Study Report

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DARWIN EU® - Suicidality incidence rates in adult male patients and in patients treated with finasteride and dutasteride

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Contents

Study title	DARWIN EU® - Suicidality incidence rates in adult male patients and in patients treated with finasteride and dutasteride
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Countries of study	Spain, United Kingdom, Denmark, Germany, The Netherlands, Croatia
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TITLE

DARWIN EU® - Suicidality incidence rates in adult male patients and in patients treated with finasteride and dutasteride

1. DESCRIPTION OF STUDY TEAM

Study team role	Names	Organisation
Study Project Manager/Principal Investigator	Marzyeh Amini Katia Verhamme	Erasmus MC
Data Scientist(s)	Ross Williams Maarten van Kessel Cesar Barboza Ger Inberg Adam Black	Erasmus MC
Epidemiologist/ Clinical Domain Expert	Marzyeh Amini Katia Verhamme Guido van Leeuwen	Erasmus MC
Data Partner*	**Names**	**Organisation**
BIFAP	Gil Garcia Miguel Jesus, Rebeca Martínez Muñoz Hermenegildo Carlos Martínez-Alcalá García Ana Llorente Garcia Miguel Angel Macia Martinez	Agencia Española de medicamentos y productos sanitarios
CPRD-Gold	Antonella Delmestri	University of Oxford
DK-DHR	Claus Møldrup Elvira Bräuner Susanne Bruun	Danish Medicines Agency
InGef RDB	Josephine Jacob Raeleesha Norris Alexander Harms Annika Vivirito	Institut für angewandte Gesundheitsforschung Berlin GmbH
IPCI	Katia Verhamme	Erasmus MC
NAJS	Jakov Vuković Maja Silobrčić-Radić Ivan Pristaš Anamaria Jurčević Pero Ivanko Marko Čavlina Antea Jezidžić	The Croatian National Institute of Public Health
SIDIAP	Talita Duarte-Salles Anna Palomar Agustina Giuliodori Picco	IDIAPJGol

*Data partners' role is only to execute code at their data source, review and approve their results. These people do not have an investigator role.

2. DATA SOURCES

This study was conducted using routinely collected data from 7 primary/secondary care data sources in the DARWIN EU® network of data partners from 6 European countries. With regards to conditions of interest, exposures and outcome, only 4 out of the 7 selected data sources have been *a priori* mapped to the OMOP CDM. Three data sources (i.e., 1, 3, and 4 in the list below) did additional mapping of the condition of interest and/or the outcome during the conduct of this study (December 2024).

Data sources

1. Pharmacoepidemiological Research Database for Public Health Systems (BIFAP), Spain
2. Clinical Practice Research Datalink (CPRD) GOLD, United Kingdom
3. Danish Data Health Registries (DK-DHR), Denmark
4. InGef Research Database (InGef RDB), Germany
5. Integrated Primary Care Information (IPCI), Netherlands
6. Croatian National Public Health Information System (NAJS), Croatia
7. The Information System for Research on Primary Care (SIDIAP), Spain

Table 1. Description of data sources used for this study and ability to answer objectives.

Country	Name of Database	Health Care setting	Type of Data	Number of active subjects	Calendar period covered by each data source
Spain	BIFAP	Primary care, inpatient hospital care	EHRs, claims, registries	16.9m	01/09/1998 - 02/05/2024
United Kingdom	CPRD-GOLD	Primary care	EHR	2.92m	01/10/1987 - 01/01/2024
Denmark	DK-DHR	Inpatient hospital care and secondary outpatient care	EHRs, registries, others	5.96m	01/01/1995 - 21/05/2024
Germany	InGef RDB	Primary care, hospital inpatient care and secondary outpatient care	Claims	7.6m	01/01/2014 - 01/04/2024
The Netherlands	IPCI	Primary Care	EHR	1.25m	01/01/2006 - 30/04/2024
Croatia	NAJS	Primary care, outpatient	Registries	4.22m*	01/08/1993 -

Country	Name of Database	Health Care setting	Type of Data	Number of active subjects	Calendar period covered by each data source
		specialist care, and inpatient care			17/11/2023
Spain	SIDIAP	Primary care	EHR	5.95m	01/01/2006 - 30/06/2023

* The person table in the NAJS data source also included both deceased individuals and those who were previously insured, meaning the number of subjects exceeds the number of currently living individuals.
CPRD= Clinical Practice Research Datalink, DK-DHR= Danish Data Health Registries, InGef RDB= InGef Research Database, IPCI= The Integrated Primary Care Information, NAJS= Croatian National Public Health Information System, SIDIAP= Information System for Research in Primary Care, EHR= Electronic Healthcare Record

3. ABSTRACT

Title

DARWIN EU® – Suicidality incidence rates in adult male patients and in patients treated with finasteride and dutasteride

Rationale and background

Finasteride is a specific inhibitor of 5α-reductase, an enzyme that converts testosterone into dihydrotestosterone. It is approved in Europe for treating benign prostatic hyperplasia (BPH) as 5 mg oral tablets and androgenetic alopecia as 1 mg oral tablets and 2.275 mg/dl cutaneous solution. Dutasteride as 0.5 mg oral capsule, another 5α-reductase inhibitor, is also approved in Europe for moderate-to-severe BPH, either alone or in combination with tamsulosin. In some non-EEA countries, dutasteride is also prescribed for androgenetic alopecia.

Signals of mood changes, including depressed mood, depression, and rarely suicidal ideation, have been reported in patients using finasteride. Depression is listed as a side effect of finasteride, along with anxiety and suicidal thoughts, though their frequency is unknown. These psychiatric effects were not identified during clinical trials but were later detected in post-marketing observational studies. There is insufficient data in the literature regarding the incidence rates of suicide related events in patients with androgenetic alopecia and BPH.

The aim of this study was to evaluate the incidence rates of suicide-related events in adult male patients exposed to finasteride or dutasteride medicines for the conditions of androgenetic alopecia and BPH. Having incidence rate data would be helpful to contextualise and to give some insight into the impact of the indication on suicide-related events. Further understanding of the safety of these medicines regarding their potential psychiatric effects can help inform regulatory decisions and the assessment of the benefit/risk profile of these medicines.

Research question and objectives

Research question

What are the incidence rates of suicide-related events in the general adult male population, adult males with newly diagnosed androgenetic alopecia, and with newly diagnosed BPH, overall and stratified by age

group, history of psychiatric disorder, history of sexual dysfunction, calendar year (for the general adult male population) and follow-up year (for indication and treatment cohorts)?

Objectives

The specific objectives were to describe incidence rates of suicide-related events, overall and stratified by age group, history of psychiatric disorder, history of sexual dysfunction, and calendar year (for the general adult male population) and follow-up year (for indication and treatment cohorts) in:

1. The general adult male population.
2. Adult male patients with newly diagnosed androgenetic alopecia.
3. Adult male patients with newly diagnosed androgenetic alopecia initiating treatment for this condition (finasteride, dutasteride, and topical minoxidil), and those with no recorded prescription for study treatments.
4. Adult male patients with newly diagnosed benign prostatic hyperplasia (BPH).
5. Adult male patients with newly diagnosed BPH initiating treatment for this condition (finasteride, dutasteride, alpha blockers, and tadalafil), and those with no recorded prescription for study treatments.

Methods

Study design

Population level cohort study.

Population

The study population included all adult male patients (≥ 18 years old) present in the data source during the study period (Objective 1).

Within this population 2 sub-cohorts were nested namely one of adult male patients newly diagnosed with androgenetic alopecia and one consisting of adult male patients newly diagnosed with BPH (Objectives 2 and 4).

Within these cohorts of adult males newly diagnosed with androgenetic alopecia and BPH, we nested cohorts of individuals initiating treatments of interest for the first time in the study period and those with no recorded prescription for study treatments (Objectives 3 and 5).

Study period

Study period started from 2010 until the end of available data. In the InGef RDB and NAJS data sources, data were available from 2014 and 2017 on, respectively.

Variables

Exposures

Conditions of interest (androgenetic alopecia and BPH) and treatments for these conditions (i.e., finasteride, dutasteride, topical minoxidil, alpha blockers, tadalafil, and tadalafil + finasteride/dutasteride).

Outcome

Outcome of interest was a composite suicidality outcome which included the first recorded occurrence of any of the following events: completed suicide, attempted suicide, suicide ideation, and intentional self-harm.

Relevant covariates

Age groups, history of psychiatric disorder, history of sexual dysfunction, and calendar year (for the general adult male population) and follow-up year (for indication and treatment cohorts).

Data source

1. Pharmaco-epidemiological Research Database for Public Health Systems (BIFAP), Spain
2. Clinical Practice Research Datalink (CPRD) GOLD, United Kingdom
3. Danish Data Health Registries (DK-DHR), Denmark
4. InGef Research Database (InGef RDB), Germany
5. Integrated Primary Care Information (IPCI), Netherlands
6. Croatian National Public Health Information System (NAJS), Croatia
7. The Information System for Research on Primary Care (SIDIAP), Spain

Sample size

No sample size was calculated as this was an exploratory study. To estimate the incidence rates of suicide-related events in adult male patients diagnosed with androgenetic alopecia and BPH, we used already collected available data. Thus, the sample size was driven by the availability of patients with conditions of interest, exposures and outcomes within each data source.

Analytical methods

Incidence rates of suicide-related events per 1,000 person-years (PYs) were estimated in the general population of adult males and in adult male patients diagnosed with androgenetic alopecia and BPH. Within these populations, incidence rates of suicide-related events per 1,000 PYs were also calculated among patients exposed to the drugs of interest (i.e., treatments of androgenetic alopecia and BPH). Overall incidence rates (and 95% Poisson confidence intervals) were reported as well as incidence rates stratified by age categories, history of psychiatric disorders, history of sexual dysfunction, and calendar year (for the general adult male population) and follow-up year (for indication and treatment cohorts). The statistical analyses were performed based on OMOP-CDM mapped data using "IncidencePrevalence" R package. A minimum cell counts of 5 were used when reporting results, with any smaller count reported as "<5".

Results

The data from InGef RDB Germany and Danish DK-DHR had limited outcome capture, which might affect the reliability of incidence rates and limit the accuracy of conclusions drawn from these results.

The overall number of the general adult male population varied across different data sources, with the highest recorded in BIFAP (8,621,220) and the lowest in IPCI (1,000,636). The overall counts of androgenetic alopecia ranged from 236 cases in inGef RDB to 5,265 in SIDIAP. BPH cases were more numerous, with counts ranging from 15,320 in IPCI to 444,795 in BIFAP across different data sources. The median age ranged: in the general population between 38 (DK-DHR and SIDIAP) and 45 (NAJS) years; between 26 (IPCI) and 35 years (DK-DHR) in the androgenetic alopecia population; and between 64 (NAJS) and 73 years (InGef RDB) in the BPH population.

The incidence rates of the composite suicidality outcome in the general adult male population varied across the data sources, with the highest rate observed in CPRD-Gold at 1.47/1,000 PYs (95% CI: 1.46, 1.49). The IPCI data source reported a rate of 0.49/1,000 PYs (95% CI: 0.47-0.51). Lower rates were reported in BIFAP at 0.42/1,000 PYs (95% CI: 0.42, 0.43) and SIDIAP at 0.34/1,000 PYs (95% CI: 0.33-0.34).

The incidence rates of suicide-related events in patients with androgenetic alopecia were consistently low across the data sources, with no suicidality cases were observed in many cohorts. In CPRD-Gold, the overall incidence rate for androgenetic alopecia patients was 2.08/1,000 PYs (95% CI: 0.76-4.54) and in SIDIAP, the overall incidence rate was 0.47/1,000 PYs (95% CI: 0.26-0.77). The incidence rates of suicidality outcome

among BPH patients varied across data sources, with highest rates reported as 0.88/1,000 PYs in CPRD-Gold and 0.12/1,000 PYs in InGef RDB.

The size of the cohorts and number of suicide-related events among patients received treatments for androgenetic alopecia were very low across all data sources, with most treatment cohorts revealed no cases due to the low number of patients. For BPH treatments, male patients treated with alpha blockers generally showed higher suicidality rates compared to those treated with finasteride, dutasteride, or tadalafil. In CPRD-Gold, the incidence rate for suicidality in patients treated with alpha blockers was 1.08/1,000 PYs, while patients treated with finasteride and dutasteride had lower rates of 0.69 and 0.65/1,000 PYs, respectively. In contrast, IPCI and SIDIAP reported no or very few suicidality-related cases for most treatment cohorts, with rates for patients treated with finasteride ranged from 0.54/1,000 PYs to 1.24 across data sources. The cohorts of patients treated with tadalafil were small, resulted in no calculable incidence rates due to the limited number of recorded outcomes.

Higher incidence rates of suicidality-related events were observed in younger age groups compared to older ones in the general adult male population. However, this trend was less obvious in BPH, where the age distribution shifted towards older individuals, and was difficult to evaluate in androgenetic alopecia due to insufficient sample size.

In the general adult male population with a history of psychiatric disorders, the incidence rates of suicide-related events ranged from 0.74/1,000 PYs in DK-DHR and highest 4.50/1,000 PYs in CPRD-Gold and were consistently higher compared to individuals without a history of psychiatric disorders. In addition, higher incidence rates of suicide-related events were observed in BPH patients with a history of sexual dysfunction in several data sources. For instance, in the CPRD-Gold data source, BPH patients with a history of sexual dysfunction had a higher incidence rate of suicide-related events (1.17/1,000 PY) compared to those without (0.82/1,000 PY), with similar patterns seen in IPCI and NAJS.

The incidence rates of composite suicidality outcomes in general adult male population over years showed varying trends, with BIFAP rising steadily from 0.2/1,000 PYs in 2010 to 0.7 by 2023 and CPRD-Gold peaking at 2.0/1,000 PYs in 2018-2019 before declining. The number of suicide related events within the androgenetic alopecia cohorts were low (between 0 and 15 across data sources) and the incidence rates were <5 or rounded to zero. In BPH patient cohorts, incidence rates of suicidality started at 0.9/1,000 PYs in BIFAP and 1.2 in CPRD Gold, declining to 0.35 and 0.7, respectively, after five years. Among treatment cohorts, alpha-blocker users experienced high initial rates which dropped later after treatment initiation in CPRD Gold (initial rate was 1.3 which dropped to 0.6 by year 4), while dutasteride and finasteride cohorts showed no clear patterns over follow-up time across data sources.

Conclusion

This analysis of suicide-related events in the general adult male population and BPH patients across European data sources, revealed variability in suicidality rates, with higher rates consistently observed in individuals with a history of psychiatric disorders and prior sexual dysfunction. Higher suicidality rates were observed in younger age groups in the general adult male population, but this trend was less obvious in BPH patients as the age distribution shifted towards older individuals. Male BPH patients treated with alpha blockers showed slightly higher rates compared to other treated groups, overall suicidality rates remained low, likely influenced by underreporting and healthcare system differences. With regards to androgenetic alopecia cohorts, there was substantial uncertainty around the incidence rates of suicide-related events due to limited sample size, which made the estimates uninformative.

4. LIST OF ABBREVIATIONS

Acronyms/term	Description
ARIs	α-reductase inhibitors
BIFAP	Pharmacoepidemiological Research Database for Public Health System
BPH	Benign Prostatic Hyperplasia
CDM	Common Data Model
CC	Coordinating centre
CIPH	Croatian Institute of Public Health
COVID-19	Coronavirus Disease 2019
CPRD	Clinical Practice Research Datalink
DARWIN EU®	Data Analysis and Real-World Interrogation Network
DK-DHR	Danish Data Health Registries
DOI	Declaration of Interests
DQD	Data Quality Dashboard
DRE	Digital Research Environment
EHR	Electronic Health Records
EMA	European Medicines Agency
ENCePP	European Network of Centres for Pharmacoepidemiology and Pharmacovigilance
EU	European Union
GDPR	General Data Protection Regulation
GP	General Practitioner
ICD	International Classification of Diseases
InGef RDB	InGef Research Database
IP	Inpatient
IPCI	Integrated Primary Care Information
NAJS	The National Public Health Information System Croatia
OHDSI	Observational Health Data Sciences and Informatics
OMOP	Observational Medical Outcomes Partnership
OP	Outpatient
RxNorm	Medical prescription normalized
SD	Standard Deviation
SIDIAP	The Information System for Research in Primary Care
SNOMED	Systematized Nomenclature of Medicine
UK	United Kingdom
WHO	World Health Organisation
WONCA	World Organization of Family Doctor

5. AMENDMENTS AND UPDATES

None.

6. MILESTONES

Study deliverable	Timelines (planned)	Timelines (actual)
Draft Study Protocol	5 November 2024	5 November 2024
Final Study Protocol	22 November 2024	04 December 2024
Creation of Analytical code	25 November 2024	11 December 2024
Execution of Analytical Code on the data	2 December 2024	15 December 2024
Interim Study Report	13 December 2024	19 December 2024
Draft Study Report	15 January 2025	06 January 2025
Final Study Report	31 January 2025	03 February 2025

7. RATIONALE AND BACKGROUND

Finasteride is a specific inhibitor of type-II 5α-reductase, an intracellular enzyme that metabolizes the androgen testosterone into dihydrotestosterone. Finasteride has been authorised in Europe since 1992 for the treatment of BPH (5mg oral tablets) and since 1998 for the treatment of androgenetic alopecia (1 mg oral tablets, 2.275 mg/dL cutaneous solution).(1-3) Another 5α-reductase inhibitor indicated for the treatment of moderate-to-severe symptoms of BPH is dutasteride. Oral dutasteride has been authorised in Europe since 2002 as monotherapy or in fixed dose combination (0.5mg) with tamsulosin (0.4 mg).(4) In some countries outside the EEA, notably South Korea and Japan, dutasteride is also authorised for androgenetic alopecia.(5, 6)

Mood alterations including depressed mood, depression and, less frequently, suicidal ideation have been reported as side effect in patients treated with finasteride.(1, 7) Additionally, anxiety and suicidal thoughts are listed among the side effects, although their frequency is unknown.(8, 9) Concerns persist about the potential continuation of psychiatric events and risks of suicide or self-injury even after discontinuing finasteride, particularly in young patients, which are being closely monitored.(10, 11) The psychiatric and suicidal adverse effects of finasteride were not found during clinical trials, but these side effects were later investigated in post-marketing observational studies.(12, 13) However, the evidence is currently scarce, and it is unclear if these psychiatric side effects could be due to the medicine itself. It is also unclear if these effects might be mediated by the potential impact on sexual side effects (sexual dysfunction) of these medicines.(12)

The aim of this study was to evaluate the incidence rates of suicide-related events in adult male patients exposed to finasteride or dutasteride for the treatment of androgenetic alopecia and BPH. Further understanding of the safety of these medicines regarding their potential psychiatric effects can help inform regulatory decisions and the assessment of the benefit/risk profile of these medicines.

8. RESEARCH QUESTION AND OBJECTIVES

Research question

What are the overall incidence rates of suicide-related events in the general adult male population, as well as in adult male patients newly diagnosed with androgenetic alopecia and benign prostatic hyperplasia (BPH), stratified by age group, history of psychiatric disorder, history of sexual dysfunction, and calendar year (for the general adult male population) and /follow-up year (for indication and treatment cohorts)?

Objectives

To describe incidence rates of suicide-related events, overall and stratified by age groups, history of psychiatric disorder, history of sexual dysfunction and calendar year (for the general adult male population) and /follow-up year (for indication and treatment cohorts) in:

1. The general adult male population.
2. Adult male patients newly diagnosed with androgenetic alopecia.
3. Adult male patients newly diagnosed with androgenetic alopecia initiating treatment for this condition (finasteride, dutasteride, and topical minoxidil), and those with no recorded prescription for study treatments.
4. Adult male patients newly diagnosed with benign prostatic hyperplasia (BPH).
5. Adult male patients newly diagnosed with BPH initiating treatments for this condition (finasteride, dutasteride, alpha blockers, tadalafil, and tadalafil + finasteride/dutasteride), and those with no recorded prescription for study treatments.

9. RESEARCH METHODS

9.1 Study type and study design

This was a population level disease epidemiology study classified as "*off-the-shelf*" and as described in the DARWIN EU® Complete Catalogue of Standard Data Analyses (**Table 2**).

Table 2. Description of potential study types and related study designs.

Study type	Study design	Study classification
Population-Level Descriptive Epidemiology	Population-Level Cohort	Off the shelf

9.2 Study setting and data sources

This study was conducted using routinely collected data from 7 primary/secondary care data sources in the DARWIN EU® network of data partners from 6 European countries.

Data sources

1. Pharmacoepidemiological Research Database for Public Health Systems (BIFAP), Spain
2. Clinical Practice Research Datalink (CPRD) GOLD, United Kingdom

3. Danish Data Health Registries (DK-DHR), Denmark
4. InGef Research Database (InGef RDB), Germany
5. Integrated Primary Care Information (IPCI), Netherlands
6. Croatian National Public Health Information System (NAJS), Croatia
7. The Information System for Research on Primary Care (SIDIAP), Spain

Data Selection

These databases fulfil the criteria required in terms of data quality, completeness, timeliness, and representativeness for population level descriptive epidemiology while covering different regions of Europe. Detailed information on the selected data sources is described in **Table 1** above.

When it comes to assessing the reliability of data sources, the data partners were asked to describe their internal data quality process on the source data as part of the DARWIN EU® onboarding procedure. To further ensure data quality, we utilised the Achilles tool,(14) which systematically characterises the data and generates data characteristics such as age distribution, condition prevalence per year, data density. Data density includes information on 1) monthly record counts by data domain (which offers insights into data collection patterns and the start date of each data source), 2) measurement value distribution (i.e. min, max, quartiles for numeric values per measurement concept and per unit and counts for discrete measurement-value pairs). The latter can be compared against expectations for the data based on predefined standards, historical trends, or known epidemiological patterns to identify potential anomalies or inconsistencies. Additionally, the data quality dashboard (DQD) provides more objective checks (see Section D1.3.5.2 on Complete Data Quality Assurance Package) on plausibility of data completeness, consistency, and conformity across the data sources.

In terms of relevance, the selection of databases was based on the availability of data on the selected conditions (androgenetic alopecia and BHP), the treatments and the outcome of interest to perform the described analyses. In addition, the databases were chosen considering their ability to support timely IRB approvals, thus ensuring alignment with the timeline established by stakeholders for the conduct of this study. The DARWIN EU® portal as well as information from the onboarding documents were used to assess whether databases have information on use of treatments and indications of interest. Data within the DARWIN EU® portal is maintained up to date by extracting the release dates for each dataset in the network and monitoring when data are out-of-date with the expected refresh cycle (typically quarterly or half-yearly). In addition, it is important to have clear understanding of the time covered by each released database, as this can vary across different domains. To facilitate this, the C*DMOnboarding* (and *Achilles*) packages (14) contain a 'data density' plot. This plot displays the number of records per OMOP domain monthly. This allows to get insights when data collection started, when new sources of data were added and until when data was included. In addition, at time of inviting data partners, they were informed about study objectives and asked whether they could participate in the study.

More general-purpose diagnostic tools, *CohortDiagnostics* (15) and *DrugExposureDiagnostics* (16), have been developed. The *CohortDiagnostics* package provides additional insights into cohort characteristics, record counts and index event misclassification. The *DrugExposureDiagnostics* package evaluates ingredient-specific attributes and patterns in drug exposure records. Upon finalisation of the study protocol and creation of the disease and drug cohorts of interest by DARWIN EU Coordination Centre, these packages were executed in each data sources by each data partners.

Pharmacoepidemiological Research Database for Public Health Systems (BIFAP), Spain

BIFAP (http://www.bifap.org/?lang=en) is a longitudinal population-based data source of medical patient records of the Spanish National Health Service. It includes data from 9 of Spain's 17 autonomous regions. Population currently included represents 36% of the total Spanish population. The Spanish National Health Service provides universal access to health services through the Regional Healthcare Services. Primary care

physicians, both general practitioners (GP) and paediatricians, act as gatekeepers of the system and exchange information with other levels of care to ensure the continuity of care. Most of the population (98.9%) is registered with a primary care physician and most drug prescriptions are written at the primary care level. BIFAP includes a collection of databases linked at individual patient level. The main one is the Primary care Database given the central role of primary care physicians in the Spanish National Health Service. Linked, there are additional important structural databases like the medicines dispensed at community pharmacies and the patients' hospital diagnosis at discharge. Additional databases are also linked for a subset of patients (hospital pharmacy, cause of death registry). BIFAP program is a non-profit program financed by the Spanish Agency of Medicines and Medical Devices (AEMPS), a government agency belonging to the Ministry of Health in collaboration with the regional health authorities. The main use of BIFAP is for research purposes to evaluate the adverse and beneficial effects of drugs and drug utilisation patterns in the general population under real conditions of use.

Clinical Practice Research Datalink GOLD, United Kingdom (University of Oxford)

The Clinical Practice Research Datalink (CPRD) GOLD is a database of anonymised electronic health records (EHR) from General Practitioner (GP) clinics in the UK that use the Vision® software system for their management.(17) The source population encompasses 98% of the UK, registered with GPs responsible for non-emergency care and referrals. Participating GPs provide CPRD EHR for all registered patients who did not specifically request to opt out of data sharing. Covering 4.6% of the current UK population, GOLD includes 4.9% of contributing GP practices, providing comprehensive information within its defined source population. GOLD contains data from all four UK constituent countries and the current regional distribution of its GP practices is 5.7% in England, 55.6% in Scotland, 28.4% in Wales, and 10.2% in Northern Ireland (May 2022).

GOLD data include patient's demographic, biological measurements, clinical symptoms and diagnoses, referrals to specialist/hospital and their outcome, laboratory tests/results, and prescribed medications. GOLD has been assessed and found broadly representative of the UK general population in terms of age, gender, and ethnicity.(17) GOLD has been widely used internationally for observational research to produce nearly 3,000 peer-reviewed publications, making GOLD the most influential UK clinical database so far.(18-20)

Danish Data Health Registries (DK-DHR), Denmark

Danish health data is collected, stored and managed in national health registers at the Danish Health Data Authority and covers the entire population which makes it possible to study the development of diseases and their treatment over time. There are no gaps in terms of gender, age and geography in Danish health data due to mandatory reporting on all patients from cradle to grave, in all hospitals and medical clinics. Personal identification numbers enable linking of data across registers, so it captures data on all Danes throughout their lives, regardless of whether they have moved around the country. High data quality due to standardisation, digitisation and documentation means that Danish health data is not based on interpretation. The Danish Health Data Authority is responsible for the national health registers and for maintaining and developing standards and classifications in the Danish healthcare system. Legislation ensures balance between personal data protection and use. The current data release includes data on the entire Danish population of 5.9 million persons from 1995. It includes data from the following registries: The central Person Registry, The National Patient Registry, The Register of Pharmaceutical Sales, The National Cancer Register, The Cause of Death registry, and Coronavirus disease 2019 test and vaccination Registries.

InGef Research Database (InGef RDB), Germany

The InGef RDB comprises anonymised longitudinal claims data of about 10 million individuals across more than 70 statutory health insurance providers (SHIs) throughout Germany. Data are longitudinally linked

over a period of currently ten years. Patients can be traced across health care sectors. All patient-level and provider-level data in the InGef RDB are anonymised to comply with German data protection regulations and German federal law. German SHI claims data available in the InGef RDB includes information on demographics (year of birth, gender, death date if applicable, region of residence on administrative district level); hospitalizations; outpatient services (diagnoses, treatments; specialities of physicians); dispensing of drugs; dispensings of remedies and aids; and sick leave and sickness allowance times. In addition, costs or cost estimates from SHI perspective are available for all important cost elements. All diagnoses in Germany are coded using the International Classification of Diseases, version 10 in the German Modification (ICD-10-GM). The persistence (membership over time) is rather high in the InGef RDB: During a time period of 5 years (2009 to 2013), 70.6% of insurance members survived and remained insured with the same SHI without any gap in their observational time. Persons leaving one of the participating SHIs and entering another participating SHI, can be linked during yearly database consistency updates and are thus not lost over time. The InGef RDB is dynamic in nature, i.e. claims data are updated in an ongoing process and new SHIs may join or leave the database.

The Integrated Primary Care Information (IPCI), the Netherlands

The Integrated Primary Care Information (IPCI) database is a longitudinal observational database containing routinely collected data extracted from computer-based patient records of a selected group of general practitioners (GPs) across the Netherlands.(21) IPCI was started in 1992 by the department of Medical Informatics of the Erasmus University Medical Center in Rotterdam. The current database includes patient records from 2006 on, when the size of the database started to increase significantly. The demographic composition of the IPCI population mirrors that of the general Dutch population in terms of age and sex. Although the geographical spread is limited, GP practices are located in urban and non-urban areas.

Patient-level data includes demographic information, patient's complaints and symptoms, diagnoses, laboratory test results, lifestyle factors and correspondence with secondary care, such as referral and discharge letters. For complaints, symptoms and diagnoses, Dutch GPs use International Classification of Primary Care (ICPC-1) coding, an international standard developed and updated by the World Organization of Family Doctors' (WONCA) International Classification Committee.

IPCI data quality has been previously documented and IPCI has proved valuable for epidemiological studies.(22-26) In terms of quality control, extensive quality control steps are performed prior to each data release. These include comparison of patient characteristics between practices and checks to identify abnormal temporal data patterns in practices. Additional checks include over 200 indicators related to population characteristics (e.g. reliability of birth and mortality rates) and medical data (e.g. availability of durations of prescriptions, completeness of laboratory results, availability of hospital letters and prescriptions, proportion of patients with blood pressure measurement, etc.(21) Based on this information, two quality scores have been created. Practices with low scores have been excluded.

National Public Health Information System (NAJS), Croatia

The National Public Health Information System (Nacionalni javnozdravstveni informacijski sustav - NAJS) is an organised system of information services by the Croatian Institute of Public Health (CIPH). This database was established in 1998, with nationwide coverage, representing approximately 5.4 million inhabitants. Settings covered include public primary, secondary/outpatient, and inpatient care. Data is retrieved primarily from EHR and holds information on demographics, inpatient and outpatient visits, conditions and procedures, drugs (outpatient and inpatient prescriptions), measurements, and inpatient and outpatient dates of death. NAJS provides linkage between medical and public health data collected and stored in health registries and other health data collections, including cancer registry, mortality, work injuries, occupational diseases, communicable and non-communicable diseases, health events, disabilities,

psychosis and suicide, diabetes, drug abuse and others. The CDM population comprises all publicly insured persons residing in Croatia starting in 2017.

Information System for Research in Primary Care (SIDIAP), Spain

The Information System for Research in Primary Care (SIDIAP) is a dynamic database of pseudo-anonymized electronic health records of the primary care patient population in Catalonia, Spain.(27) It contains data of approximately 80% of the Catalan population registered in over 280 primary care practices throughout Catalonia since 2005.

The database contains data recorded in primary care centres on a daily basis. Additionally, it integrates data from external sources including biomarkers data from laboratories and records of drug prescription and dispensation. The dataset covers demographics, all-cause mortality, disease diagnoses classified under the International Classification of Diseases 10th revision (ICD-10), prescription and dispensation records of drugs, results of laboratory tests, socio-economic indicators, vaccination records, lifestyle information, parent–child linkage and various clinical parameters. Additional data from other data sources such as hospital discharges, mental health centres or specific disease registries can be obtained through diverse linkages. The demographic composition within SIDIAP closely mirrors that of the broader Catalan population, encompassing a representative spectrum of geographic distribution, age, and sex proportions. The database is updated every 6 months.

SIDIAP data quality has been previously documented and SIDIAP has proved valuable for epidemiological studies.(28-36) In terms of data integrity and reliability, SIDIAP has been subject to rigorous evaluation. Quality checks have been implemented including central identification of duplicate patient ID and visual inspection for temporal patterns in the registry of a certain variable. Furthermore, the data undergoes assessment for availability (longitudinally and reliability), plausibility (range checks and unusual values) and consistency using visualization tools. Specifically, for biochemistry data, consistency for measurements taken in different laboratories is assessed, and unit conversion is undertaken when needed.

9.3 Study period

The start of the study was set to 2010 when most of the data sources had enough data on the treatments of interest until the end of available data. It should be noted that in the InGef RDB and NAJS data sources, the availability of data started from 2014 and 2017, respectively.

9.4 Follow-up

- For the cohort of general adult male population (Objective 1): Follow-up started on the first date, within the study period, when an individual became eligible to enter the study (i.e., index date as defined in), and continued until the earliest of the following: first date of the study outcome of interest, loss to follow-up, death, end of observation period (the most recent data available) in the data source.
- For the cohorts of adult male patients with incident androgenetic alopecia or BPH (Objectives 2 and 4): Follow-up started from the index date (i.e., first diagnosis ever of androgenetic alopecia or BPH diagnosis recorded during the study period) and continued until the earliest of the following: first date of the study outcome of interest, loss to follow-up, death, end of observation period (the most recent data available) in the data source.
- For the cohorts of adult male patients with androgenetic alopecia or BPH who initiated treatments for these conditions (Objective 3 and 5): Follow-up started from index date (i.e., date of initiation of first treatment of interest) any time following incident androgenetic alopecia and BPH diagnosis during the study period, and continued up until the earliest of the following: first date of the study outcome of

interest event, the date of treatment discontinuation plus six months, switching to another treatment cohort, loss to follow-up, death, end of observation period (the most recent data available) in the data source.

- For the cohorts of adult male patients with androgenetic alopecia or BPH who had no recorded prescription for study treatments related to these conditions (Objective 3 and 5): Follow-up started from index date (i.e., first diagnosis ever of androgenetic alopecia or BPH diagnosis recorded during the study period), and continued up until the earliest of the following: first date of the study outcome of interest event, the first date recorded of treatment with study treatments, loss to follow-up, death, end of observation period (the most recent data available) in the data source.

Operational definition of the index dates for each of the cohorts mentioned above and other primary time anchors are described in **Table 3**.

Table 3. Operational definition of time 0 (index date).

Study population name(s)	Time Anchor Description (time 0 or index date)	Number of entries	Type of entry	Washout window	Care Setting[1]	Code Type[2]	Diagnosis position	Incident with respect to…	Measurement characteristics/validation	Source of algorithm
General adult male population older than 18 years old (objective 1)	First date during the study period, on which individuals are minimum 18 years of age and have sufficient prior data availability (minimum 365 days)	Single	n/a	n/a	OP	n/a	n/a	n/a	n/a	n/a
Adult males with incident androgenetic alopecia (objective 2)	First diagnosis of androgenetic alopecia, during the study period, and sufficient prior data availability (minimum 365 days) (incident diagnosis)	Single	Incident	Any time prior to study entry date	OP	Clinical finding	n/a	Prior androgenetic alopecia diagnosis	n/a	n/a
Adult males with incident BPH (objective 4)	First diagnosis of BPH, during the study period, and sufficient prior data availability (minimum 365 days)	Single	Incident	Any time prior to study entry date	OP	Clinical finding	n/a	Prior BPH diagnosis	n/a	n/a

Study population name(s)	Time Anchor Description (time 0 or index date)	Number of entries	Type of entry	Washout window	Care Setting[1]	Code Type[2]	Diagnosis position	Incident with respect to…	Measurement characteristics/validation	Source of algorithm
	(incident diagnosis)									
Adult males with incident androgenetic alopecia (objective 3) initiating treatment with any of the medicines of interest	Date of first treatment with topical minoxidil, finasteride or dutasteride (see Section 8.6.1) any time following the diagnosis of androgenetic alopecia, during study period, and sufficient prior data availability (minimum 365 days).	Single	Incident	Any time prior to study entry date	OP	Treatment	n/a	Prior selected treatments of interest,	n/a	n/a
Adult males with incident BPH (objective 5) initiated treatment with any of the medicines of interest	Date of first treatment with alpha blocker, finasteride, dutasteride or tadalafil (see Section 8.6.1) any time following the diagnosis of BPH, during study period, and sufficient prior	Single	Incident	Any time prior to study entry date	OP	Treatment	n/a	Prior selected treatments of interest,	n/a	n/a

Study population name(s)	Time Anchor Description (time 0 or index date)	Number of entries	Type of entry	Washout window	Care Setting[1]	Code Type[2]	Diagnosis position	Incident with respect to…	Measurement characteristics/validation	Source of algorithm
	data availability (minimum 365 days).									

[1] IP = inpatient, OP = outpatient, ED = emergency department, OT = other, n/a = not applicable

[2] The type(s) of clinical codes that are used to define the time 0 (or another primary anchor) criterion

BPH= Benign Prostatic Hyperplasia

9.5 Inclusion and exclusion criteria

The study population was defined as follows for each cohort:

For the cohort of general adult male population (Objective 1):

Inclusion criteria:

- All male patients aged ≥18 years observed in one of the participating data sources during the study period.
- Study participants were required to have minimum 365 days of prior history before contributing follow-up time in the study. This was to ensure a minimum prior observation time to identify a history of any of the outcomes of interest at the time on which a participant enters the study.

Exclusion criteria:

- Patients with a recorded history of suicide-related or self-harm-related events (as defined in Outcome section, composite suicidality outcome) prior to index-date.

For the cohorts of adult male patients with incident androgenetic alopecia or BPH (Objectives 2 and 4):

Within the general adult male population, two sub-cohorts were nested, one for each condition of interest (i.e., androgenetic alopecia and BPH).

Inclusion criteria:

- Same as described above for the general adult male population.
- Patients newly diagnosed (first diagnosis recorded in the data source) with:
  - Androgenetic alopecia, OR
  - BPH.
- Study participants were required to have minimum 365 days of prior history before contributing follow-up time in the study. This was to ensure a minimum prior observation time to identify androgenetic alopecia or BPH and to identify a history of any of the outcomes of interest at the time on which a participant enters the study.

Exclusion criteria:

- Same as described above for the general adult male population.
- A previous diagnosis of androgenetic alopecia OR BPH before index date (to ensure index-date represents an incident diagnosis).

For the cohorts of adult male patients with androgenetic alopecia or BPH who initiated treatments for these conditions (Objective 3 and 5):

Within the cohorts of adult males newly diagnosed with androgenetic alopecia and BPH, cohorts of patients initiating treatment for these conditions any time following diagnosis were nested.

Inclusion criteria:

- Same as described above for the male patients with incident androgenetic alopecia or BPH.
- Patients initiating treatments of interest (see Section 8.6.1) for the first time following the first diagnosis of androgenetic alopecia or BPH.
- Study participants were required to have minimum 365 days of prior history before contributing follow-up time in the study. This was to ensure a minimum prior observation time to identify

androgenetic alopecia or BPH and to identify a history of any of the outcomes of interest at the time on which a participant enters the study.

Exclusion criteria:

- Same as described above for the general adult male population.
- For the treatment cohorts of patients initiating finasteride or dutasteride for androgenetic alopecia, previous treatment with any of the study treatments except minoxidil before index date.
- For the treatment cohort of patients initiating minoxidil for androgenetic alopecia, previous treatment with any of the study treatments before index date.
- For the treatment cohorts of patients initiating finasteride, dutasteride or tadalafil for BPH, previous treatment with any study treatments except alpha-blockers (see Section 8.6.1) before index date.
- For the treatment cohorts of patients initiating alpha-blockers for BPH, previous treatment with any study treatments (see Section 8.6.1) before index date.

For the cohorts of adult male patients with androgenetic alopecia or BPH who did not have a recorded prescription for study treatments for these conditions (Objective 3 and 5):
Within the cohorts of adult males newly diagnosed with androgenetic alopecia and BPH, cohorts of patients who did not have a recorded prescription for study treatments for these conditions following diagnosis were nested.

Inclusion criteria:

- Same as described above for the male patients with incident androgenetic alopecia or BPH.
- Patients who did not have a recorded prescription for study treatments (see Section 8.6.1) for these conditions following the first diagnosis of androgenetic alopecia or BPH.
- Study participants were required to have minimum 365 days of prior history before contributing follow-up time in the study. This was to ensure a minimum prior observation time to identify androgenetic alopecia or BPH and to identify a history of any of the outcomes of interest at the time on which a participant enters the study.

Exclusion criteria:

- Same as described above for the general adult male population.
- Previous treatment with any study treatments (see Section 8.6.1) before index date.

Operational definition of the inclusion and exclusion criteria for each of the cohorts mentioned above are described in **Table 4** and **Table 5**, respectively

Table 4. Operational definitions of inclusion criteria.

Criterion	Details	Order of application*	Assessment window	Care Settings[1]	Code Type	Diagnosis position [2]	Applied to study populations:	Measurement characteristics/ validation	Source for algorithm
Observation period in the data source during the study period	All adult male individuals present in the study period	After study start date	n/a	OP, OT	n/a	n/a	All adult male individuals within selected data sources	n/a	n/a
Prior database history of one year	Study participants will be required to have a year of prior history observed before contributing observation time	Before index date/study start date	[-365, -1]	OP, OT	n/a	n/a	All adult male individuals within selected data sources (except for general adult male population cohort)	n/a	n/a
Adult	Aged ≥18 years at index date	After study start date	On index date	OP	n/a	n/a	All cohorts	n/a	n/a
Sex	Male	After study start date	On index date	OP	n/a	n/a	All cohorts	n/a	n/a
Androgenetic alopecia	Diagnosis records of androgenetic alopecia	After study start date	On index date	OP, OT	SNOMED	n/a	Androgenetic alopecia cohort	n/a	n/a

Criterion	Details	Order of application*	Assessment window	Care Settings[1]	Code Type	Diagnosis position [2]	Applied to study populations:	Measurement characteristics/ validation	Source for algorithm
BPH	Diagnosis records of androgenetic alopecia	After study start date	On index date	OP, OT	SNOMED	n/a	BPH cohort	n/a	n/a
Initiating treatments of interest for androgenetic alopecia	Treatment with finasteride, dutasteride, topical minoxidil after androgenetic alopecia diagnosis.	After condition index date	On index date	OP, OT	RxNorm	n/a	Androgenetic alopecia treatment cohorts	n/a	n/a
Initiating treatments of interest for BPH	Treatment with finasteride, dutasteride, alpha blocker, tadalafil, after BPH diagnosis.	After condition index date	On index date	OP, OT	RxNorm	n/a	BPH treatment cohorts	n/a	n/a

[1] OP = outpatient, OT = other, n/a = not applicable

[2] The type(s) of clinical codes that are used to define the inclusion criteria.

BPH= Benign Prostatic Hyperplasia

*Order of application specifies whether the eligibility criterion is applied before or after selection of the study entry date. For example, selecting "before" means that all possible study entry dates are identified, and then one or more is chosen. For instance, selecting 'after' means that the first possible study entry date is chosen, followed by the application of the inclusion and/or exclusion criteria. If the patient does not meet the criterion, then the patient drops out.

Table 5. Operational definitions of exclusion criteria.

Criterion	Details	Order of application	Assessment window	Care Settings[1]	Code Type[2]	Diagnosis position	Applied to study populations:	Measurement characteristics/ validation	Source for algorithm
Observation	Less than 365 days of observation prior to the index date	After	[-365,0]	OP, IP, and OT	n/a	N/A	All cohorts (except for general adult male population cohort)	n/a	n/a
Previous history of composite suicidality outcomes	Recorded history of suicide-related or self-harm-related events (as defined in outcome section, composite suicidality outcome) prior to the index-date	Before	any time prior to index date	IP, OP, and OT	RxNorm	n/a	All cohorts	n/a	n/a
Previous diagnosis of androgenetic alopecia before index date	Diagnosis records of androgenetic alopecia prior to the index date.	Before	any time prior to index date	OP, OT	SNOMED	n/a	Androgenetic alopecia cohort	n/a	n/a
Previous diagnosis of BPH before index date	Diagnosis records of BPH prior to the index date	Before	any time prior to index date	OP, OT	SNOMED	n/a	BPH cohort	n/a	n/a
Previous treatment with any of the study treatments except minoxidil before index date	Treatment with index drug, finasteride or dutasteride prior to the index date for androgenetic alopecia	Before	any time prior to index date	OP, OT	RxNorm	n/a	For the Treatment cohorts initiating finasteride or	n/a	n/a

Criterion	Details	Order of application	Assessment window	Care Settings[1]	Code Type[2]	Diagnosis position	Applied to study populations:	Measurement characteristics/ validation	Source for algorithm
							dutasteride for androgenetic alopecia		
Previous treatment with any of the study treatments before index date	Treatment with index drug, prior to the index date for androgenetic alopecia	Before	any time prior to index date	OP, OT	RxNorm	n/a	Treatment cohorts initiating minoxidil for androgenetic alopecia	n/a	n/a
Previous treatments of interest for BPH except alpha-blockers prior index date	Treatment with index drug, finasteride, dutasteride, or tadalafil prior to index date for BPH	Before	any time prior to index date	OP, OT	RxNorm	n/a	Treatment cohorts initiating finasteride, dutasteride, or tadalafil for BPH	n/a	n/a
Previous treatments of interest for BPH prior index date	Treatment cohorts with index drug, alpha-blockers prior to index date for BPH	Before	any time prior to index date	OP, OT	RxNorm	n/a	Treatment cohorts of patients initiating alpha-blockers for BPH	n/a	

[1] OP = outpatient, OT = other, n/a = not applicable

[2] The type(s) of clinical codes that are used to define the inclusion criteria.

9.6 Variables

9.6.1 Exposures

Cohorts of conditions of interest were defined as follows in **Table 6**.

Table 6. Operational definitions of exposure to conditions of interest.

Condition of interest	Definition	Follow-up (censoring)
Androgenetic alopecia	Individuals with a first diagnosis of androgenetic alopecia	Follow-up started from the date of incident androgenetic alopecia diagnosis during the study period (after a minimum of 365 days of database history). Follow up ended at the earliest date of 1) outcome of interest occurrence, 2) loss to follow-up, 3) death, 4) end of observation period (the most recent data available) in the data source.
Benign prostatic hyperplasia (BPH)	Individuals with a first diagnosis of BPH	Follow-up started from the date of incident BPH diagnosis during the study period (after a minimum of 365 days of database history). Follow up ended at the earliest date of 1) outcome of interest occurrence, 2) loss to follow-up, 3) death, 4) end of observation period (the most recent data available) in the data source.

Cohorts of treatments of interest were defined as follows in **Table 7**.

Table 7. Operational definitions of exposure to treatment of interest

Treatment cohorts	Definition	Follow-up (censoring)
Androgenetic alopecia indication		
Finasteride	Individuals who initiated finasteride, after the first diagnosis of androgenetic alopecia. Treatments other than dutasteride (mainly topical, including minoxidil) were allowed before or during follow-up.	Follow-up started at first finasteride prescription any time following the first diagnosis of androgenetic alopecia. Follow-up ended at the date of treatment discontinuation plus six months or when the patient switched to (i.e., initiates) dutasteride, if this came before the first outcome event or any other previously described censoring event.
Dutasteride	Individuals who initiated dutasteride, after the first diagnosis of androgenetic alopecia. Treatments other than finasteride (mainly topical, including minoxidil) were allowed before or during follow-up.	Follow-up started at first dutasteride prescription any time following the first diagnosis of androgenetic alopecia. Follow-up ended at the date of treatment discontinuation plus six months or when patient switched to (i.e., initiated) finasteride, if this comes before the first outcome event or any other previously described censoring event.

Treatment cohorts	Definition	Follow-up (censoring)
Topical minoxidil	Individuals who initiated topical minoxidil, after the first diagnosis of androgenetic alopecia. Treatments other than finasteride or dutasteride were allowed before or during follow-up.	Follow-up started at first topical minoxidil prescription any time following the first diagnosis of androgenetic alopecia. Follow-up ended at the date of treatment discontinuation plus six months or when the participants initiated finasteride or dutasteride, if this came before the first outcome event or any other previously described censoring event.
No recorded prescription for study treatments	Individuals who did not initiate any of the above-mentioned treatments for androgenetic alopecia. Treatments other than those mentioned above were allowed before or during follow-up.	Follow-up started at first androgenetic alopecia diagnosis. Follow-up ended at the earliest date of 1) outcome of interest occurrence, 2) loss to follow-up, 3) death, 4) end of observation period (the most recent data available) in the data source, 5) initiation of any study treatment for androgenetic alopecia.
BPH indication		
Finasteride	Individuals who initiated finasteride, either alone or in combination with alpha blockers, after first BPH diagnosis. Treatments other than dutasteride and tadalafil were also allowed before or during follow-up.	Follow-up started at first finasteride prescription any time following first BPH diagnosis. Follow-up ended at the date of treatment discontinuation plus six months or the participant initiated dutasteride or tadalafil, if this came before the first outcome event or any other previously described censoring event.
Dutasteride	Individuals who initiated dutasteride, either alone or in combination with alpha blockers, after first BPH diagnosis. Treatments other than finasteride and tadalafil were also allowed before or during follow-up.	Follow-up started at first dutasteride prescription any time following first BPH diagnosis. Follow-up ended at the date of treatment discontinuation plus six months or the date on which participant initiated finasteride or tadalafil, if this comes before the first outcome event or any other previously described censoring event.
Alpha blockers	Individuals who initiated any alpha blocker after first BPH diagnosis. Treatments other than finasteride, dutasteride and tadalafil were also allowed before or during follow-up.	Follow-up started at first alpha blocker prescription within any time following first BPH diagnosis. Participants were allowed to switch between alpha blockers. Follow-up ended at the date of treatment discontinuation plus six months or the participant initiated dutasteride, finasteride or tadalafil, if this came before the first outcome event or any other previously described censoring event.

Treatment cohorts	Definition	Follow-up (censoring)
Tadalafil	Individuals who initiated tadalafil, either alone or in combination with alpha blockers, after first BPH diagnosis. Treatments other than finasteride and dutasteride were also allowed before or during follow-up.	Follow-up started at first tadalafil prescription any time following first BPH diagnosis. Follow-up ended on the date of treatment discontinuation plus six months or on the date when participants initiated finasteride or dutasteride, if this came before the first outcome event or any other previously described censoring event.
Tadalafil + Finasteride/Dutasteride	Individuals who initiated tadalafil in combination with finasteride or dutasteride and possibly in combination with alpha blockers, after first BPH diagnosis. Other treatments (anti-cholinergic, beta 3 agonists, herbals) were also allowed before or during follow-up.	Follow-up started at first tadalafil + finasteride/dutasteride prescription any time following the first BPH diagnosis. Follow-up ended at the date of treatment discontinuation plus six months or any other previously described censoring event. Switching was not a censoring event.
No recorded prescription for study treatments	Individuals who did not initiate any of the above mentioned BPH treatments. Treatments other than those mentioned above were allowed before or during follow-up (anti-inflammatory, anti-cholinergic, beta-3 agonists, herbal etc.).	Follow-up started at first BPH diagnosis. Follow-up ended at the earliest date of 1) outcome of interest occurrence, 2) loss to follow-up, 3) death, 4) end of observation period (the most recent data available) in the data source, 5) initiation of any study treatment for BPH.

A list of conditions and exposure concepts can be seen in **Appendix I. Table S 1.**

9.6.2 Outcome

The outcome of interest was a composite suicidality outcome which included the first recorded occurrence of any of the following events: completed suicide, attempted suicide, suicide ideation, and intentional self-harm.

All lists of codes for identifying the outcomes of interest are available in **Appendix I. Table S 3**.

These were refined during the study execution following the DARWIN EU® phenotyping standard processes, which involved the review of code lists by clinical experts, and the review of phenotypes after their execution in the participating data sources.

Furthermore, we described the counts of the constituent parts which make up the composite suicidality outcome, i.e., the number of outcomes which were attributed to suicide, suicide attempt, suicide ideation, and self-harm.

The operational definition of the outcome is presented in **Table 8**.

Table 8. Operational definition of outcomes.

Outcome name	Details	Primary outcome?	Type of outcome	Washout window	Care Settings[1]	Code Type	Diagnosis Position	Applied to study populations	Measurement characteristics/ validation	Source of algorithm
Composite suicidality outcome	First condition/observation record of any of the following events of completed suicide, attempted suicide, suicide ideation, and intentional self-harm	Yes	Binary	[-inf, -1]	IP, OP, and OT	SNOMED	n/a	All cohorts	n/a	n/a

* Infinite wash out was applied which means we included only incident cases and not allowing outcome event any time before index date
[1] IP = inpatient, OP = outpatient, ED = emergency department, OT = other, n/a = not applicable

9.6.3 Other covariates, including confounders, effect modifiers and other variables

- Age at index date namely:
  - 18-30 years
  - 31-40 years
  - 41-50 years
  - 51-60 years
  - 61-70 years
  - 71+years

- History of psychiatric disorders, which included any of the following conditions:
  - Depression
  - Anxiety
  - Bipolar disorder
  - Post-traumatic stress disorder (PTSD)
  - Eating disorders
  - Psychotic disorders

- History of sexual dysfunction, which included any of the following conditions:
  - Sexual pain disorder
  - Sexual arousal disorder
  - Sexual desire disorder
  - Psychosexual disorder

- Calendar/follow-up year: calendar year for the general adult male population and follow-up year for indication and treatment cohorts.

List of codes for identifying the psychiatric disorders and sextual dysfunction are described in **Appendix I. Table S 1**.

The operational definitions of the covariates are described in the **Table 9**.

Table 9. Operational definitions of covariates.

Characteristic	Details	Type of variable	Assessment window	Care Settings[1]	Code Type	Diagnosis Position	Applied to study populations	Measurement characteristics/ validation	Source for algorithm
Demographics	Age at index date	Numeric continuous	At index date	IP, OP, and OT	n/a	n/a	All cohorts	n/a	n/a
Psychiatric disorders of interest	Diagnosis records prior index date	Binary	All history	OP	SNOMED	n/a	All cohorts	n/a	n/a
Sexual dysfunction	Diagnosis records prior index date	Binary	All history	OP	SNOMED	n/a	All cohorts	n/a	n/a
Calendar/follow-up year	Calendar year for the general adult male population and follow-up year for indication and treatment cohorts	Numeric	At index date and during follow-up	IP, OP, and OT	n/a	n/a	All cohorts	n/a	n/a

[1] IP = inpatient, OP = outpatient, ED = emergency department, OT = other, n/a = not applicable

BPH= Benign Prostatic Hyperplasia

9.7 Study size

No sample size has been calculated as this was an exploratory study which was not intended to test a specific hypothesis. In addition, to estimate the incidence rates of suicide-related events in adult male patients diagnosed with androgenetic alopecia and BPH, we used already collected data. Thus, the sample size was driven by the availability of patients with conditions of interest, exposures and outcomes within each data source.

9.8 Data transformation

Analyses were conducted separately for each database. Before study initiation, test runs of the analytics were performed on a subset of the data sources and quality control checks were performed. Once all the tests passed (see section 11 Quality Control), the final package was released in the version-controlled Study Repository for execution against all the participating data sources.

The data partners locally executed the analytics against the OMOP-CDM in R Studio and reviewed and approved the - by default - aggregated results.

The study results of all data sources were checked after which they were made available to the team and the Dissemination Phase started. All results were locked and timestamped for reproducibility and transparency.

9.9 Statistical methods

9.9.1 Patient privacy protection

Cell suppression was applied as required by databases to protect individual's privacy. Cell counts <5 was masked.

9.9.2 Main summary measures

Results were presented by counts, percentages, median, range, and incidence rates. Incidence rates of suicide-related outcomes (with 95% confidence intervals) were estimated.

9.9.3 Main statistical methods

The main analysis included the calculation of incidence rates, as described below. The type of analysis by study type is presented in **Table 10**.

Table 10. Description of study type and type of analysis.

Study type	Study classification	Type of analysis
Population-level descriptive epidemiology	Off-the-shelf	- Incidence rates of the condition of interest

R-packages

The incidence rates were calculated based on OMOP-CDM mapped data using the "*IncidencePrevalence*" R package, developed by DARWIN EU®.(37)

Descriptive analysis

Distribution (number and %, median and IQR) of patient characteristics for each cohort of interest were described by data sources. This included the general adult male population, the androgenetic alopecia cohort, the treated androgenetic alopecia cohort, the non-treated androgenetic alopecia cohort (i.e., patients with no recorded prescription for the study treatments), the BPH cohort, the treated BPH cohort and the non-treated BPH cohort (i.e., patients with no recorded prescription for the study treatments before or at index date).

Furthermore, we described the counts of the constituent parts which made up the composite suicidality outcome, i.e., the number of outcomes which were attributed to suicide, suicide attempt, suicide ideation, and self-harm.

Main analysis

Overall incidence rates of the outcomes of interest were calculated as the number of newly diagnosed individuals with the outcome of interest divided by the person-years as contributed by the population at risk of the outcome of interest during the study period. Follow-up was censored at the earliest occurrence of the following: the outcome of interest, loss to follow-up, death, or the end of the observation period. For treatment cohorts, follow-up was additionally censored six months after treatment discontinuation or when patients switch to another treatment. For non-treated cohorts (i.e., patients with no recorded prescription for the study treatments before or at index date), follow-up was additionally censored at initiation of any study treatment.

Incidence rates were presented per 1,000 PYs together with 95% Poisson confidence intervals. **Figure 1** represents an example of incidence rate estimation.

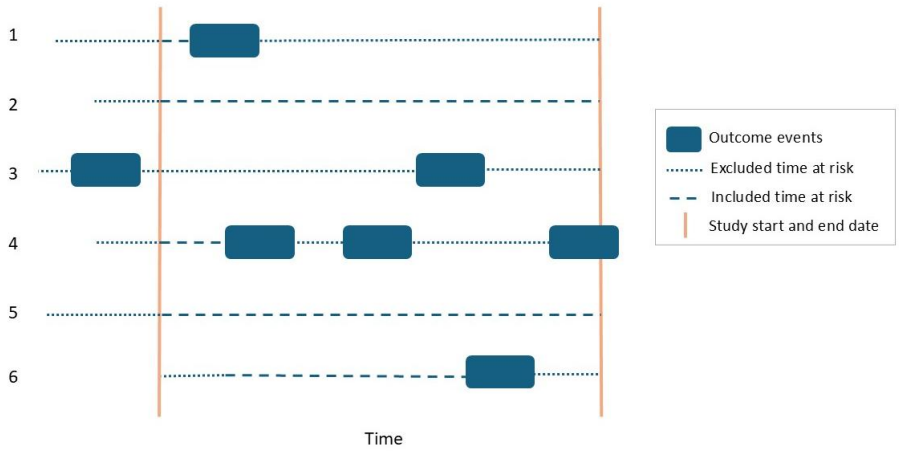


Figure 1. Examples of incidence rate estimation.

Patient IDs 1 and 4 contributed time at risk between the study start until they have an incident outcome of interest. Patient IDs 2 and 5 contributed time at risk between the study start and end date as no outcome of interest was observed between this period nor before the study start date. Patient ID 6 contributed time at risk from date where he had enough history of data (365 days) until he had an incident outcome of interest. Individuals should not have had a history of the suicidality to ensure that only new instances of the events were captured for analysis. Patient ID 3 was excluded due to having a prior history of the suicidality-related event.

Supplementary analyses

Incidence rates were stratified by:

- Age groups (18-30, 31-40, 41-50, 51-60, 61-70, 71+).
- History of psychiatric disorder
- History of sexual dysfunction
- Calendar year for the general adult male population and follow-up year for indication and treatment cohorts: For the general adult male population, the study entry date was random, allowing yearly incidence rates to be analysed by calendar year. However, for condition and treatment cohorts, follow-up time scale was more relevant, allowing one to look at how incidence rates changed over time since the disease or treatment initiation.

9.9.3 Missing values

For the disease epidemiology studies, we assume that the absence of a diagnosis record means that the person did not receive the diagnosis.

9.9.4 Sensitivity analysis

There were no sensitivity analyses in this study.

10. DATA MANAGEMENT

10.1 Data management

All databases have previously mapped their data to the OMOP common data model. This enabled the use of standardised analytics and using DARWIN EU® tools across the network since the structure of the data and the terminology system was harmonised. The OMOP CDM was developed and maintained by the Observational Health Data Sciences and Informatics (OHDSI) initiative and is described in detail on the wiki page of the CDM: https://ohdsi.github.io/CommonDataModel and in The Book of OHDSI: http://book.ohdsi.org

The analytic code for this study was written in R and used standardized analytics wherever possible. Each data partner executed the study code against their database containing patient-level data and then returned the results (csv files) which only contained aggregated data. The results from each of the contributing data sites were then combined in tables and figures for the study report.

10.2 Data storage and protection

For this study, personal data from individuals in various EU member states were processed, using information collected from national/regional electronic health record databases. Due to the sensitive nature of this personal medical data, it is important to be fully aware of ethical and regulatory aspects and to strive to take all reasonable measures to ensure compliance with ethical and regulatory issues on privacy.

All databases used in this study were already used for pharmaco-epidemiological research and have a well-developed mechanism to ensure that European and local regulations dealing with ethical use of the data and adequate privacy control are adhered to. In agreement with these regulations, rather than combining

person level data and performing only a central analysis, local analyses were run, which generate non-identifiable aggregate summary results.

11. QUALITY CONTROL

General database quality control

A number of open-source quality control mechanisms for the OMOP CDM have been developed (see Chapter 15 of The Book of OHDSI http://book.ohdsi.org/DataQuality.html). In particular, all data partners ran the OHDSI Data Quality Dashboard tool (https://github.com/OHDSI/DataQualityDashboard). This tool provides numerous checks relating to the conformance, completeness and plausibility of the mapped data. Conformance focuses on checks that describe the compliance of the representation of data against internal or external formatting, relational, or computational definitions. Completeness in the sense of data quality is solely focused on quantifying missingness, or the absence of data, while plausibility seeks to determine the believability or truthfulness of data values. Each of these categories has one or more subcategories and are evaluated in two contexts: validation and verification. Validation relates to how well data align with external benchmarks with expectations derived from known true standards, while verification relates to how well data conform to local knowledge, metadata descriptions, and system assumptions.

Study specific quality control

The SNOMED codes of the conditions and outcomes of interest were derived from ATLAS. The codes were then reviewed by two clinical epidemiologists to consider their relevance and accuracy. In addition, the "*CohortDiagnostics*" R package (https://github.com/OHDSI/CohortDiagnostics) was run to assess the use of different codes across the databases contributing to the study and identify any codes potentially omitted in error. This allowed for a consideration of the validity of the study cohort of patients with the selected conditions and outcomes in each of the databases and informed decisions around whether multiple definitions were required.

12. RESULTS

The full set of results for this study is available through an interactive web-application "shiny app" at https://data.darwin-eu.org/p3-c1-019-results-app/.

The data sources InGef RDB Germany and Danish DK-DHR had limited counts of outcomes, which might affect the reliability of incidence rates and limit the accuracy of conclusions drawn from their results.

12.1 Participants

Table 11 describes the characteristics of study participants in terms of counts, demographics and comorbidities of interests within the different cohorts of interest.

The overall number of the general adult male population varied across different data sources as follows, BIFAP (8,621,220), InGef RDB (4,063,229), CPRD-Gold (4,336,324), SIDIAP (3,316,543), DK-DHR (2,916,174), Croatian NAJS (1,918,950), and IPCI (1,000,636). The median age in the general adult male population ranged between 38 years (DK-DHR and SIDIAP) and 45 (NAJS) years. The proportion of individuals with a history of psychiatric disorders was very low in InGef RDB (1.69%) and was up to 11.13% in NAJS. The proportion of males with a history of sexual dysfunction was less than 1% in BIFAP, InGef RDB, and NAJS and highest 4.60 in DK-DHR in the general adult male population.

The cohort of individuals with newly diagnosed androgenetic alopecia consisted of 9,280 in BIFAP, 5,265 in SIDIAP, 1,949 in IPCI, 1,640 in NAJS, 629 in CPRD-Gold, 452 in DK-DHR and 236 in InGef RDB. The median age at time of diagnosis ranged between 26 years (IPCI) and 35 years (DK-DHR). The proportion of individuals with a history of psychiatric disorders was much higher compared to the general adult male population and ranged between 11.4% (InGef RDB) and 31.45% in IPCI. The proportion of individuals with a history of sexual dysfunction ranged between 0% (InGef RDB) and 10.2 % (DK-DHR) (**Table 11**).

A large number of individuals had no recorded study treatment on the day of their first androgenetic alopecia diagnosis, thus could participate with follow-up to the non-treated cohort. In total 77% of the individuals newly diagnosed with androgenetic alopecia had no recorded study treatment for finasteride (1 mg), dutasteride or topical minoxidil on the day of their diagnosis. Data on treatment for androgenetic alopecia was mainly present in BIFAP, CPRD-Gold, IPCI and SIDIAP. In CPRD-Gold, 23.5% were treated with finasteride 1mg and 4.3% were treated with topical minoxidil. In IPCI, 31.0% were treated with finasteride 1mg and 15.6% were treated with topical minoxidil. In SIDIAP, 3.4% and 8.6% of patients received treatment with finasteride 1 mg and topical minoxidil, respectively. In all data sources, the use of dutasteride for the treatment of androgenetic alopecia was low or not recorded. Individuals who initiated finasteride or dutasteride were somewhat older than the androgenetic alopecia patients who had no recorded prescriptions for study treatments. This pattern was observed in CPRD Gold (finasteride), IPCI (dutasteride), NAJS (dutasteride) and SIDIAP (dutasteride and finasteride 1mg).

The total number of individuals with newly diagnosed BPH across different data sources was distributed as follows: BIFAP (444,795), SIDIAP (313,797), NAJS (279,363), InGef RDB (163,278), DK-DHR (93,919), CPRD-Gold (74,558), and IPCI (15,320). The median age at time of BPH diagnosis ranged between 64 (NAJS) and 73 (InGef RDB) years. The proportion of patients with a history of psychiatric disorders was much higher compared to the general adult male population and ranged between 10.4% (InGef RDB) and 28.8% in NAJS. The proportion of patients with a history of sexual dysfunction was high in DK-DHR (25.8%) and lower in CPRD-Gold (7.39%), SIDIAP (6.1%), and IPCI (7.2%). The proportion of patients with a history of sexual dysfunction was lowest in InGef RDB (0.1%) and NAJS (0.6%) (**Table 11**).

Across various data sources, high proportion of patients newly diagnosed with BPH first initiated treatment with alpha-blockers before initiating any 5-alpha-reductare-inhibitors (ARI). For example, 32.3% of newly diagnosed males with BPH in DK-DHR and 62% in CPRD-Gold and NAJS. In CPRD Gold, 21.3% of individuals newly diagnosed with BPH initiated finasteride as the first 5-ARI following diagnosis vs. only 0.7% in BIFAP. In NAJS, 29.7% of individuals newly diagnosed with BPH were treated with dutasteride as the first 5-ARI after first indication diagnosis. Also, in IPCI (9.5% of newly diagnosed BPH) and SIDIAP (11.5%) use of dutasteride was substantial whereas the proportion of BPH males treated with dutasteride was lower in DK-DHR (8.9%), CPRD-Gold (4.5%), and InGef RDB (3.1%). Use of tadalafil for treatment of BPH was much lower (0.5% of newly diagnosed BPH in InGef RDB to 2.2% in CPRD). High proportion of (>46%) of individuals with newly diagnosed BPH had no recorded prescriptions for study treatments on the date of their diagnosis., ranging from 46.0% in DK-DHR to 88.0% in IPCI across data sources (**Table 11**).

Regarding the characteristics of the exposure cohorts for the treatment of BPH, median age was the lowest for the tadalafil exposure cohorts (64 years in CPRD-Gold – and 65 years in IPCI, InGef RDB and SIDIAP) and the median age was the highest in the finasteride exposure cohorts (71 years for SIDIAP – 76 years in InGef RDB). The proportion of patients with a recorded history of psychiatric disorders was higher in the tadalafil exposure cohort (16.0% InGef RDB – 32.8% in SIDIAP) compared to the other exposure cohorts. This trend was even stronger for a recorded history of sexual dysfunction in the tadalafil exposure cohort with proportions ranging between 55.6% for SIDIAP and 66.2% for CPRD-Gold. The proportion of male patients recorded with history of sexual dysfunction was low in InGef RDB in all exposure cohorts (**Table 11**).

Table 11. Distribution of study participants' characteristics (number and %, median and IQR) per cohorts of interest by data source.

Data source	Characteristic	General adult male population	Androgenetic alopecia (first ever) diagnosis	Finasteride for androgenetic alopecia	Dutasteride for androgenetic alopecia	Topical minoxidil for androgenetic alopecia	Non-treated androgenetic alopecia	BPH (first ever) diagnosis	Finasteride for BPH	Dutasteride for BPH	Alpha blockers for BPH	Tadalafil for BPH	Tadalafil + finasteride/ Dutasteride for BPHdo	Non-treated BPH
BIFAP	Overall, N	8,621,220	9,280	1,139	216	supp	8930	444,795	3,203	91,574	158,870	4,418	NC	348,518
	Median age (IQR) at index date	41 (28 - 57)	31 (24 - 40)	34 (27 - 41)	33 (27 - 42)	supp	31 (24 - 40)	70 (61 - 79)	75 (67 - 82)	72 (65 - 79)	71 (63 - 78)	64 (58 - 69)	NC	68 (60 - 76)
	Mean age (SD) at index date	43.48 (19.01)	33.19 (11.00)	34.82 (10.12)	35.71 (12.04)	supp	33.21 (11.14)	69.82 (11.69)	74.13 (10.69)	72.16 (9.84)	70.58 (10.17)	63.36 (7.78)	NC	68.17 (11.55)
	Age groups, in year N (%)													
	18-30	1,620,132 (18.79)	4,390 (47.31)	448 (39.33)	91 (42.13)	supp	4,250 (47.59)	357 (0.08)	NC	7 (0.01)	14 (0.01)	NC	NC	354 (0.10)
	31-40	1,667,717 (19.34)	2,569 (27.68)	362 (31.78)	63 (29.17)	NC	2,437 (27.29)	1,914 (0.43)	9 (0.28)	36 (0.04)	196 (0.12)	15 (0.34)	NC	1,872 (0.54)
	41-50	1,483,672 (17.21)	1,525 (16.43)	242 (21.25)	37 (17.13)	NC	1,446 (16.19)	18,844 (4.24)	72 (2.25)	1,004 (1.10)	3,260 (2.05)	198 (4.48)	NC	18,182 (5.22)
	51-60	1,175,316 (13.63)	546 (5.88)	69 (6.06)	16 (7.41)	NC	536 (6.00)	78,338 (17.61)	279 (8.71)	10,347 (11.30)	23,178 (14.59)	1,358 (30.74)	NC	71,636 (20.55)
	61-70	867,002 (10.06)	148 (1.59)	12 (1.05)	5 (2.31)	NC	159 (1.78)	132,873 (29.87)	752 (23.48)	28,698 (31.34)	52,472 (33.03)	2,047 (46.33)	NC	111,396 (31.96)
	71+	912,197 (10.58)	26 (0.28)	supp	supp	NC	27 (0.30)	212,465 (47.77)	2,091 (65.28)	51,482 (56.22)	79,750 (50.20)	800 (18.11)	NC	145,074 (41.63)
	History of psychiatric disorder (%)	512,636 (5.95)	1,662 (17.91)	228 (20.02)	42 (19.44)	supp	1,600 (17.92)	81,833 (18.40)	575 (17.95)	17,326 (18.92)	29,961 (18.86)	1,195 (27.05)	NC	63,231 (18.14)
	History of sexual	49,264 (0.57)	185 (1.99)	13 (1.14)	7 (3.24)	supp	178 (1.99)	18,925 (4.25)	81 (2.53)	4,291 (4.69)	7,423 (4.67)	1,455 (32.93)	NC	14,618 (4.19)

Data source	Characteristic	General adult male population	Androgenetic alopecia (first ever) diagnosis	Finasteride for androgenetic alopecia	Dutasteride for androgenetic alopecia	Topical minoxidil for androgenetic alopecia	Non-treated androgenetic alopecia	BPH (first ever) diagnosis	Finasteride for BPH	Dutasteride for BPH	Alpha blockers for BPH	Tadalafil for BPH	Tadalafil + finasteride/ Dutasteride for BPHdo	Non-treated BPH
	dysfunction (%)													
	Median index year (IQR)	2012-01-01 (2010-01-01 - 2019-02-21)	2021-02-04 (2018-06-11 - 2022-11-11)	2020-08-25 (2019-11-14 - 2021-07-24)	2021-04-21 (2020-02-26 - 2021-12-24)	supp	2021-02-16 (2018-04-27 - 2022-11-21)	2018-01-31 (2014-10-27 - 2021-03-27)	2016-04-18 (2013-02-12 - 2019-07-31)	2019-04-05 (2015-11-26 - 2021-12-20)	2018-12-10 (2015-10-14 - 2021-08-26)	2021-05-31 (2020-02-28 - 2022-06-03)	NC	2018-01-08 (2014-09-04 - 2021-03-18)
CPRD-Gold	Overall, N	4,336,324	629	148	supp	27	469	74,558	15,869	3,332	46,058	1,630	NC	57,944
	Median age (IQR) at index date	41 (28 - 57)	27 (23 - 36)	29 (24 - 37)	supp	26 (23 - 31)	27 (22 - 35)	68 (61 - 75)	72 (65 - 78)	71 (64 - 77)	68 (61 - 76)	64 (58 - 70)	NC	67 (60 - 75)
	Mean age (SD) at index date	43.15 (18.60)	30.72 (11.41)	31.43 (9.77)	supp	29.22 (11.84)	30.22 (11.24)	67.90 (10.67)	71.45 (9.69)	70.68 (9.43)	68.36 (10.32)	64.00 (8.63)	NC	66.99 (10.74)
	Age groups, in year N (%)													
	18-30	1,330,033 (30.67)	379 (60.25)	77 (52.03)	supp	20 (74.07)	293 (62.47)	90 (0.12)	supp	NC	14 (0.03)	supp	NC	89 (0.15)
	31-40	807,806 (18.63)	152 (24.17)	48 (32.43)	NC	supp	109 (23.24)	409 (0.55)	11 (0.07)	5 (0.15)	144 (0.31)	10 (0.61)	NC	386 (0.67)
	41-50	746,579 (17.22)	58 (9.22)	17 (11.49)	supp	supp	38 (8.10)	3,413 (4.58)	233 (1.47)	49 (1.47)	1,806 (3.92)	87 (5.34)	NC	3,131 (5.40)
	51-60	577,467 (13.32)	20 (3.18)	supp	NC	NC	14 (2.99)	14,152 (18.98)	1,896 (11.95)	415 (12.45)	8,455 (18.36)	451 (27.67)	NC	12,152 (20.97)
	61-70	459,936 (10.61)	12 (1.91)	supp	NC	NC	11 (2.35)	26,030 (34.91)	5,093 (32.09)	1,180 (35.41)	16,233 (35.24)	734 (45.03)	NC	20,484 (35.35)
	71+	414,503 (9.56)	8 (1.27)	supp	supp	supp	supp	30,464 (40.86)	8,635 (54.41)	1,683 (50.51)	19,406 (42.13)	346 (21.23)	NC	21,702 (37.45)
	History of psychiatric	469,397 (10.82)	151 (24.01)	40 (27.03)	supp	supp	109 (23.24)	15,038 (20.17)	3,063 (19.30)	754 (22.63)	9,065 (19.68)	439 (26.93)	NC	11,591 (20.00)

Data source	Characteristic	General adult male population	Androgenetic alopecia (first ever) diagnosis	Finasteride for androgenetic alopecia	Dutasteride for androgenetic alopecia	Topical minoxidil for androgenetic alopecia	Non-treated androgenetic alopecia	BPH (first ever) diagnosis	Finasteride for BPH	Dutasteride for BPH	Alpha blockers for BPH	Tadalafil for BPH	Tadalafil + finasteride/ Dutasteride for BPHdo	Non-treated BPH
	disorder (%)													
	History of sexual dysfunction (%)	158,423 (3.65)	26 (4.13)	5 (3.38)	supp	supp	22 (4.69)	12,965 (17.39)	2,234 (14.08)	449 (13.48)	6,187 (13.43)	1,079 (66.20)	NC	7,606 (13.13)
	Median index year (IQR)	2010-01-01 (2010-01-01 - 2014-01-01)	2013-07-23 (2011-10-24 - 2017-02-11)	2014-04-30 (2012-03-19 - 2017-03-23)	supp	2013-11-19 (2011-09-24 - 2016-04-24)	2013-05-10 (2011-10-06 - 2016-11-15)	2014-03-24 (2011-12-22 - 2018-01-23)	2015-11-10 (2013-02-22 - 2019-06-28)	2014-01-24 (2011-12-23 - 2017-05-02)	2014-07-30 (2012-03-28 - 2018-05-01)	2015-04-29 (2013-01-09 - 2019-01-30)	NC	2014-02-24 (2011-12-01 - 2017-11-30)
DK-DHR	Overall, N	2,916,174	452	71	supp	12	366	93,919	25,738	8,350	30,372	5,559	NC	43,233
	Median age (IQR) at index date	38 (23 - 55)	35 (27 - 43)	30 (25 - 38)	supp	27 (22 - 42)	35 (27 - 44)	71 (64 - 77)	72 (66 - 78)	71 (65 - 78)	70 (64 - 77)	66 (59 - 72)	NC	69 (63 - 76)
	Mean age (SD) at index date	40.72 (19.04)	36.00 (11.67)	32.54 (9.21)	supp	31.83 (12.97)	36.68 (12.09)	70.25 (10.15)	71.83 (9.40)	71.26 (9.13)	70.01 (9.55)	65.26 (9.95)	NC	69.32 (10.22)
	Age groups, in year N (%)													
	18-30	1,130,630 (37.63)	162 (35.84)	36 (50.70)	supp	6 (50.00)	127 (34.70)	218 (0.23)	47 (0.18)	NC	17 (0.06)	29 (0.52)	NC	63 (0.15)
	31-40	472,834 (15.74)	141 (31.19)	21 (29.58)	supp	supp	112 (30.60)	446 (0.47)	42 (0.16)	6 (0.07)	81 (0.27)	60 (1.08)	NC	230 (0.53)
	41-50	457,610 (15.23)	100 (22.12)	10 (14.08)	NC	supp	84 (22.95)	2,230 (2.37)	333 (1.29)	106 (1.27)	614 (2.02)	316 (5.68)	NC	1,206 (2.79)
	51-60	378,408 (12.59)	30 (6.64)	supp (supp)	NC	supp	27 (7.38)	11,778 (12.54)	2,382 (9.25)	904 (10.83)	4,035 (13.29)	1,182 (21.26)	NC	6,465 (14.95)
	61-70	329,863 (10.98)	8 (1.77)	NC	NC	NC	8 (2.19)	32,063 (34.14)	8,215 (31.92)	2,862 (34.28)	10,863 (35.77)	2,266 (40.76)	NC	15,596 (36.07)

Data source	Characteristic	General adult male population	Androgenetic alopecia (first ever) diagnosis	Finasteride for androgenetic alopecia	Dutasteride for androgenetic alopecia	Topical minoxidil for androgenetic alopecia	Non-treated androgenetic alopecia	BPH (first ever) diagnosis	Finasteride for BPH	Dutasteride for BPH	Alpha blockers for BPH	Tadalafil for BPH	Tadalafil + finasteride/ Dutasteride for BPHdo	Non-treated BPH
	71+	235,155 (7.83)	7 (1.55)	NC	NC	NC	7 (1.91)	47,183 (50.24)	14,719 (57.19)	4,472 (53.56)	14,762 (48.60)	1,706 (30.69)	NC	19,672 (45.50)
	None	322 (0.01)	supp	NC	NC	supp	supp	supp	NC	NC	NC	NC	NC	supp
	History of psychiatric disorder (%)	271,092 (9.02)	61 (13.50)	9 (12.68)	supp	supp	44 (12.02)	17,197 (18.31)	4,593 (17.85)	1,414 (16.93)	5,317 (17.51)	1,102 (19.82)	NC	7,139 (16.51)
	History of sexual dysfunction (%)	140,846 (4.69)	46 (10.18)	10 (14.08)	supp	supp	36 (9.84)	24,206 (25.77)	4,444 (17.27)	1,342 (16.07)	4,990 (16.43)	3,045 (54.78)	NC	6,075 (14.05)
	Median index year (IQR)	2010-01-01 (2010-01-01 - 2012-12-10)	2015-10-27 (2013-08-21 - 2018-09-13)	2018-07-13 (2016-12-17 - 2021-09-18)	supp	2016-07-06 (2014-05-26 - 2021-06-18)	2015-10-27 (2013-09-06 - 2018-09-04)	2016-08-01 (2013-02-26 - 2020-09-09)	2017-11-15 (2014-08-14 - 2021-04-22)	2016-02-04 (2012-11-23 - 2019-12-22)	2017-01-12 (2013-08-29 - 2020-10-24)	2022-02-04 (2019-03-11 - 2023-07-19)	NC	2015-09-29 (2012-08-22 - 2019-08-28)
IPCI	Overall, N	1,000,636	1,949	605	15	304	1,315	15,320	567	1,462	9,103	324	NC	13,487
	Median age (IQR) at index date	44 (29 - 59)	26 (21 - 34)	26 (22 - 32)	32 (24 - 44)	25 (21 - 33)	25 (21 - 33)	67 (60 - 74)	72 (65 - 79)	70 (64 - 77)	68 (61 - 75)	65 (60 - 70)	NC	67 (60 - 73)
	Mean age (SD) at index date	44.68 (18.64)	29.38 (11.14)	28.78 (9.79)	36.40 (16.71)	28.58 (10.38)	29.16 (11.90)	66.97 (9.88)	71.63 (9.36)	69.88 (9.42)	67.47 (9.96)	64.60 (7.67)	NC	66.48 (9.86)
	Age groups, in year N (%)													
	18-30	278,804 (27.86)	1,266 (64.96)	420 (69.42)	7 (46.67)	208 (68.42)	876 (66.62)	11 (0.07)	NC	NC	5 (0.05)	supp	NC	10 (0.07)
	31-40	170,561 (17.05)	351 (18.01)	98 (16.20)	supp	48 (15.79)	219 (16.65)	31 (0.20)	NC	supp	18 (0.20)	supp	NC	30 (0.22)

Data source	Characteristic	General adult male population	Androgenetic alopecia (first ever) diagnosis	Finasteride for androgenetic alopecia	Dutasteride for androgenetic alopecia	Topical minoxidil for androgenetic alopecia	Non-treated androgenetic alopecia	BPH (first ever) diagnosis	Finasteride for BPH	Dutasteride for BPH	Alpha blockers for BPH	Tadalafil for BPH	Tadalafil + finasteride/ Dutasteride for BPHdo	Non-treated BPH
	41-50	170,093 (17.00)	173 (8.88)	53 (8.76)	supp	27 (8.88)	103 (7.83)	645 (4.21)	supp	27 (1.85)	368 (4.04)	10 (3.09)	NC	623 (4.62)
	51-60	153,752 (15.37)	85 (4.36)	23 (3.80)	supp	14 (4.61)	48 (3.65)	3,346 (21.84)	68 (11.99)	219 (14.98)	1,879 (20.64)	75 (23.15)	NC	3,123 (23.16)
	61-70	124,565 (12.45)	28 (1.44)	supp	NC	supp	25 (1.90)	5,721 (37.34)	181 (31.92)	511 (34.95)	3,337 (36.66)	163 (50.31)	NC	5,064 (37.55)
	71+	102,861 (10.28)	11 (0.56)	supp	supp	NC	16 (1.22)	5,566 (36.33)	314 (55.38)	704 (48.15)	3,496 (38.40)	74 (22.84)	NC	4,637 (34.38)
	History of psychiatric disorder (%)	86,958 (8.69)	613 (31.45)	208 (34.38)	8 (53.33)	104 (34.21)	391 (29.73)	3,212 (20.97)	143 (25.22)	302 (20.66)	1,963 (21.56)	100 (30.86)	NC	2,824 (20.94)
	History of sexual dysfunction (%)	10,368 (1.04)	50 (2.57)	14 (2.31)	supp	9 (2.96)	33 (2.51)	1,097 (7.16)	27 (4.76)	75 (5.13)	464 (5.10)	187 (57.72)	NC	670 (4.97)
	Median index year (IQR)	2015-06-01 (2012-02-29 - 2019-05-01)	2018-05-01 (2014-10-16 - 2021-06-07)	2018-08-10 (2015-01-28 - 2021-10-22)	2019-05-27 (2013-07-27 - 2021-03-22)	2020-01-26 (2016-08-25 - 2022-06-24)	2018-04-18 (2014-09-13 - 2021-04-29)	2017-06-19 (2014-01-21 - 2020-07-21)	2019-04-04 (2015-12-15 - 2021-08-02)	2017-08-22 (2014-05-03 - 2020-09-03)	2017-10-02 (2014-05-02 - 2020-10-30)	2019-04-26 (2016-01-20 - 2021-07-27)	NC	2017-07-12 (2014-02-13 - 2020-08-12)
InGef RDB	Overall, N	4,063,229	236	supp	NC	NC	230	163,278	5,256	4,998	96,199	869	NC	137,195
	Median age (IQR) at index date	42 (28 - 55)	29 (23 - 41)	supp	NC	NC	29 (23 - 40)	73 (65 - 81)	76 (69 - 82)	76 (68 - 82)	74 (66 - 81)	65 (59 - 72)	NC	73 (64 - 80)
	Mean age (SD) at index date	43.03 (17.92)	33.89 (14.86)	supp	NC	NC	33.18 (13.75)	72.47 (10.72)	74.94 (9.27)	74.72 (9.19)	73.01 (10.29)	65.64 (9.45)	NC	72.04 (10.88)
	Age groups, in year N (%)													

Data source	Characteristic	General adult male population	Androgenetic alopecia (first ever) diagnosis	Finasteride for androgenetic alopecia	Dutasteride for androgenetic alopecia	Topical minoxidil for androgenetic alopecia	Non-treated androgenetic alopecia	BPH (first ever) diagnosis	Finasteride for BPH	Dutasteride for BPH	Alpha blockers for BPH	Tadalafil for BPH	Tadalafil + finasteride/ Dutasteride for BPHdo	Non-treated BPH
	18-30	1,224,847 (30.14)	120 (50.85)	supp	NC	NC	119 (51.74)	86 (0.05)	NC	NC	22 (0.02)	NC	NC	85 (0.06)
	31-40	684,233 (16.84)	53 (22.46)	NC	NC	NC	52 (22.61)	452 (0.28)	supp	NC	136 (0.14)	supp	NC	448 (0.33)
	41-50	761,623 (18.74)	27 (11.44)	NC	NC	NC	27 (11.74)	3,054 (1.87)	27 (0.51)	21 (0.42)	1,446 (1.50)	42 (4.83)	NC	2,925 (2.13)
	51-60	681,154 (16.76)	13 (5.51)	NC	NC	NC	13 (5.65)	20,648 (12.65)	378 (7.19)	380 (7.60)	10,961 (11.39)	235 (27.04)	NC	18,628 (13.58)
	61-70	364,543 (8.97)	13 (5.51)	NC	NC	NC	13 (5.65)	42,809 (26.22)	1,203 (22.89)	1,186 (23.73)	24,573 (25.54)	327 (37.63)	NC	36,634 (26.70)
	71+	346,829 (8.54)	7 (2.97)	NC	NC	NC	supp	96,227 (58.93)	3,647 (69.39)	3,411 (68.25)	59,061 (61.39)	263 (30.26)	NC	78,473 (57.20)
	History of psychiatric disorder (%)	68,615 (1.69)	27 (11.44)	supp	NC	NC	28 (12.17)	16,907 (10.35)	590 (11.23)	623 (12.46)	11,774 (12.24)	139 (16.00)	NC	14,845 (10.82)
	History of sexual dysfunction (%)	305 (0.01)	supp	supp	NC	NC	supp	133 (0.08)	supp	5 (0.10)	80 (0.08)	10 (1.15)	NC	116 (0.08)
	Median index year (IQR)	2016-01-01 (2016-01-01 - 2017-03-01)	2019-09-11 (2017-12-14 - 2021-12-21)	supp	NC	NC	2019-09-17 (2017-12-15 - 2022-01-05)	2020-01-30 (2017-12-25 - 2022-06-18)	2020-06-04 (2018-07-18 - 2022-09-10)	2021-10-22 (2020-01-27 - 2023-03-21)	2019-10-16 (2017-05-31 - 2022-04-25)	2022-06-23 (2020-10-06 - 2023-09-29)	NC	2020-01-16 (2017-12-12 - 2022-06-01)
NAJS	Overall, N	1,918,950	1,640	12	7	NC	1,705	279,363	7,687	83,055	173,087	NC	NC	249,257
	Median age (IQR) at index date	45 (29 - 60)	27 (22 - 35)	26 (23 - 30)	46 (36 - 54)	NC	27 (22 - 37)	64 (56 - 71)	73 (67 - 80)	67 (60 - 74)	67 (60 - 74)	NC	NC	63 (56 - 71)

Data source	Characteristic	General adult male population	Androgenetic alopecia (first ever) diagnosis	Finasteride for androgenetic alopecia	Dutasteride for androgenetic alopecia	Topical minoxidil for androgenetic alopecia	Non-treated androgenetic alopecia	BPH (first ever) diagnosis	Finasteride for BPH	Dutasteride for BPH	Alpha blockers for BPH	Tadalafil for BPH	Tadalafil + finasteride/ Dutasteride for BPHdo	Non-treated BPH
	Mean age (SD) at index date	45.18 (18.88)	30.25 (11.67)	27.67 (8.36)	46.00 (13.81)	NC	31.41 (12.90)	63.40 (11.58)	72.77 (9.17)	66.84 (10.43)	67.08 (10.46)	NC	NC	63.05 (11.47)
	Age groups, in year N (%)													
	18-30	522,761 (27.24)	996 (60.73)	9 (75.00)	Supp	NC	993 (58.24)	1,713 (0.61)	7 (0.09)	139 (0.17)	302 (0.17)	NC	NC	1,584 (0.64)
	31-40	314,846 (16.41)	371 (22.62)	Supp	Supp	NC	370 (21.70)	5,947 (2.13)	Supp	688 (0.83)	1,462 (0.84)	NC	NC	5,374 (2.16)
	41-50	302,242 (15.75)	138 (8.41)	Supp	Supp	NC	155 (9.09)	28,210 (10.10)	87 (1.13)	4,113 (4.95)	8,404 (4.86)	NC	NC	25,979 (10.42)
	51-60	317,881 (16.57)	50 (3.05)	NC	Supp	NC	73 (4.28)	73,650 (26.36)	616 (8.01)	16,823 (20.26)	33,777 (19.51)	NC	NC	67,449 (27.06)
	61-70	255,655 (13.32)	47 (2.87)	NC	Supp	NC	67 (3.93)	95,210 (34.08)	2,294 (29.84)	31,147 (37.50)	64,108 (37.04)	NC	NC	85,609 (34.35)
	71+	205,472 (10.71)	14 (0.85)	NC	NC	NC	23 (1.35)	74,619 (26.71)	4,679 (60.87)	30,144 (36.29)	65,032 (37.57)	NC	NC	63,249 (25.38)
	None	93 (0.00)	24 (1.46)	NC	NC	NC	24 (1.41)	14 (0.01)	-	Supp	Supp	NC	NC	13 (0.01)
	History of psychiatric disorder (%)	213,510 (11.13)	276 (16.83)	Supp	Supp	NC	307 (18.01)	80,332 (28.76)	2,071 (26.94)	27,971 (33.68)	54,789 (31.65)	NC	NC	71,200 (28.56)
	History of sexual dysfunction (%)	1,712 (0.09)	5 (0.30)	Supp	supp	NC	9 (0.53)	1,574 (0.56)	22 (0.29)	623 (0.75)	1,111 (0.64)	NC	NC	1,395 (0.56)
	Median index year (IQR)	2016-03-02 (2016-01-15 - 2017-02-08)	2020-07-31 (2018-03-20 - 2022-09-27)	2021-11-18 (2019-07-23 - 2023-02-10)	2021-06-17 (2018-03-04 - 2023-03-18)	NC	2020-07-31 (2018-03-26 - 2022-09-21)	2018-12-15 (2017-03-09 - 2021-09-09)	2017-11-14 (2016-02-01 - 2019-08-22)	2020-07-09 (2018-02-21 - 2023-01-04)	2019-01-11 (2016-11-16 - 2021-11-29)	NC	NC	2018-12-04 (2017-03-13 - 2021-08-09)

Data source	Characteristic	General adult male population	Androgenetic alopecia (first ever) diagnosis	Finasteride for androgenetic alopecia	Dutasteride for androgenetic alopecia	Topical minoxidil for androgenetic alopecia	Non-treated androgenetic alopecia	BPH (first ever) diagnosis	Finasteride for BPH	Dutasteride for BPH	Alpha blockers for BPH	Tadalafil for BPH	Tadalafil + finasteride/ Dutasteride for BPHdo	Non-treated BPH
SIDIAP	Overall, N	3,316,543	5,265	181	97	466	4,573	313,797	15,588	36,164	163,225	3,659	NC	270,850
	Median age (IQR) at index date	38 (27 - 53)	30 (24 - 38)	33 (27 - 41)	35 (29 - 43)	28 (23 - 37)	30 (24 - 37)	68 (60 - 76)	71 (65 - 78)	71 (65 - 78)	68 (61 - 76)	65 (59 - 70)	NC	67 (59 - 75)
	Mean age (SD) at index date	41.36 (18.36)	31.88 (10.44)	34.87 (10.68)	37.63 (11.45)	30.42 (9.44)	31.90 (10.85)	67.87 (11.30)	71.41 (9.86)	71.16 (9.40)	68.59 (10.54)	64.63 (7.84)	NC	66.90 (11.14)
	Age groups, in year N (%)													
	18-30	1,086,604 (32.76)	2,720 (51.66)	71 (39.23)	31 (31.96)	263 (56.44)	2,404 (52.57)	236 (0.08)	12 (0.08)	supp	51 (0.03)	supp	NC	218 (0.08)
	31-40	747,335 (22.53)	1,532 (29.10)	64 (35.36)	32 (32.99)	124 (26.61)	1,291 (28.23)	1,834 (0.58)	21 (0.13)	26 (0.07)	449 (0.28)	8 (0.22)	NC	1,754 (0.65)
	41-50	529,361 (15.96)	651 (12.36)	32 (17.68)	20 (20.62)	63 (13.52)	526 (11.50)	16,244 (5.18)	202 (1.30)	375 (1.04)	6,112 (3.74)	130 (3.55)	NC	15,775 (5.82)
	51-60	371,110 (11.19)	233 (4.43)	11 (6.08)	9 (9.28)	10 (2.15)	210 (4.59)	65,063 (20.73)	1,887 (12.11)	4,402 (12.17)	30,520 (18.70)	952 (26.02)	NC	61,093 (22.56)
	61-70	280,440 (8.46)	72 (1.37)	supp	supp	supp	81 (1.77)	103,482 (32.98)	5,080 (32.59)	12,437 (34.39)	56,448 (34.58)	1,735 (47.42)	NC	92,327 (34.09)
	71+	301,693 (9.10)	16 (0.30)	supp	supp	NC	22 (0.48)	126,936 (40.45)	8,386 (53.80)	18,920 (52.32)	69,644 (42.67)	833 (22.77)	NC	99,681 (36.80)
	None	NC	41 (0.78)	NC	NC	supp	39 (0.85)	supp	NC	NC	supp	NC	NC	supp (supp)
	History of psychiatric disorder (%)	211,030 (6.36)	1,073 (20.38)	39 (21.55)	34 (35.05)	109 (23.39)	910 (19.90)	60,162 (19.17)	3,321 (21.30)	7,729 (21.37)	34,211 (20.96)	1,200 (32.80)	NC	52,374 (19.34)
	History of sexual	18,943 (0.57)	145 (2.75)	supp	5 (5.15)	12 (2.58)	129 (2.82)	19,017 (6.06)	1,134 (7.27)	2,583 (7.14)	11,143 (6.83)	2,035 (55.62)	NC	16,209 (5.98)

Data source	Characteristic	General adult male population	Androgenetic alopecia (first ever) diagnosis	Finasteride for androgenetic alopecia	Dutasteride for androgenetic alopecia	Topical minoxidil for androgenetic alopecia	Non-treated androgenetic alopecia	BPH (first ever) diagnosis	Finasteride for BPH	Dutasteride for BPH	Alpha blockers for BPH	Tadalafil for BPH	Tadalafil + finasteride/ Dutasteride for BPHdo	Non-treated BPH
	dysfunction (%)													
	Median index year (IQR)	2010-01-01 (2010-01-01 - 2011-06-23)	2016-10-31 (2013-09-13 - 2020-11-09)	2017-08-23 (2013-10-01 - 2020-10-02)	2022-01-31 (2020-04-01 - 2022-09-29)	2021-05-02 (2018-05-11 - 2022-07-08)	2016-03-10 (2013-05-30 - 2020-01-07)	2016-02-23 (2013-01-21 - 2019-07-08)	2017-08-01 (2015-01-01 - 2020-04-01)	2018-10-24 (2015-02-11 - 2021-07-01)	2017-04-01 (2013-12-01 - 2020-07-13)	2021-03-16 (2019-01-26 - 2022-06-20)	NC	2016-03-11 (2013-02-11 - 2019-07-10)

Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.

BPH=Benign Prostatic Hyperplasia.

NC= No Person Count.

Supp= Person counts <5 was suppressed to protect patients' confidentiality.

12.2 Incidence rates of composite suicidality events

Appendix II. Table S 30 describes the distribution of the individual suicide related events (completed suicide, attempted suicide, suicidal ideation and intentional self-harm) that contributed to the composite outcome by data source for the general population and indication cohorts of interest (androgenetic alopecia and BPH). In the general adult male population, the highest number of suicide related events were found in CPRD-Gold (37,773 events consisting of suicidal ideation (n=23,614), intentional self-harm (n=15,392), attempted suicide (n=10,952) and completed suicide (n=86)). Also, in the general adult male population of BIFAP, the number of outcomes was high with 26,385 events of suicide ideation, 8,749 attempted suicide and 6,059 intentional self-harm. In IPCI (n=2,091) and NAJS (7,508) mainly attempted suicide was reported. In SIDIAP, the composite outcome consisted of attempted suicide (n=5,967), suicidal ideation (n=3,600) and intentional self-harm (n=2,993). When narrowing down to the BPH cohort and androgenetic alopecia, the number of outcome events were much lower.

Table 12-18 and **Figure 2-8** show the incidence rates of the suicidality composite outcome across cohorts of interest for each data source.

The incidence rates of the suicidality composite outcome in the **general adult male population** varied across the data sources, with the highest rate observed in CPRD-Gold at 1.47/1,000 PYs (95% CI: 1.46, 1.49), based on 37,773 incident suicide-related events from 4.3 million participants. Lower rates were reported in IPCI at 0.49/1,000 PYs (95% CI: 0.47-0.51), BIFAP at 0.42/1,000 PYs (95% CI: 0.42, 0.43), and SIDIAP at 0.34/1,000 PYs (95% CI: 0.33-0.34). The lowest rates were observed in DK-DHR (0.18/1,000 PYs) and InGef RDB (0.07/1,000 PYs), likely due to limited outcome capture in these data sources (**Table 12-18**).

Although the number of composite suicidality outcomes in **the androgenetic alopecia patient** cohorts was low -resulting in imprecise estimates- the point estimate incidence rates were higher than those reported for the general population in some data sources. In CPRD-Gold, the overall incidence rate for androgenetic alopecia patients was 2.08/1,000 PYs (95% CI: 0.76-4.54). In BIFAP and SIDIAP, the overall incidence rate was 0.49/1,000 PYs (95% CI: 0.29-0.79) and 0.47 (95% CI: 0.26-0.77), respectively. In DK-DHR, IPCI, In-Gef RDB, and NAJS, no suicidality events were recorded in individuals newly diagnosed with androgenetic alopecia (**Table 12-18)**.

The incidence rates of composite suicidality outcome among patients who received **treatments for androgenetic alopecia** were very low across the data sources. In most cases, no suicidality-related events were reported among treated patients due to the small cohort sizes. (**Table 12-18)**. For the non-treated cohort (i.e., patients with no recorded prescription for the study treatments), though the follow-up time was considerably larger than for the treated cohorts, the number of suicidality related events was very limited (≤15) across data sources.

The incidence rates of suicidality outcome among **BPH** patients varied across data sources, with rates of 0.88/1,000 PYs in CPRD-Gold, 0.71 in Croatian NAJS, 0.56 in BIFAP, 0.50 in IPCI, 0.42 in SIDIAP (**Table 12-18**).

The incidence rates of suicidality among patients who received **treatments for BPH** varied across treatment cohorts and data sources. In CPRD-Gold, patients treated with alpha blockers had an incidence rate of 1.08/1,000 PYs (95% CI: 0.88-1.31). The rate among patients treated with finasteride was 0.69 (95% CI: 0.47-0.99), while patients who were prescribed with dutasteride had a rate of 0.65 (95% CI: 0.24-1.41). In IPCI, all treatment groups (including those treated with finasteride, dutasteride, and alpha blockers) reported either no suicide-related cases or very low number of cases and therefore no incidence rates could be calculated. In BIFAP, male patients treated with alpha blockers had an incidence rates of 0.42/1,000 PYs (95% CI: 0.33-0.53), 1.26 for those treated with finasteride and 0.53 for those treated with dutasteride. The Croatian NAJS data source reported 1.24/1,000 PY for treated patients with finasteride, and 0.87 for treated with dutasteride, while SIDIAP showed a rate of 0.54 for patients treated with finasteride and 0.34 for dutasteride. Across data sources, the cohorts of patients treated with tadalafil were small and number of outcomes was too low to calculate incidence rates. (**Table 12-18**).

The incidence rates of suicidality events in the general adult male population across different **age groups** and data sources are shown in **Appendix II. Table S 1**. CPRD-Gold showed the highest rate of 2.54/ 1,000 PYs in the 18–30 age group, decreasing to 0.73 in those over 71 years old. BIFAP reported stable rates around 0.45 in younger groups, dropping to 0.26 in the 61–70 age group. SIDIAP showed rates starting at 0.40 in the youngest and declining to 0.22 before slightly rising to 0.27 in older adults. The precision of incidence rates of the composite suicidality outcome in patients with androgenetic alopecia (and within the different treatment cohorts) stratified by age category was very low given the limited follow-up time and the absent or scarce number of events. In many of the cohorts, it was not possible to calculate the incidence rates (**Appendix II. Tables S2-S8** and **Appendix II. Figure S 1- S 7**). Similarly, the precision of incidence rates of the composite suicidality outcome in BPH patients, stratified by age category and treatment cohorts, were lowest in young adults (18-30 years). The rates were higher in middle-aged groups compared to the extreme age groups (<31 and 71+) in all data sources but Croatian NAJS. (**Appendix II. Table S 9-S 15** and **Appendix II. Figure S 8-S 14**).

Appendix II. Table S 16-S 22 present the incidence rates of composite suicidality outcomes in the general adult male population, in male patients newly diagnosed with androgenetic alopecia and BPH (and within respective treatment cohort) per data source and stratified in individuals **with or without a history of psychiatric disorders**. The incidence rates of composite suicidality outcomes in the general adult male population with a history of psychiatric disorders ranged from lowest of 0.74/1,000 PYs in DK-DHR and highest 4.50/1,000 PYs in CPRD-Gold, with higher rates observed in this group in compared with those without a history of psychiatric disorders (0.06-1.11/1,000 PYs in InGef RDB and CPRD-Gold, respectively). The incidence rates of composite suicidality outcome in the androgenetic alopecia population with or without history of psychiatric disorders and related treatment cohorts were generally low, within most data sources reporting zero events and very limited follow-up time. Only in the SIDIAP data source, androgenetic alopecia patients had a rate of 0.26/1,000 PYs (95% CI: 0.11-0.54) in patients without history of psychiatric disorders and rate of 1.44/1,000 PYs (95% CI: 0.62-2.84) in patients with a history of psychiatric disorders. Similarly, in BIFAP, the rate was 1.75 in patients with history of psychiatric disorder and 0.27 in without history of psychiatric disorders. Similar pattern was observed in patients with no recorded prescription for the study treatments.

The incidence rates of suicidality in BPH patients were consistently higher among those with a history of psychiatric disorders compared to those without, across all data sources. In IPCI, the rate was 0.78/1,000 PYs in patients with a history of psychiatric disorders versus 0.43 in those without. In BIFAP, patients with a history of psychiatric disorders had a rate of 1.47 compared to 0.38 in those without. Croatian NAJS reported a rate of 1.32 in patients with a history of psychiatric disorders compared to 0.48 in those without. Similarly, SIDIAP showed a rate of 1.20 in patients with a history of psychiatric disorders compared to 0.27 in those without. The incidence rates of suicide-related events in **treated BPH patients** varied by treatment and psychiatric history across data sources, with higher rates generally observed in patients with a history of psychiatric disorders. In IPCI, no suicide-related events were recorded for treated patients, regardless of psychiatric history. In Croatian NAJS, patients treated with finasteride and history of psychiatric disorders had a higher rate (2.98/1,000 PYs) compared to no events in those without. Similarly, patients treated with dutasteride, and history of psychiatric disorders had a rate of 1.48, compared to 0.57 in those without. In SIDIAP, rates for finasteride-treated patients with history of psychiatric disorders were 1.01/1,000 PYs versus 0.43 in those without, and for patients treated with dutasteride, the rates were 0.68 and 0.26, respectively. Among patients with no recorded prescription for the study treatments, incidence rates of suicide related events were higher in patients with history of psychiatric disorders than those without across all data sources (**Appendix II. Table S 16-S 22**).

Appendix II. Table S 23-S 29 present the incidence rates of composite suicidality outcomes in the general male population, in males newly diagnosed with androgenetic alopecia and BPH (and within respective

treatment cohort) per data source and stratified in patients **with or without a history of sexual dysfunction**. In the male general population, incidence rates were higher in patients with history of sexual dysfunction than in patients without in BIFAP (0.61/1,000 PY vs 0.42/1,000 PY, respectively), DK-DHR (0.23 vs. 0.18) (IPCI (0.74 vs 0.48), Croatian NAJS (1.11 vs 0.58), and SIDIAP (0.50 vs 0.34). Among androgenic alopecia patients, incidence rates were uninformative due to none/very low event counts and very limited follow-up time. Among BPH patients, incidence rates were higher in patients with history of sexual dysfunction than in patients without in BIFAP (0.81/1,000 PY vs 0.55/1,000 PY, respectively), CPRD-Gold (1.17 vs 0.82), DK-DHR (0.19 vs. 0.12), Croatian NAJS (1.69 vs 0.70), and SIDIAP (0.58 vs. 0.41). Regarding treatment cohorts, no clear pattern was found in the incidence rates of patients with history of sexual dysfunction and patients without as estimates were affected by low counts of events and limited follow-up time in most of the data sources.

The incidence rates of composite suicidality outcomes in the general adult male population (**Appendix II. Figure S 15-S21**) showed varying trends across data sources **over calendar years**. BIFAP data showed a steady increase from 0.2/1,000 PYs in 2010 to around 0.7/1,000 PYs by 2023. In CPRD-Gold, the rates remained stable around 1.5–2.0/1,000 PYs, peaking in 2018-2019 before slightly declining by 2024. DK-DHR presented a declining trend, starting at 0.3/1,000 PYs in 2012 and dropping below 0.1/1,000 PYs by 2024. IPCI exhibited moderate fluctuation, with rates between 0.4/1,000 PYs and 0.6/1,000 PYs, peaking around 2018 and 2023. NAJS reported declining in the incidence rates from around 0.8/1,000 PYs in 2017 to 0.3 by 2021, then dropped sharply to near 0.1 in 2022, remaining low through 2024. Meanwhile, SIDIAP displayed a steady rise from 0.2/1,000 PYs in 2010 to approximately 0.8/1,000 PYs in 2023, particularly increasing after 2017.

The incidence rates of composite suicidality events for androgenetic alopecia remained consistently at zero across all **follow-up years** and data sources. Regardless of the treatment cohorts analysed, there was no evidence of risk of suicide events among individuals treated for alopecia. For BPH, the incidence rates in BIFAP started at 0.90/1,000 PYs and declined to 0.40 by year 5, fluctuating between 0.35 and 0.50 in later years. CPRD-Gold showed a higher initial rate of 1.20/1,000 PYs, dropping to 0.70 by year 5 and stabilizing between 0.6 and 0.85 afterward. The SIDIAP data start at 0.55 in year 1 and fluctuated between 0.30 and 0.50 in subsequent follow up years. Among treatment cohorts, alpha-blocker users experienced high initial rates which dropped later after treatment initiation in CPRD Gold (initial rate was 1.3 which dropped to 0.6 by year 4). Dutasteride and finasteride treated patients' cohorts showed inconsistent rates over follow up across different data sources. Rates in BPH patients' cohorts with no records of prescription of the study treatments at index date displayed fluctuated rates, with CPRD-Gold between 1.2-0.4 and SIDIAP between 0.6-0.3 over 7 years. (**Appendix II. Figure S 15-S21**).

Table 12. Incidence rates of composite suicidality outcome per 1,000 person- years by indication and treatment in each cohort during the study period in BIFAP data source.

Cohorts	Number of participants	Follow-up (person-years)	Number of incident cases (suicide related events)	Incidence Rate/1,000 PYs (95% CI)
General adult male population	8,621,220	74,292,952.53	31,235	0.42 (0.42, 0.43)
Androgenetic alopecia				
All patients	9,280	34,588.17	17	0.49 (0.29, 0.79)
Patients treated with finasteride	1,139	supp	<5	supp
Patients treated with dutasteride	216	supp	<5	supp
Patients treated with topical minoxidil	<5	supp	<5	supp
Non-treated	8,930	30,147.17	15	0.50 (0.28, 0.82)
BPH				
All patients	444,795	2,208,981.48	1,233	0.56 (0.53, 0.59)
Patients treated with finasteride	3,203	7,907.51	10	1.26 (0.61, 2.33)
Patients treated with dutasteride	91,574	237,635.49	125	0.53 (0.44, 0.63)
Patients treated with alpha blockers	158,870	175,186.80	74	0.42 (0.33, 0.53)
Patients treated with tadalafil	4,418	supp	<5	supp
Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
Non-treated	348,518	1,458,111.57	810	0.56 (0.52, 0.60)

Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.
NC= No person count; supp= If the number of participants or incident cases was <5; associated statistics have been suppressed to protect patients' confidentiality.

Table 13. Incidence rates of composite suicidality outcome per 1,000 person- years by indication and treatment in each cohort during the study period in CPRD-Gold data source.

Cohorts	Number of participants	Follow-up (person-years)	Number of incident cases (suicide related events)	Incidence Rate/1,000 PYs (95% CI)
General adult male population	4,336,324	25,634,004.59	37,773	1.47 (1.46, 1.49)
Androgenetic alopecia				
All patients	629	2,878.34	6	2.08 (0.76, 4.54)
Patients treated with finasteride	148	supp	<5	supp
Patients treated with dutasteride	<5	supp	<5	supp
Patients treated with topical minoxidil	27	supp	<5	supp
Non-treated	469	supp	<5	supp
BPH				
All patients	74,558	363,112.43	318	0.88 (0.78, 0.98)
Patients treated with finasteride	15,869	44,643.14	31	0.69 (0.47, 0.99)
Patients treated with dutasteride	3,332	9,242.46	6	0.65 (0.24, 1.41)
Patients treated with alpha blockers	46,058	94,863.79	102	1.08 (0.88, 1.31)
Patients treated with tadalafil	1,630	supp	<5	supp
Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
Non-treated	57,944	217,443.52	200	0.92 (0.80, 1.06)

Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.

NC= No person count; supp= If the number of participants or incident cases was <5; associated statistics have been suppressed to protect patients' confidentiality.

Table 14. Incidence rates of composite suicidality outcome per 1,000 person- years by indication and treatment in each cohort during the study period in DK-DHR data source.

Cohorts	Number of participants	Follow-up (person-years)	Number of incident cases (suicide related events)	Incidence Rate/1,000 PYs (95% CI)
General adult male population	2,916,154	32,354,227.56	5,901	0.18 (0.18, 0.19)
Androgenetic alopecia				
All patients	452	supp	<5	supp
Patients treated with finasteride	71	supp	<5	supp
Patients treated with dutasteride	<5	supp	<5	supp
Patients treated with topical minoxidil	12	supp	<5	supp
Non-treated	366	supp	<5	supp
BPH				
All patients	93,919	572,717.68	77	0.13 (0.11, 0.17)
Patients treated with finasteride	25,738	72,869.27	5	0.07 (0.02, 0.16)
Patients treated with dutasteride	8,350	supp	<5	supp
Patients treated with alpha blockers	30,372	47,238.49	8	0.17 (0.07, 0.33)
Patients treated with tadalafil	5,559	supp	<5	supp
Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
Non-treated	43,233	220,408.58	32	0.15 (0.10, 0.20)

Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.
NC= No person count; supp= If the number of participants or incident cases was <5; associated statistics have been suppressed to protect patients' confidentiality.

Table 15. Incidence rates of composite suicidality outcome per 1,000 person- years by indication and treatment in each cohort during the study period in IPCI data source.

Cohorts	Number of participants	Follow-up (person-years)	Number of incident cases (suicide related events)	Incidence Rate/1,000 PYs (95% CI)
General adult male population	1,000,636	5,036,462.64	2,451	0.49 (0.47, 0.51)
Androgenetic alopecia				
All patients	1,949	supp	<5	supp
Patients treated with finasteride	605	supp	<5	supp
Patients treated with dutasteride	15	supp	<5	supp
Patients treated with topical minoxidil	304	supp	<5	supp
Non-treated	1,315	supp	<5	supp
BPH				
All patients	15,320	66,322.14	33	0.50 (0.34, 0.70)
Patients treated with finasteride	567	supp	<5	supp
Patients treated with dutasteride	1,462	supp	<5	supp
Patients treated with alpha blockers	9,103	supp	<5	supp
Patients treated with tadalafil	324	supp	<5	supp
Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
Non-treated	13,487	50,917.24	24	0.47 (0.30, 0.70)

Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.
NC= No person count; supp= If the number of participants or incident cases was <5; associated statistics have been suppressed to protect patients' confidentiality.

Table 16. Incidence rates of composite suicidality outcome per 1,000 person- years by indication and treatment in each cohort during the study period in InGef RDB data source.

Cohorts	Number of participants	Follow-up (person-years)	Number of incident cases (suicide related events)	Incidence Rate/1,000 PYs (95% CI)
General adult male population	4,063,229	25,781,939.87	1,795	0.07 (0.07, 0.07)
Androgenetic alopecia				
All patients	236	supp	<5	supp
Patients treated with finasteride	<5	supp	<5	supp
Patients treated with dutasteride	NC	NC	NC	NC
Patients treated with topical minoxidil	NC	NC	NC	NC
Non-treated	230	supp	<5	supp
BPH				
All patients	163,278	544,015.18	68	0.12 (0.10, 0.16)
Patients treated with finasteride	5,256	supp	<5	supp
Patients treated with dutasteride	4,998	supp	<5	supp
Patients treated with alpha blockers	96,199	220,548.42	36	0.16 (0.11, 0.23)
Patients treated with tadalafil	869	supp	<5	supp
Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
Non-treated	137,195	427,343.25	71	0.17 (0.13, 0.21)

Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.
NC= No person count; supp= If the number of participants or incident cases was <5; associated statistics have been suppressed to protect patients' confidentiality.

Table 17. Incidence rates of composite suicidality outcome per 1,000 person- years by indication and treatment in each cohort during the study period in NAJS data source.

Cohorts	Number of participants	Follow-up (person-years)	Number of incident cases (suicide related events)	Incidence Rate/1,000 PYs (95% CI)
General adult male population	1,918,950	13,320,081.04	7,714	0.58 (0.57, 0.59)
Androgenetic alopecia				
All patients	1,640	supp	<5	supp
Patients treated with finasteride	12	supp	<5	supp
Patients treated with dutasteride	7	supp	<5	supp
Patients treated with topical minoxidil	NC	NC	NC	NC
Non-treated	1,705	supp	<5	supp
BPH				
All patients	279,363	1,239,372.25	879	0.71 (0.66, 0.76)
Patients treated with finasteride	7,687	12,128.20	15	1.24 (0.69, 2.04)
Patients treated with dutasteride	83,055	114,195.54	99	0.87 (0.70, 1.06)
Patients treated with alpha blockers	173,087	164,919.41	128	0.78 (0.65, 0.92)
Patients treated with tadalafil	NC	NC	NC	NC
Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
Non-treated	249,257	899,218.20	569	0.63 (0.58, 0.69)

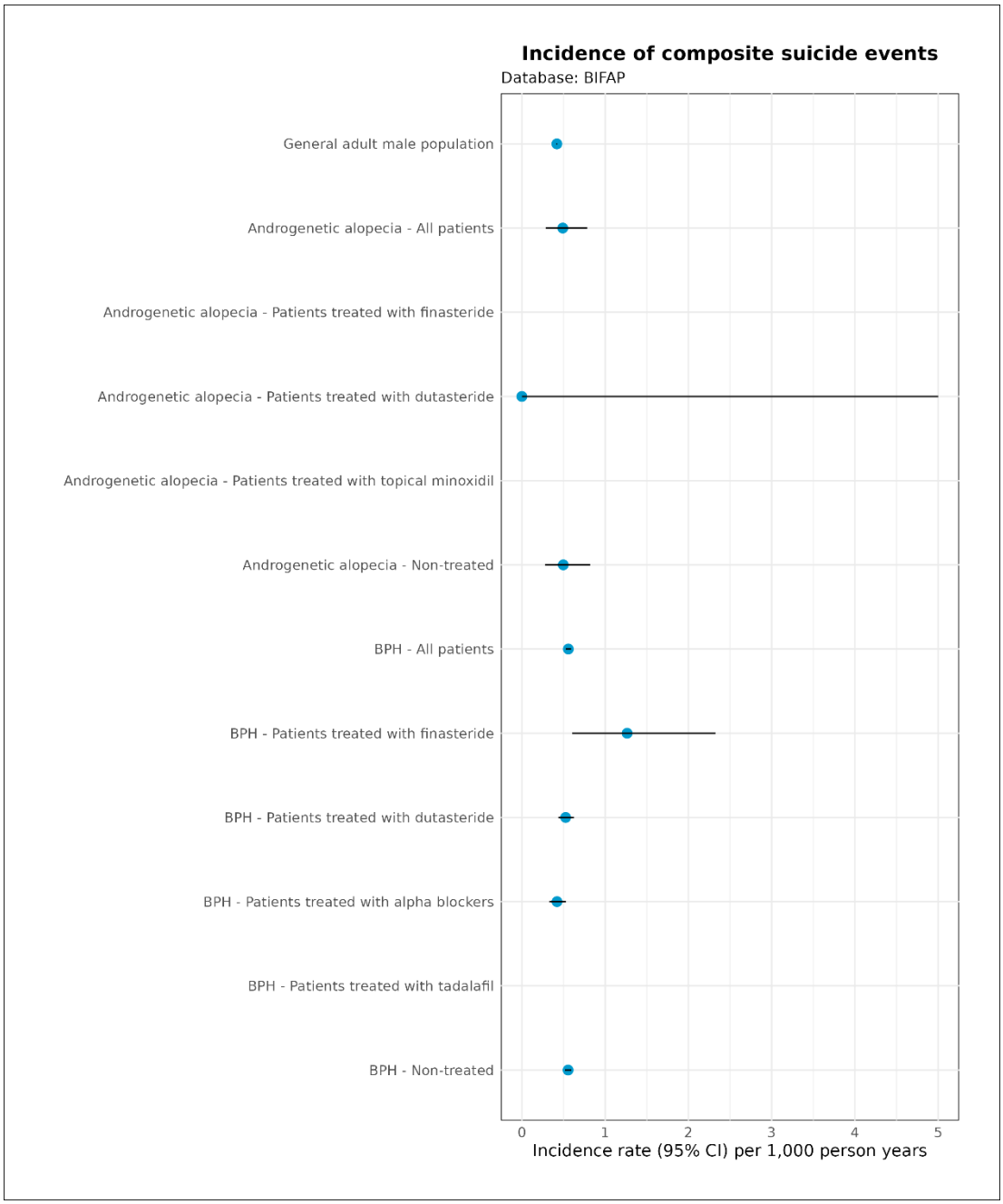
Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.

NC= No person count; supp= If the number of participants or incident cases was <5; associated statistics have been suppressed to protect patients' confidentiality.

Table 18. Incidence rates of composite suicidality outcome per 1,000 person- years by indication and treatment in each cohort during the study period in SIDIAP data source.

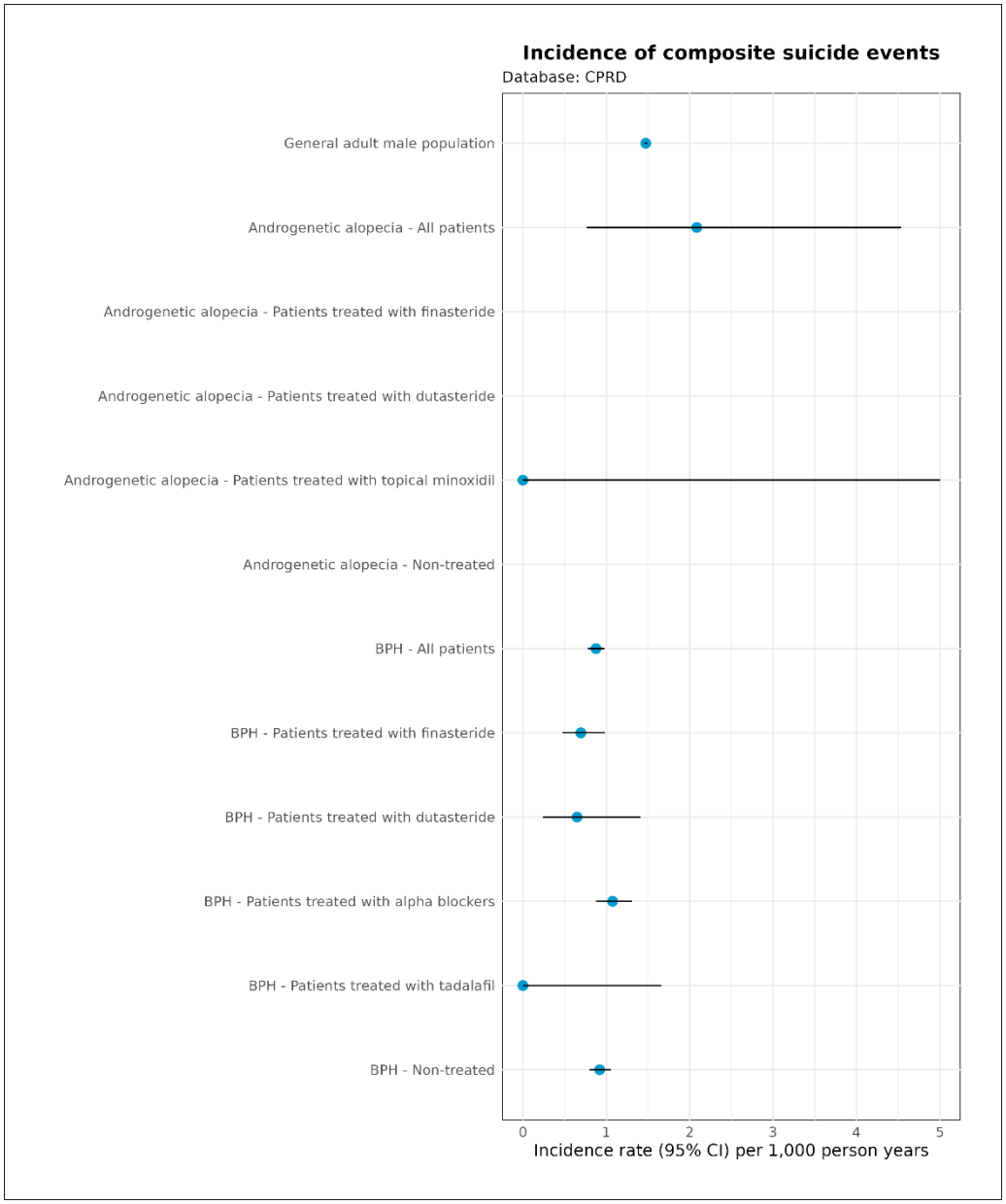
Cohorts	Number of participants	Follow-up (person-years)	Number of incident cases (suicide related events)	Incidence Rate/1,000 PYs (95% CI)
General adult male population	3,316,543	31,627,938.30	10,675	0.34 (0.33, 0.34)
Androgenetic alopecia				
All patients	5,265	32,130.94	15	0.47 (0.26, 0.77)
Patients treated with finasteride	181	supp	<5	supp
Patients treated with dutasteride	97	supp	<5	supp
Patients treated with topical minoxidil	466	supp	<5	supp
Non-treated	4,573	28,491.85	10	0.35 (0.17, 0.65)
BPH				
All patients	313,797	1,839,919.43	768	0.42 (0.39, 0.45)
Patients treated with finasteride	15,588	42,564.19	23	0.54 (0.34, 0.81)
Patients treated with dutasteride	36,164	89,010.19	30	0.34 (0.23, 0.48)
Patients treated with alpha blockers	163,225	448,524.48	208	0.46 (0.40, 0.53)
Patients treated with tadalafil	3,659	supp	<5	supp
Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
Non-treated	270,850	1,377,893.65	588	0.43 (0.39, 0.46)

Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.
NC= No person count; supp= If the number of participants or incident cases was <5; associated statistics have been suppressed to protect patients' confidentiality.



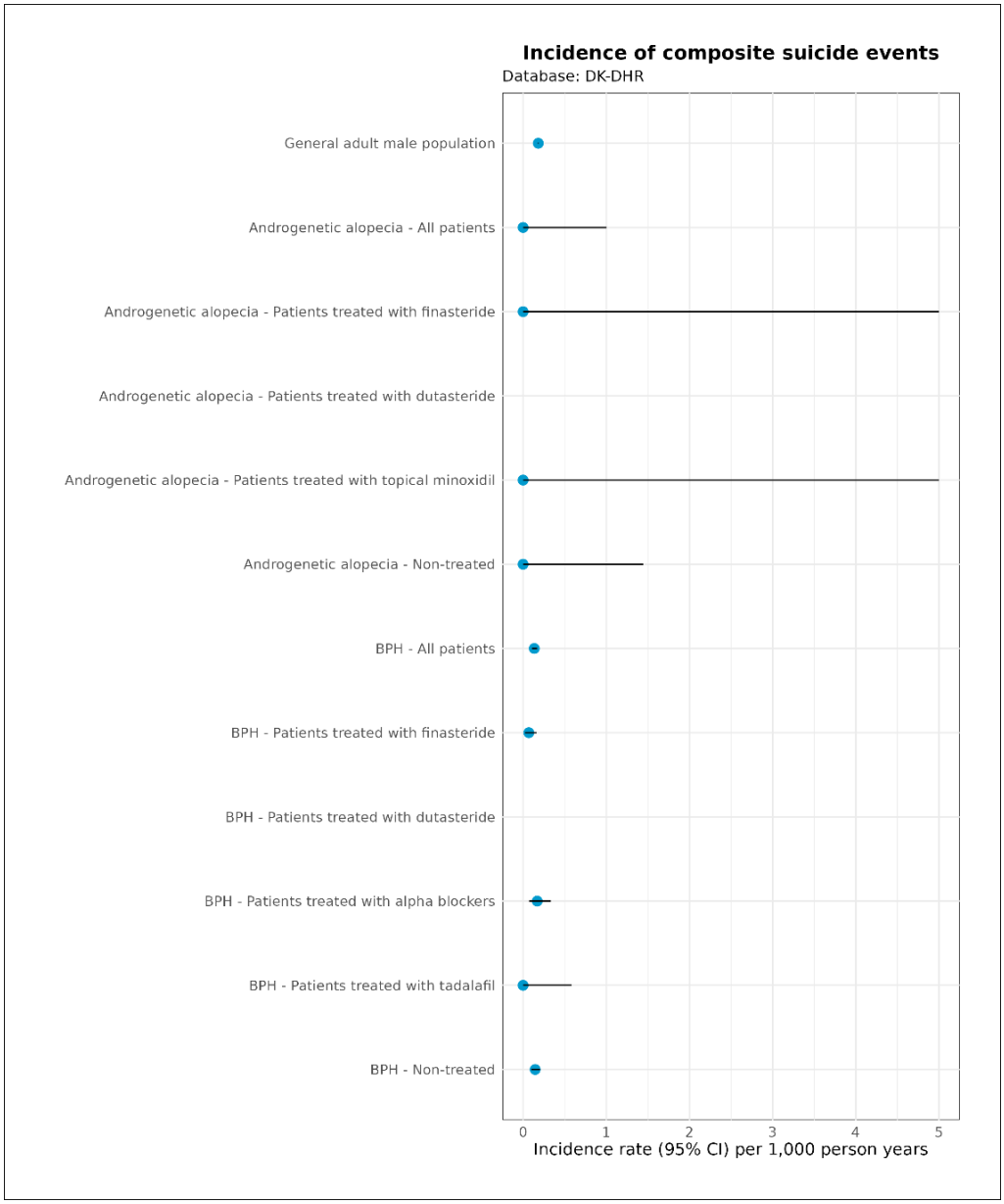
Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.

Figure 2. Incidence rates (95% CI) of composite suicidality events per 1,000 PYs in BIFAP data source.



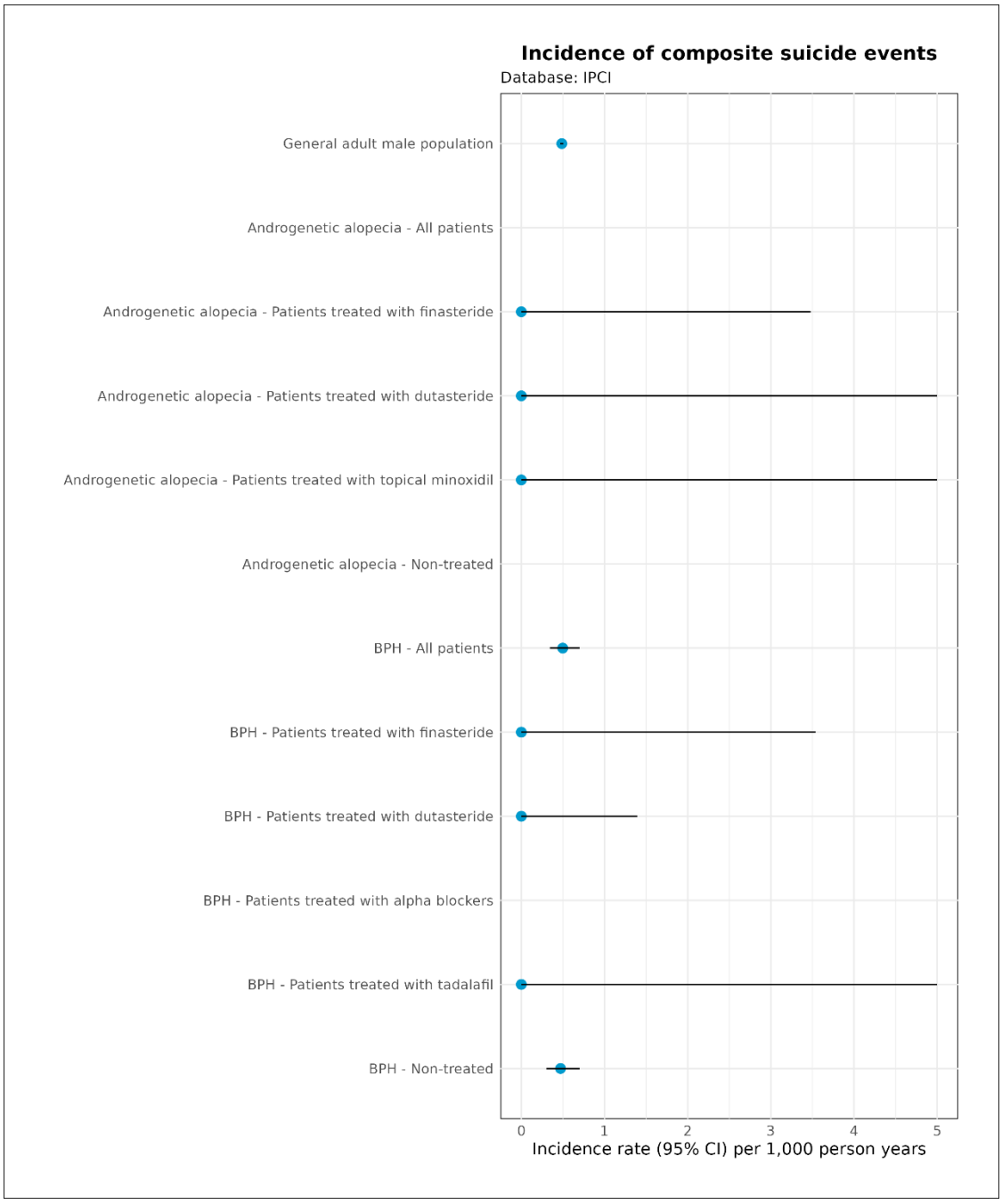
Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.

Figure 3. Incidence rates (95% CI) of composite suicidality events per 1,000 PYs in CPRD Gold data source.



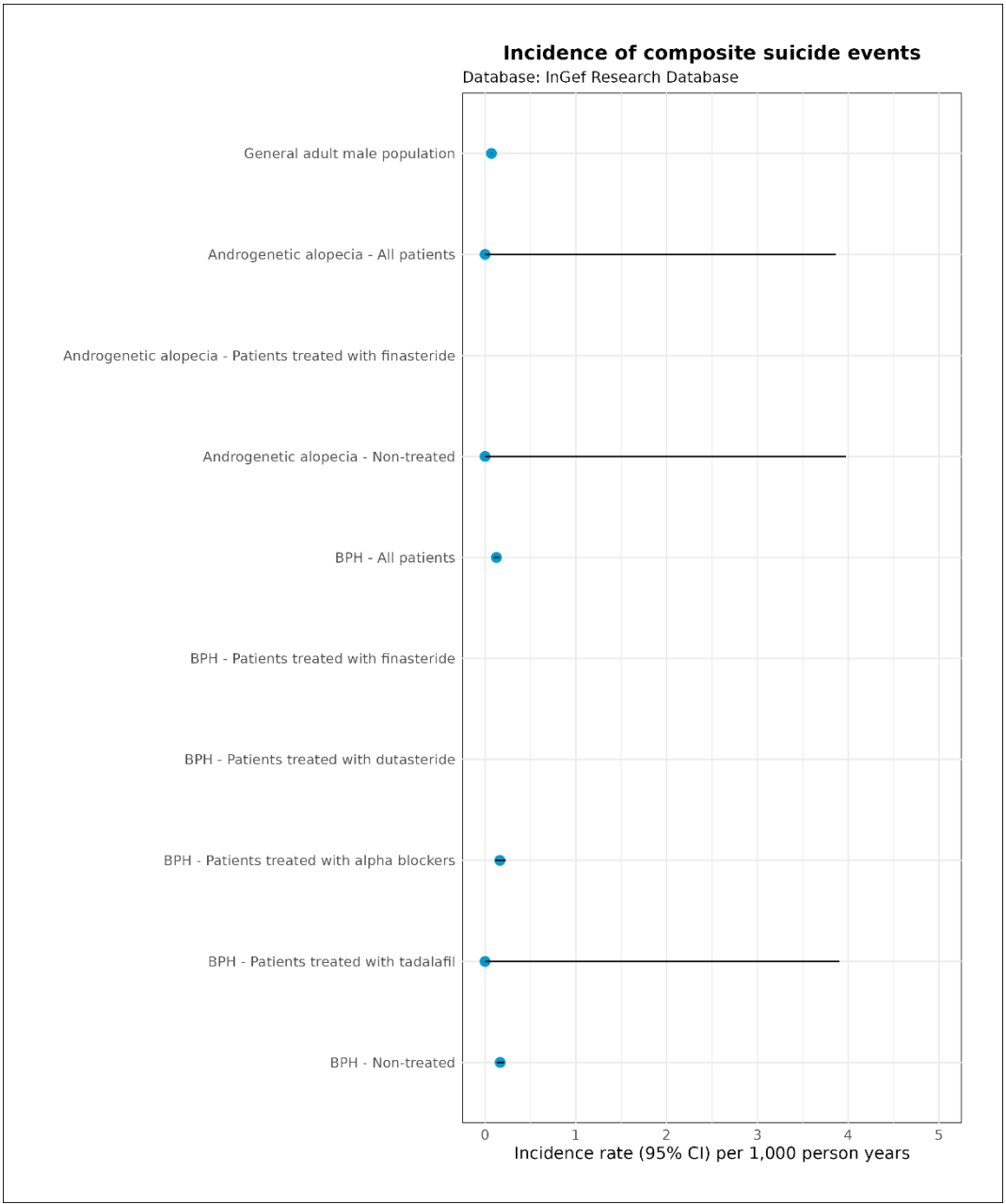
Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.

Figure 4. Incidence rates (95% CI) of composite suicidality events per 1,000 PYs in DK-DHR data source.



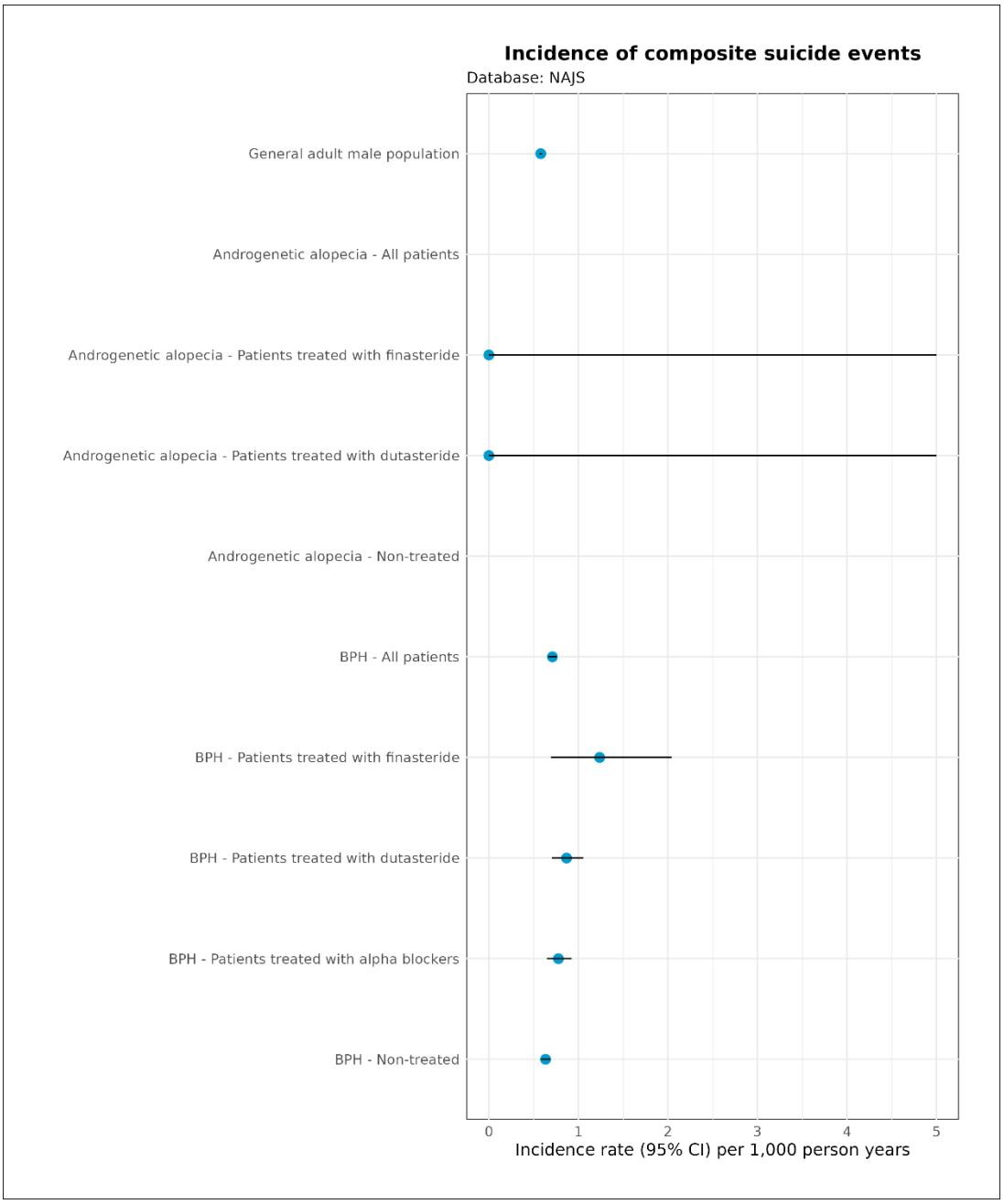
Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.

Figure 5. Incidence rates (95% CI) of composite suicidality events per 1,000 PYs in IPCI data source.



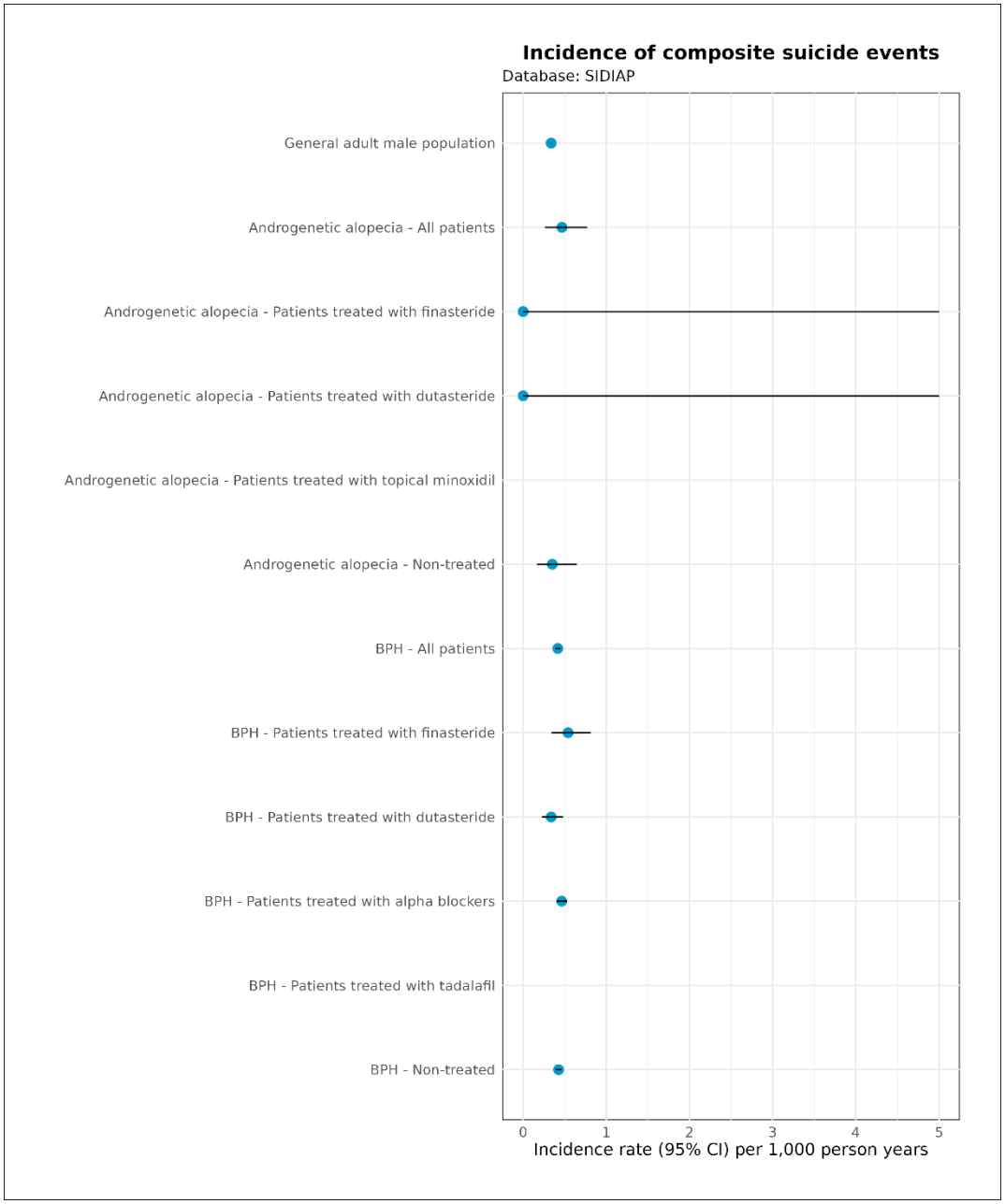
Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.

Figure 6. Incidence rates (95% CI) of composite suicidality events per 1,000 PYs in In-Gef RDB data source.



Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.

Figure 7. Incidence rates (95% CI) of composite suicidality events per 1,000 PYs in NAJS data source.



Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.

Figure 8. Incidence rates (95% CI) of composite suicidality events per 1,000 PYs in SIDIAP data source.

13. MANAGEMENT AND REPORTING OF ADVERSE EVENTS/ADVERSE REACTIONS

Adverse events/adverse reactions were not collected or analysed as part of this evaluation. The nature of this non-interventional evaluation, through the use of secondary data, does not fulfil the criteria for reporting adverse events, according to module VI, VI.C.1.2.1.2 of the Good Pharmacovigilance Practices (https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/guideline-good-pharmacovigilance-practices-gvp-module-vi-collection-management-submission-reports_en.pdf).

Only in case of prospective data collection, there is a need to describe the procedures for the collection, management and reporting of individual cases of adverse events/adverse reactions.

14. DISCUSSION

14.1 Key results

The data sources InGef RDB Germany and Danish DK-DHR had limited outcome capture, which might affect the reliability of incidence rates and limit the accuracy of conclusions drawn from their results

The overall number of the general adult male population varies across different data sources, with the highest recorded in BIFAP (8,621,220) and the lowest in IPCI (1,000,636). The overall counts of androgenetic alopecia range from 236 cases InGef RDB to 5,265 in SIDIAP. BPH cases are more numerous, with counts ranging from 15,320 in IPCI to 444,795 in BIFAP across different data sources. The median age in the general population ranged between 38 (DK-DHR and SIDIAP) and 45 (NAJS) years, between 26 (IPCI) and 35 years (DK-DHR) in the androgenetic alopecia population and between 64 (NAJS) and 73 years (InGef RDB) in the BPH population.

The incidence rates of composite suicidality outcome in the general adult male population varied across the data sources, with the highest rate observed in CPRD-Gold at 1.47/1,000 PYs (95% CI: 1.46, 1.49), based on 37,773 incident suicide-related events from 4.3 million participants. The NAJS reported a rate of 0.58/1,000 PYs based on 7,714 incident suicide-related events from 1.2 million participants. Lower rates were reported in IPCI at 0.49/1,000 PYs (95% CI: 0.47-0.51), BIFAP at 0.42/1,000 PYs (95% CI: 0.42, 0.43), and SIDIAP at 0.34/1,000 PYs (95% CI: 0.33-0.34).

The precision of incidence rates of suicide-related events in patients with androgenetic alopecia was low across the data sources or there was insufficient data to calculate the incidence rates. In CPRD-Gold, the overall incidence rate of suicide-related events for the androgenetic alopecia patients was 2.08/1,000 PYs (95% CI: 0.76-4.54) and in SIDIAP, the overall incidence rate was 0.47/1,000 PYs (95% CI: 0.26-0.77). The incidence rates of suicidality among patients receiving treatments for androgenetic alopecia were even more affected by the very limited size of the cohorts. The high uncertainty reflected by the very wide 95% confidence intervals preclude a meaningful interpretation of these estimates.

The incidence rates of suicide-related events among BPH patients varied across data sources, with rates of 0.88/1,000 PYs in CPRD-Gold, 0.71 in Croatian NAJS, 0.56 in BIFAP, 0.50 in IPCI, 0.42 in SIDIAP. In CPRD-Gold, patients treated with alpha blockers had an incidence rate of 1.08/1,000 PYs (95% CI: 0.88-1.31), patients treated with finasteride had an incidence rate of 0.69/1,000 PY (95% CI: 0.47-0.99), and 0.65/1,000 PY (95% CI: 0.24-1.41) in patients treated with dutasteride. In IPCI, the estimates of all treatment groups (including finasteride, dutasteride, and alpha blockers) were affected by a very limited follow-up time. In BIFAP, male patients treated with alpha blockers had an incidence rates of 0.42/1,000 PYs, 1.26 for those

treated with finasteride and 0.53 for those treated with dutasteride. In the Croatian NAJS, the estimated incidence rate was 1.24/1,000 PY in patients treated with finasteride, 0.87 in dutasteride cohort, and 0.78 in the alpha blockers cohort. In SIDIAP, the incidence rate of suicide-related events was 0.54 in patients treated with finasteride, 0.34 in those treated with dutasteride, and 0.46 in those treated with alpha blockers. Across data sources, the tadalafil cohorts were small and number of outcomes were absent or too low to calculate incidence rates.

Higher incidence rates of suicidality-related events were observed in younger age groups compared to older ones in the general adult male population. However, this trend was less obvious in BPH, where the age distribution shifted towards older individuals, and was difficult to evaluate in androgenetic alopecia due to insufficient sample size. The incidence rates of composite suicidality outcomes in the general adult male population with a history of psychiatric disorders ranged from lowest of 0.74/1,000 PYs in DK-DHR and highest 4.50/1,000 PYs in CPRD-Gold, with higher rates observed in this group in compared with those without a history of psychiatric disorders (0.06-1.11/1,000 PYs). The precision of incidence rates of composite suicidality outcomes in the androgenetic alopecia population with or without history of psychiatric disorders and related treatment cohorts were generally low, within many data sources reporting zero events. The incidence rates for adult males with BPH with a history of psychiatric disorders was higher compared those without and ranged between 0.47/1,000 PY (DK-DHR and InGefRDB) and 2.71 (CPRD-Gold).

Higher incidence rates were observed in patients with a history of sexual dysfunction in several data sources. For instance, in the CPRD-Gold data source, BPH patients with a history of sexual dysfunction had a higher incidence rate of suicide-related events (1.17/1,000 PY) compared to those without history of sexual dysfunction (0.82/1,000 PY), with similar patterns in BIFAP, and NAJS and SIDIAP.

The incidence rates of composite suicidality outcomes in general adult male population showed varying trends over years, with BIFAP rising steadily from 0.2/1,000 PYs in 2010 to 0.7 by 2023 and CPRD-Gold peaking at 2.0/1,000 PYs in 2018-2019 before declining. In BPH cohorts, incidence rates of suicidality started at 0.9/1,000 PYs in BIFAP and 1.2 in CPRD Gold, declining to 0.35 and 0.7, respectively, after five years. Among treatment cohorts, alpha-blocker treatment users experienced high initial rates (e.g., 1.5 in CPRD Gold), which dropped to 0.55 by year 4, while dutasteride and finasteride cohorts showed inconsistent trends across data sources.

14.2 Limitations of the research methods

The study was conducted using routinely collected health care data; therefore, data quality issues must be considered. In particular, the recording of the outcome events may vary across data sources. While relatively few false positives suicide-related events would be expected, false negatives may be more likely, especially for data sources without patient-level linkage to secondary care data (e.g., CPRD-Gold, IPCI, SIDIAP). This is because the recording of completed suicide event is often under-reported in primary care records due to various factors like social stigma, misclassification of cases (e.g., recorded as accidental), not admission in hospital, the prioritization of physical over mental health symptoms, and cultural attitudes. While linkage to death certification data could improve reporting complete suicide, it would still fall short of a true "gold standard", as the deficiencies in coding of suicide on death certificates are well documented.(38-42) Additionally, it would fail to capture cases of suicidal ideation that do not result in death. Also, not all data sources had information on type of suicide events of interest, e.g. InGef RDB only had information on intentional self-harm and DK-DHR on intentional self-harm and attempted suicide, due to national coding practices and discrepancies in data mapping. Due to these limitations, it is expected that any biases arising from incomplete ascertainment of outcomes would be differential across the different cohorts of interest.

For this study, we used data sources containing routinely collected health care data. Electronic health records (EHRs) have certain inherent limitations because they are collected for clinical purpose rather than primarily for research use. The under-recording of androgenetic alopecia in healthcare data sources can significantly affect the validity of incidence rate estimates. Many individuals with androgenetic alopecia may not seek formal medical care, viewing it as a cosmetic issue, leading to incomplete capture of diagnoses in EHRs. Additionally, the use of over the counter (OTC) treatments or medications such as (topical) finasteride and (topical) minoxidil purchased online, would underestimate the number of individuals exposed to the drug of interest. The potential off-label use of finasteride, particularly in men over 40, is another limitation in studies evaluating its effects. While commonly prescribed for androgenetic alopecia or BPH, it is also used for purposes beyond these indications, such as delaying hair loss or for anti-aging effects, which may not be accurately recorded in medical data sources.(43)

While OMOP provides mapping to established vocabularies like SNOMED, inaccuracies or gaps in these mappings can occur, impacting the accuracy and completeness of data in different data sources. Outcome misclassification may also occur due to coding limitations. Certain data sources like InGef RDB and IPCI include fewer specific codes for certain outcomes of interest, increasing the risk of misclassification.

Another limitation of InGef RDB claims data source is the potential misclassification of the dates of diagnosis for conditions diagnosed outside of a hospital setting. Unlike inpatient diagnoses, which are associated with an exact diagnosis date and mapped directly to standard concepts, outpatient diagnoses are recorded on a quarterly basis without a specific date. All outpatient diagnoses within a given quarter are documented as occurring on the last day of that period. For example, a BPH diagnosis made by a general practitioner on February 5, 2010, would appear in the data source as March 31, 2010. Similarly, a diagnosis of suicidal ideation made on July 1, 2012, outside the hospital would be recorded as September 30, 2012. This misclassification can lead to a time lag of up to three months between the date of actual diagnosis and the recorded date in the data source.

Regarding the history of psychiatric disorders and sexual dysfunction, differences between data sources were found, for instance, a high proportion of individuals with sexual dysfunction in CPRD and much lower proportions in InGef RDB and NAJS. Although we do not know the reason for this difference, this might be related to country specific differences in prevalence of these disorders but could also be related to inadequate capture of this information or under-reporting within the different data sources. E.g. whereas CPRD is a primary care data source, NAJS and InGef RDB are claims data sources which might explain differences in availability and/or recording of this information.

The proportion of individuals with a history of sexual dysfunction was higher in the tadalafil exposure cohort with proportions ranging between 55.6% for SIDIAP and 66.2% for CPRD-Gold compared to the other exposure cohorts. This high proportion of individuals with a history of sexual dysfunction in the tadalafil exposure cohort demonstrates the potential misclassification of the indication of use where tadalafil is initiated for treatment of sexual dysfunction and not (only) for the treatment of BPH.

Another limitation of the study is the potential for residual or unmeasured confounding when comparing the incidence rates of suicide-related events across the general adult male population, men with newly diagnosed androgenetic alopecia, and those with BPH. Although the study provides descriptive analysis and stratifications by factors such as age, sexual dysfunction, and psychiatric history, there may still be underlying differences between these groups that were not captured.

14.3 Interpretation

The incidence rates of composite suicidality outcomes among adult male population show notable variability across different European healthcare data sources. The highest rate was observed in the CPRD-

Gold data source [1.47/1,000 PYs (95% CI: 1.46, 1.49)], which aligns with findings from another UK-based study that highlight a relatively high prevalence of suicidality in the general population, potentially due to more comprehensive reporting systems and cultural or socio-economic factors influencing mental health outcomes.(44) The lower incidence rates in other data sources (e.g., NAJS, IPCI and SIDIAP) might be partially explained by underreporting or differences in access to mental health care services in these regions.(45, 46)

There was considerable uncertainty regarding the incidence rates of suicide-related events among androgenetic alopecia patients in most data sources. This was due to the scarcity of events and the limited cohort sizes, which rendered the data largely uninformative. Additionally, the diagnosis of androgenetic alopecia appears to be under-ascertained, suggesting that a portion of the general male population may be affected but not formally recorded as such.(47) The absence of recorded suicidality cases in DK-DHR (Denmark), IPCI (Netherlands), InGef RDB (Germany), and NAJS (Croatia) may reflect low absolute risk, short follow-up periods in combination with small sample size, and underreporting in these data sources. While psychological distress, anxiety, and depression have been linked to hair loss conditions like androgenetic alopecia,(48) the low incidence of suicidality observed in these datasets suggests that androgenetic alopecia-related suicidality is likely rare. However, it is essential to recognize that individual cases of psychological distress due to hair loss may still warrant psychiatric screening and support, particularly in patients with pre-existing mental health conditions.(49)

The incidence rates of suicidality among patients with BPH varied across data sources, ranging from 0.12 to 0.88/1,000 PYs. These differences may reflect differences in healthcare systems in terms of access to mental health services, the integration of psychiatric assessments into routine care, and the availability of specialized support for at-risk individuals.(50) The overall rates suggest that BPH patients may have a slightly elevated risk of suicidality compared to the general population. This increased risk could be attributed to the psychological burden associated with lower urinary tract symptoms, which can significantly impact quality of life. Additionally, BPH patients often experience related comorbidities and may have higher levels of healthcare utilization, both of which may contribute to increased awareness and diagnosis of mental health conditions.(51, 52) However, the low incidence rates across most data sources indicate that BPH itself may not be a primary risk factor for suicidality.

The incidence rates of suicidality among BPH patients varied across different treatment types, with alpha blockers generally showing higher rates. These findings align with previous research suggesting that alpha blockers may contribute to psychological distress through side effects such as hypotension and fatigue.(53, 54). It is worth noting that the overall risk remains low across all treatment cohorts. In a nationwide cohort study in France the risk of suicide or hospitalization for self-harm among men with BPH was investigated. In this French study, the incidence rates of these outcomes were higher than those observed in our study. However, the outcomes they examined differ from our study, which may account for the discrepancy in the incidence rates.(13)

The results suggest no clear age-related differences in suicidality incidence rates among individuals with BPH. The incidence rates of suicidality were higher among adult males with BPH and with a history of psychiatric disorders ranging between 0.47 and 2.71 across data sources. While some studies suggest potential associations between certain treatments (e.g., finasteride and 5-ARI) and increased suicidality, especially in individuals with pre-existing mood disorders, the evidence was not conclusive.(13, 55) We observed higher suicidality incidence rates in BPH patients with a history of sexual dysfunction, particularly in the CPRD-Gold, IPCI, and NAJS data sources, aligning with evidence that sexual dysfunction is a known risk factor for psychological distress and suicidal behavior.(56) The small cohort sizes and low event counts across many groups limit the interpretation, but the findings emphasize the importance of considering sexual health history when assessing suicidality risk in clinical practice.

14.4 Generalisability

This study included data from seven data sources of six different European countries (UK, Spain, Denmark, Germany, Croatia, and the Netherlands) and included primary and secondary healthcare data; thus, represent different aspects of the healthcare pathway.

While these results may be considered largely representative of individuals newly diagnosed BPH, results should not be completely generalised to the entire Europe or regions outside of Europe, as differences in population characteristics and guidelines on diagnosis and treatment, may vary by country and the results estimated from this study were only reflect the populations from the included data sources.

14.5 Other information

There is no further information to report.

15. CONCLUSION

In this epidemiological analysis of suicide-related events among adult male patients with androgenetic alopecia and BPH, treated with medicines of interest, as well as the general male population in the UK, the Netherlands, Spain, Croatia, Germany, and Denmark, we observed variability in suicidality incidence rates across European healthcare data sources. Higher incidence rates were consistently reported among patients with a history of psychiatric disorders across all cohorts. Also, higher incidence rates were reported among patients with prior sexual dysfunction and a diagnosis of BPH, however, estimates for treatment cohorts were affected by low counts of events and limited follow-up time in most of the data sources. Higher suicidality rates were observed in younger age groups in the general adult male population, but this trend was less obvious in BPH patients as the age distribution shifted towards older individuals. There was substantial uncertainty around the incidence rates of suicide-related events for androgenetic alopecia patients and those prescribed with finasteride, dutasteride, or minoxidil due to the scarcity of events and the limited size of cohorts, which made these estimates uninformative.

Although certain treatment groups, such as patients receiving alpha blockers for BPH, exhibited slightly higher rates, the overall findings suggest that suicidality risks in these populations remain low and not different to rates as reported in the general male population, with possible underreporting and differences in healthcare systems contributing to variations across regions.

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17. ANNEXES

Appendix I: Concepts set for study cohorts

Conditions concept name and concept IDs definition is listed in the **Appendix I. Table S 1**.

Appendix I. Table S 1. List of concept IDs for conditions exposure and covariate conditions definition.

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Androgenetic alopecia	Male pattern alopecia	4339092		SNOMED
BPH	Benign prostatic hyperplasia	198803		SNOMED
	Prostatism	4016155		SNOMED
	Prostatic obstruction	4188305		SNOMED
	Lower urinary tract symptoms due to benign prostatic hypertrophy	45770925		SNOMED
	Hyperplasia of prostate	197032		SNOMED
Mental health disorders	Depressed mood	40546087		
	Anxiety	441542		SNOMED
	Bipolar disorder	436665		SNOMED
	Eating disorder	439002	4143677, 46285098	SNOMED
	Psychotic disorder	436073		SNOMED
Sexual dysfunction	Psychosexual dysfunction	440068		SNOMED
	Sexual disorder	4335174		SNOMED
	Psychosexual disorder	436666		SNOMED

List of drug concepts definition is provided in the **Appendix I. Table S 2.**

Appendix I. Table S 2. List of concept IDs for treatments exposure definition.

Substance Name	Concept name	Ingredient Concept ID including descendants	Vocabulary
Finasteride	finasteride	996416	RxNorm
	finasteride delayed release oral tablet	43158527	RxNorm

	finasteride oral capsule	35874759	RxNorm
	finasteride oral powder	40727856	RxNorm
	finasteride oral suspension	21112185	RxNorm
	finasteride oral tablet	40039832	RxNorm
Dutasteride	dutasteride	989482	RxNorm
	dutasteride / tamsulosin delayed release oral capsule	36269492	RxNorm
	dutasteride / tamsulosin extended-release oral capsule	43269047	RxNorm
	dutasteride / tamsulosin oral capsule	40222570	RxNorm
	dutasteride extended-release oral capsule	35766105	RxNorm
	dutasteride oral capsule	40033414	RxNorm
	dutasteride oral solution	21101685	RxNorm
	dutasteride oral tablet	2074253	RxNorm
Topical minoxidil	minoxidil topical foam	40134989	RxNorm
	minoxidil topical gel	40065459	RxNorm
	minoxidil topical lotion	40065460	RxNorm
	minoxidil topical ointment	41142871	RxNorm
	minoxidil topical powder	40743375	RxNorm
	minoxidil topical solution	40065461	RxNorm
	minoxidil topical spray	44818151	RxNorm
Alpha blockers	terazosin	1341238	RxNorm
	tamsulosin	924566	RxNorm
	silodosin	19012925	RxNorm
	alfuzosin	930021	RxNorm
	doxazosin	1363053	RxNorm
Tadalafil	tadalafil	1336926	RxNorm
	tadalafil delayed release oral tablet	43207191	RxNorm
	tadalafil oral capsule	1830694	RxNorm
	tadalafil oral suspension	741670	RxNorm
	tadalafil oral tablet	40102137	RxNorm

Tadalafil + finasteride	finasteride / tadalafil pill	702486	RxNorm

Outcomes concept name and concept IDs definition is listed in the **Appendix I. Table S 3**.

Appendix I. Table S 3. List of concept IDs for outcome definition.

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Suicide	Suicide	440925	4198985	SNOMED
Suicide attempt	Suicide attempt	4219484	4206010	SNOMED
	Injury due to suicide attempt	4257906		
	Self-administered poisoning	4181216		
	Intentional overdose	607149		
	Suicide deliberate poisoning	444362		
Suicide ideation	Threatening suicide	4216115	602870, 4190444	SNOMED
	Suicidal thoughts	4273391		
	Harmful thoughts	4037303		
	Feeling suicidal	4021339		
	At risk for suicide	4021336		
	Suicide risk	37399733		
	Suicide plan	600767		
Intentional self-harm	Self-inflicted injury	439235	440925, 42536693, 42573140, 42596336, 4206010, 42573949	SNOMED
	Self-destructive behaviour	608248		
	Late effect of self-inflicted injury	435446		
	Intentionally harming self	4303690		
	Suicide deliberate poisoning	444362		
	Self-administrated poisoning	4181216		
	Intentional overdose of prescription only medication	44802958		

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
	Intentional overdose	607149		
Composite Suicidality Outcome	Suicide	440925	4206010, 42596336, 42536693, 42573140, 42573949	SNOMED
	Suicide attempt	4219484		
	Injury due to suicide attempt	4257906		
	Suicidal thoughts	4273391		
	Harmful thoughts	4037303		
	Feeling suicidal	4021339		
	At risk for suicide	4021336		
	Suicide risk	37399733		
	Threatening suicide	4216115		
	Suicide plan	600767		
	Self-inflicted injury	439235		
	Self-destructive behaviour	608248		
	Late effect of self-inflicted injury	435446		
	Intentionally harming self	4303690		
	Self-administered poisoning	4181216		
	Intentional overdose	607149		
	Suicidal deliberate poisoning	444362		

Appendix II: Supplementary analyses

Appendix II. Table S 1. Incidence rates of composite suicidality outcome per 1,000 person- years in the general adult male population by age group.

Data source	Age group	Number of participants	Follow-up (person-years)	Number of incident cases (suicide related events)	Incidence Rate/1,000 PYs (95% CI)
BIFAP	18-30	1,620,132	14,514,187.74	6,466	0.45 (0.43, 0.46)
	31-40	1,667,717	15,892,181.36	7,136	0.45 (0.44, 0.46)
	41-50	1,483,672	13,909,476.57	6,600	0.47 (0.46, 0.49)
	51-60	1,175,316	10,720,202.62	3,543	0.33 (0.32, 0.34)
	61-70	867,002	7,796,370.21	2,053	0.26 (0.25, 0.27)
	71+	912,197	6,277,841.86	2,427	0.39 (0.37, 0.40)
CPRD-Gold	18-30	1,330,033	6,891,936.45	17,487	2.54 (2.50, 2.58)
	31-40	807,806	4,571,834.16	7,549	1.65 (1.61, 1.69)
	41-50	746,579	4,964,457.36	6,770	1.36 (1.33, 1.40)
	51-60	577,467	3,948,591.60	3,424	0.87 (0.84, 0.90)
	61-70	459,936	3,095,837.20	1,468	0.47 (0.45, 0.50)
	71+	19,406	38,337.83	28	0.73 (0.49, 1.06)
DK-DHR	18-30	1,089,490	10,062,327.72	2,532	0.25 (0.24, 0.26)
	31-40	466,905	5,635,712.11	1,065	0.19 (0.18, 0.20)
	41-50	454,117	5,905,908.82	1,073	0.18 (0.17, 0.19)
	51-60	376,704	4,860,138.73	619	0.13 (0.12, 0.14)
	61-70	329,227	3,987,874.54	352	0.09 (0.08, 0.10)
	71+	234,971	1,899,518.19	259	0.14 (0.12, 0.15)
IPCI	18-30	278,804	1,229,986.26	598	0.49 (0.45, 0.53)
	31-40	170,561	815,822.32	409	0.50 (0.45, 0.55)
	41-50	170,093	979,911.42	521	0.53 (0.49, 0.58)

	51-60	153,752	873,116.00	480	0.55 (0.50, 0.60)
	61-70	124,565	688,649.05	252	0.37 (0.32, 0.41)
	71+	102,861	448,977.59	191	0.43 (0.37, 0.49)
InGef	18-30	1,224,847	6,427,931.70	600	0.09 (0.09, 0.10)
	31-40	684,233	4,205,944.76	293	0.07 (0.06, 0.08)
	41-50	761,623	5,365,942.19	334	0.06 (0.06, 0.07)
	51-60	681,154	4,946,921.36	273	0.06 (0.05, 0.06)
	61-70	364,543	2,661,822.57	123	0.05 (0.04, 0.06)
	71+	346,829	2,173,377.29	172	0.08 (0.07, 0.09)
NAJS	18-30	522,761	3,343,654.30	1,681	0.50 (0.48, 0.53)
	31-40	314,846	2,326,190.40	1,200	0.52 (0.49, 0.55)
	41-50	302,242	2,266,463.81	1,312	0.58 (0.55, 0.61)
	51-60	317,881	2,384,493.50	1,380	0.58 (0.55, 0.61)
	61-70	255,655	1,826,999.60	1,021	0.56 (0.53, 0.59)
	71+	205,472	1,171,815.84	1,120	0.96 (0.90, 1.01)
SIDIAP	18-30	1,086,604	8,967,682.80	3,593	0.40 (0.39, 0.41)
	31-40	747,335	7,435,025.38	2,734	0.37 (0.35, 0.38)
	41-50	529,361	5,736,753.76	2,140	0.37 (0.36, 0.39)
	51-60	371,110	4,140,933.62	909	0.22 (0.21, 0.23)
	61-70	280,440	3,014,039.37	658	0.22 (0.20, 0.24)
	71+	301,693	2,333,503.38	641	0.27 (0.25, 0.30)

Appendix II. Table S 2. Incidence rates of composite suicidality outcome per 1,000 person- years in androgenetic alopecia patients by age group and by treatment in BIFAP data source.

Age group	Cohorts*	Number of participants	Follow-up (person-years)	Number of incident cases (suicide related events)	Incidence Rate/1,000 PYs (95% CI)
18-30	All patients	4,390	18,364.22	7	0.38 (0.15, 0.79)
	Patients treated with finasteride	448	supp	<5	supp
	Patients treated with dutasteride	91	supp	<5	supp
	Patients treated with topical minoxidil	<5	supp	<5	supp
	Non-treated	4,250	16,456.26	7	0.43 (0.17, 0.88)
31-40	All patients	2,569	9,196.85	6	0.65 (0.24, 1.42)
	Patients treated with finasteride	362	supp	<5	supp
	Patients treated with dutasteride	63	supp	<5	supp
	Patients treated with topical minoxidil	NC	NC	NC	NC
	Non-treated	2,437	7,762.10	5	0.64 (0.21, 1.50)
41-50	All patients	1,525	supp	<5	supp
	Patients treated with finasteride	242	supp	<5	supp
	Patients treated with dutasteride	37	supp	<5	supp
	Patients treated with topical minoxidil	NC	NC	NC	NC
	Non-treated	1,446	supp	<5	supp
51-60	All patients	546	supp	<5	supp
	Patients treated with finasteride	69	supp	<5	supp
	Patients treated with dutasteride	16	supp	<5	supp
	Patients treated with topical minoxidil	NC	NC	NC	NC
	Non-treated	536	supp	<5	supp

61-70	All patients	148	supp	<5	supp
	Patients treated with finasteride	12	supp	<5	supp
	Patients treated with dutasteride	5	supp	<5	supp
	Patients treated with topical minoxidil	NC	NC	NC	NC
	Non-treated	159	supp	<5	supp
71+	All patients	26	supp	<5	supp
	Patients treated with finasteride	<5	supp	<5	supp
	Patients treated with dutasteride	<5	supp	<5	supp
	Patients treated with topical minoxidil	NC	NC	NC	NC
	Non-treated	27	supp	<5	supp

* Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.
NC= No person counts
supp= If the number of participants or incident cases was <5; associated statistics have been suppressed to protect patients' confidentiality.

Appendix II. Table S 3. Incidence rates of composite suicidality outcome per 1,000 person- years in androgenetic alopecia patients by age group and by treatment in CPRD-Gold data source.

Age group	Cohorts*	Number of participants	Follow-up (person-years)	Number of incident cases (suicide related events)	Incidence Rate/1,000 PYs (95% CI)
18-30	All patients	379	supp	<5	supp
	Patients treated with finasteride	77	supp	<5	supp
	Patients treated with dutasteride	<5	supp	<5	supp
	Patients treated with topical minoxidil	20	supp	<5	supp
	Non-treated	293	supp	<5	supp
31-40	All patients	152	supp	<5	supp
	Patients treated with finasteride	48	supp	<5	supp

	Patients treated with dutasteride	NC	NC	NC	NC
	Patients treated with topical minoxidil	<5	supp	<5	supp
	Non-treated	109	supp	<5	supp
41-50	All patients	58	supp	<5	supp
	Patients treated with finasteride	17	supp	<5	supp
	Patients treated with dutasteride	<5	supp	<5	supp
	Patients treated with topical minoxidil	<5	supp	<5	supp
	Non-treated	38	supp	<5	supp
51-60	All patients	20	supp	<5	supp
	Patients treated with finasteride	<5	supp	<5	supp
	Patients treated with dutasteride	NC	NC	NC	NC
	Patients treated with topical minoxidil	NC	NC	NC	NC
	Non-treated	14	supp	<5	supp
61-70	All patients	12	supp	<5	supp
	Patients treated with finasteride	<5	supp	<5	supp
	Patients treated with dutasteride	NC	NC	NC	NC
	Patients treated with topical minoxidil	NC	NC	NC	NC
	Non-treated	11	supp	<5	supp
71+	All patients	8	supp	<5	supp
	Patients treated with finasteride	<5	supp	<5	supp
	Patients treated with dutasteride	<5	supp	<5	supp
	Patients treated with topical minoxidil	<5	supp	<5	supp
	Non-treated	<5	supp	<5	supp

* Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.

NC= No person counts

supp= If the number of participants or incident cases was <5; associated statistics have been suppressed to protect patients' confidentiality.

Appendix II. Table S 4. Incidence rates of composite suicidality outcome per 1,000 person- years in androgenetic alopecia patients by age group and by treatment in DK-DHR data source.

Age group	Cohorts*	Number of participants	Follow-up (person-years)	Number of incident cases (suicide related events)	Incidence Rate/1,000 PYs (95% CI)
18-30	All patients	161	supp	<5	supp
	Patients treated with finasteride	36	supp	<5	supp
	Patients treated with dutasteride	<5	supp	<5	supp
	Patients treated with topical minoxidil	6	supp	<5	supp
	Non-treated	126	supp	<5	supp
31-40	All patients	140	supp	<5	supp
	Patients treated with finasteride	20	supp	<5	supp
	Patients treated with dutasteride	<5	supp	<5	supp
	Patients treated with topical minoxidil	<5	supp	<5	supp
	Non-treated	111	supp	<5	supp
41-50	All patients	99	supp	<5	supp
	Patients treated with finasteride	10	supp	<5	supp
	Patients treated with dutasteride	NC	NC	NC	NC
	Patients treated with topical minoxidil	<5	supp	<5	supp
	Non-treated	83	supp	<5	supp
51-60	All patients	30	supp	<5	supp
	Patients treated with finasteride	<5	supp	<5	supp
	Patients treated with dutasteride	NC	NC	NC	NC
	Patients treated with topical minoxidil	<5	supp	<5	supp
	Non-treated	27	supp	<5	supp
61-70	All patients	8	supp	<5	supp

	Patients treated with finasteride	NC	NC	NC	NC
	Patients treated with dutasteride	NC	NC	NC	NC
	Patients treated with topical minoxidil	NC	NC	NC	NC
	Non-treated	8	supp	<5	supp
71+	All patients	7	supp	<5	supp
	Patients treated with finasteride	NC	NC	NC	NC
	Patients treated with dutasteride	NC	NC	NC	NC
	Patients treated with topical minoxidil	NC	NC	NC	NC
	Non-treated	7	supp	<5	supp

* Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.

NC= No person counts

supp= If the number of participants or incident cases was <5; associated statistics have been suppressed to protect patients' confidentiality.

Appendix II. Table S 5. Incidence rates of composite suicidality outcome per 1,000 person- years in androgenetic alopecia patients by age group and by treatment in IPCI data source.

Age group	Cohorts*	Number of participants	Follow-up (person-years)	Number of incident cases (suicide related events)	Incidence Rate/1,000 PYs (95% CI)
18-30	All patients	1,266	supp	<5	supp
	Patients treated with finasteride	420	supp	<5	supp
	Patients treated with dutasteride	7	supp	<5	supp
	Patients treated with topical minoxidil	208	supp	<5	supp
	Non-treated	876	supp	<5	supp
31-40	All patients	351	supp	<5	supp
	Patients treated with finasteride	98	supp	<5	supp
	Patients treated with dutasteride	<5	supp	<5	supp

	Patients treated with topical minoxidil	48	supp	<5	supp
	Non-treated	219	supp	<5	supp
41-50	All patients	173	supp	<5	supp
	Patients treated with finasteride	53	supp	<5	supp
	Patients treated with dutasteride	<5	supp	<5	supp
	Patients treated with topical minoxidil	27	supp	<5	supp
	Non-treated	103	supp	<5	supp
51-60	All patients	85	supp	<5	supp
	Patients treated with finasteride	23	supp	<5	supp
	Patients treated with dutasteride	<5	supp	<5	supp
	Patients treated with topical minoxidil	14	supp	<5	supp
	Non-treated	48	supp	<5	supp
61-70	All patients	28	supp	<5	supp
	Patients treated with finasteride	<5	supp	<5	supp
	Patients treated with dutasteride	<5	supp	<5	supp
	Patients treated with topical minoxidil	<5	supp	<5	supp
	Non-treated	25	supp	<5	supp
71+	All patients	11	supp	<5	supp
	Patients treated with finasteride	<5	supp	<5	supp
	Patients treated with dutasteride	<5	supp	<5	supp
	Patients treated with topical minoxidil	NC	NC	NC	NC
	Non-treated	16	supp	<5	supp

* Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.
NC= No person counts
supp= If the number of participants or incident cases was <5; associated statistics have been suppressed to protect patients' confidentiality.

Appendix II. Table S 6. Incidence rates of composite suicidality outcome per 1,000 person- years in androgenetic alopecia patients by age group and by treatment in InGef RDB data source.

Age group	Cohorts*	Number of participants	Follow-up (person-years)	Number of incident cases (suicide related events)	Incidence Rate/1,000 PYs (95% CI)
18-30	All patients	120	supp	<5	supp
	Patients treated with finasteride	<5	supp	<5	supp
	Patients treated with dutasteride	NC	NC	NC	NC
	Patients treated with topical minoxidil	NC	NC	NC	NC
	Non-treated	119	supp	<5	supp
31-40	All patients	53	supp	<5	supp
	Patients treated with finasteride	<5	supp	<5	supp
	Patients treated with dutasteride	NC	NC	NC	NC
	Patients treated with topical minoxidil	NC	NC	NC	NC
	Non-treated	52	supp	<5	supp
41-50	All patients	27	supp	<5	supp
	Patients treated with finasteride	27	supp	<5	supp
	Patients treated with dutasteride	NC	NC	NC	NC
	Patients treated with topical minoxidil	NC	NC	NC	NC
	Non-treated	27	supp	<5	supp
51-60	All patients	13	supp	<5	supp
	Patients treated with finasteride	375	supp	<5	supp
	Patients treated with dutasteride	NC	NC	NC	NC
	Patients treated with topical minoxidil	NC	NC	NC	NC
	Non-treated	13	supp	<5	supp
61-70	All patients	12	supp	<5	supp

	Patients treated with finasteride	1,194	supp	<5	supp
	Patients treated with dutasteride	NC	NC	NC	NC
	Patients treated with topical minoxidil	NC	NC	NC	NC
	Non-treated	12	supp	<5	supp
71+	All patients	7	supp	<5	supp
	Patients treated with finasteride	3,624	supp	<5	supp
	Patients treated with dutasteride	NC	NC	NC	NC
	Patients treated with topical minoxidil	NC	NC	NC	NC
	Non-treated	supp	supp	<5	supp

* Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.
NC= No person counts
supp= If the number of participants or incident cases was <5; associated statistics have been suppressed to protect patients' confidentiality.

Appendix II. Table S 7. Incidence rates of composite suicidality outcome per 1,000 person- years in androgenetic alopecia patients by age group and by treatment in NAJS data source.

Age group	Cohorts*	Number of participants	Follow-up (person-years)	Number of incident cases (suicide related events)	Incidence Rate/1,000 PYs (95% CI)
18-30	All patients	996	supp	<5	supp
	Patients treated with finasteride	9	supp	<5	supp
	Patients treated with dutasteride	<5	supp	<5	supp
	Patients treated with topical minoxidil	NC	NC	NC	NC
	Non-treated	993	supp	<5	supp
31-40	All patients	371	supp	<5	supp
	Patients treated with finasteride	<5	supp	<5	supp
	Patients treated with dutasteride	<5	supp	<5	supp
	Patients treated with topical minoxidil	NC	NC	NC	NC

	Non-treated	370	supp	<5	supp
41-50	All patients	138	supp	<5	supp
	Patients treated with finasteride	<5	supp	<5	supp
	Patients treated with dutasteride	<5	supp	<5	supp
	Patients treated with topical minoxidil	NC	NC	NC	NC
	Non-treated	155	supp	<5	supp
51-60	All patients	50	supp	<5	supp
	Patients treated with finasteride	NC	NC	NC	NC
	Patients treated with dutasteride	<5	supp	<5	supp
	Patients treated with topical minoxidil	NC	NC	NC	NC
	Non-treated	73	supp	<5	supp
61-70	All patients	47	supp	<5	supp
	Patients treated with finasteride	NC	NC	NC	NC
	Patients treated with dutasteride	<5	supp	<5	supp
	Patients treated with topical minoxidil	NC	NC	NC	NC
	Non-treated	67	supp	<5	supp
71+	All patients	14	supp	<5	supp
	Patients treated with finasteride	NC	NC	NC	NC
	Patients treated with dutasteride	NC	NC	NC	NC
	Patients treated with topical minoxidil	NC	NC	NC	NC
	Non-treated	23	supp	<5	supp

* Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.
NC= No person counts
supp= If the number of participants or incident cases was <5; associated statistics have been suppressed to protect patients' confidentiality.

Appendix II. Table S 8. Incidence rates of composite suicidality outcome per 1,000 person- years in androgenetic alopecia patients by age group and by treatment in SIDIAP data source.

Age group	Cohorts*	Number of participants	Follow-up (person-years)	Number of incident cases (suicide related events)	Incidence Rate/1,000 PYs (95% CI)
18-30	All patients	2,72	17,500.36	10	0.57 (0.27, 1.05)
	Patients treated with finasteride	71	supp	<5	supp
	Patients treated with dutasteride	31	supp	<5	supp
	Patients treated with topical minoxidil	263	supp	<5	supp
	Non-treated	2,404	15,711.00	6	0.38 (0.14, 0.83)
31-40	All patients	1,532	supp	<5	supp
	Patients treated with finasteride	64	supp	<5	supp
	Patients treated with dutasteride	32	supp	<5	supp
	Patients treated with topical minoxidil	124	supp	<5	supp
	Non-treated	1,291	supp	<5	supp
41-50	All patients	651	supp	<5	supp
	Patients treated with finasteride	32	supp	<5	supp
	Patients treated with dutasteride	20	supp	<5	supp
	Patients treated with topical minoxidil	63	supp	<5	supp
	Non-treated	526	supp	<5	supp
51-60	All patients	233	supp	<5	supp
	Patients treated with finasteride	11	supp	<5	supp
	Patients treated with dutasteride	9	supp	<5	supp
	Patients treated with topical minoxidil	10	supp	<5	supp
	Non-treated	210	supp	<5	supp
61-70	All patients	72	supp	<5	supp

	Patients treated with finasteride	<5	supp	<5	supp
	Patients treated with dutasteride	<5	supp	<5	supp
	Patients treated with topical minoxidil	<5	supp	<5	supp
	Non-treated	81	supp	<5	supp
71+	All patients	16	supp	<5	supp
	Patients treated with finasteride	<5	supp	<5	supp
	Patients treated with dutasteride	<5	supp	<5	supp
	Patients treated with topical minoxidil	NC	NC	NC	NC
	Non-treated	22	supp	<5	supp

* Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.
NC= No person counts
supp= If the number of participants or incident cases was <5; associated statistics have been suppressed to protect patients' confidentiality.

Appendix II. Table S 9. Incidence rates of composite suicidality outcome per 1,000 person- years in BPH patients by age group and by treatment in BIFAP data source.

Age group	Cohorts*	Number of participants	Follow-up (person-years)	Number of incident cases (suicide related events)	Incidence Rate/1,000 PYs (95% CI)
18-30	All patients	357	supp	<5	supp
	Patients treated with finasteride	NC	NC	NC	NC
	Patients treated with dutasteride	7	supp	<5	supp
	Patients treated with alpha blockers	14	supp	<5	supp
	Patients treated with tadalafil	NC	NC	NC	NC
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	354	supp	<5	supp
31-40	All patients	1,914	10,067.35	6	0.60 (0.22, 1.30)

	Patients treated with finasteride	9	supp	<5	supp
	Patients treated with dutasteride	36	supp	<5	supp
	Patients treated with alpha blockers	196	supp	<5	supp
	Patients treated with tadalafil	15	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	1,872	9,657.60	6	0.62 (0.23, 1.35)
41-50	All patients	18,844	102,954.76	89	0.86 (0.69, 1.06)
	Patients treated with finasteride	72	supp	<5	supp
	Patients treated with dutasteride	1,004	supp	<5	supp
	Patients treated with alpha blockers	3,260	supp	<5	supp
	Patients treated with tadalafil	198	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	18,182	91,908.99	70	0.76 (0.59, 0.96)
51-60	All patients	78,338	439,245.63	252	0.57 (0.51, 0.65)
	Patients treated with finasteride	279	supp	<5	supp
	Patients treated with dutasteride	10,347	23,084.52	19	0.82 (0.50, 1.29)
	Patients treated with alpha blockers	23,178	27,299.52	24	0.88 (0.56, 1.31)
	Patients treated with tadalafil	1,358	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	71,636	345,429.83	193	0.56 (0.48, 0.64)
61-70	All patients	132,873	743,555.77	299	0.40 (0.36, 0.45)
	Patients treated with finasteride	752	supp	<5	supp
	Patients treated with dutasteride	28,698	77,290.33	34	0.44 (0.30, 0.61)
	Patients treated with alpha blockers	52,472	62,412.97	16	0.26 (0.15, 0.42)

	Patients treated with tadalafil	2,047	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	111,396	506,395.52	202	0.40 (0.35, 0.46)
71+	All patients	212,465	911,357.82	585	0.64 (0.59, 0.70)
	Patients treated with finasteride	2,091	5,250.91	6	1.14 (0.42, 2.49)
	Patients treated with dutasteride	51,482	135,573.11	68	0.50 (0.39, 0.64)
	Patients treated with alpha blockers	79,750	81,517.08	32	0.39 (0.27, 0.55)
	Patients treated with tadalafil	800	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	145,074	502,940.44	337	0.67 (0.60, 0.75)

* Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.
NC= No person counts
supp= If the number of participants or incident cases was <5; associated statistics have been suppressed to protect patients' confidentiality.

Appendix II. Table S 10. Incidence rates of composite suicidality outcome per 1,000 person- years in BPH patients by age group and by treatment in CPRD-Gold data source.

Age group	Cohorts*	Number of participants	Follow-up (person-years)	Number of incident cases (suicide related events)	Incidence Rate/1,000 PYs (95% CI)
18-30	All patients	90	supp	<5	supp
	Patients treated with finasteride	<5	supp	<5	supp
	Patients treated with dutasteride	NC	NC	NC	NC
	Patients treated with alpha blockers	NC	NC	NC	NC
	Patients treated with tadalafil	<5	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC

	Non-treated	89	supp	<5	supp
31-40	All patients	409	supp	<5	supp
	Patients treated with finasteride	11	supp	<5	supp
	Patients treated with dutasteride	5	supp	<5	supp
	Patients treated with alpha blockers	NC	NC	NC	NC
	Patients treated with tadalafil	10	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	386	supp	<5	supp
41-50	All patients	3,413	18,198.92	42	2.31 (1.66, 3.12)
	Patients treated with finasteride	233	supp	<5	supp
	Patients treated with dutasteride	49	supp	<5	supp
	Patients treated with alpha blockers	NC	NC	NC	NC
	Patients treated with tadalafil	87	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	3,131	14,756.22	32	2.17 (1.48, 3.06)
51-60	All patients	14,152	74,596.86	98	1.31 (1.07, 1.60)
	Patients treated with finasteride	1,896	4,742.89	6	1.27 (0.46, 2.75)
	Patients treated with dutasteride	415	supp	<5	supp
	Patients treated with alpha blockers	NC	NC	NC	NC
	Patients treated with tadalafil	451	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	12,152	50,955.41	69	1.35 (1.05, 1.71)
61-70	All patients	26,030	136,763.12	90	0.66 (0.53, 0.81)
	Patients treated with finasteride	5,093	15,573.09	7	0.45 (0.18, 0.93)
	Patients treated with dutasteride	1,180	3,532.36	5	1.42 (0.46, 3.30)
	Patients treated with alpha blockers	NC	NC	NC	NC

	Patients treated with tadalafil	734	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	20,484	80,097.55	49	0.61 (0.45, 0.81)
71+	All patients	30,464	131,181.62	83	0.63 (0.50, 0.78)
	Patients treated with finasteride	8,635	23,813.72	17	0.71 (0.42, 1.14)
	Patients treated with dutasteride	1,683	supp	<5	supp
	Patients treated with alpha blockers	NC	NC	NC	NC
	Patients treated with tadalafil	346	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	21,702	69,500.82	46	0.66 (0.48, 0.88)

* Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.
NC= No person counts
supp= If the number of participants or incident cases was <5; associated statistics have been suppressed to protect patients' confidentiality.

Appendix II. Table S 11. Incidence rates of composite suicidality outcome per 1,000 person- years in BPH patients by age group and by treatment in DK-DHR data source.

Age group	Cohorts*	Number of participants	Follow-up (person-years)	Number of incident cases (suicide related events)	Incidence Rate/1,000 PYs (95% CI)
18-30	All patients	216	supp	<5	supp
	Patients treated with finasteride	47	supp	<5	supp
	Patients treated with dutasteride	NC	NC	NC	NC
	Patients treated with alpha blockers	16	supp	<5	supp
	Patients treated with tadalafil	29	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	62	supp	<5	supp

31-40	All patients	440	supp	<5	supp
	Patients treated with finasteride	42	supp	<5	supp
	Patients treated with dutasteride	6	supp	<5	supp
	Patients treated with alpha blockers	81	supp	<5	supp
	Patients treated with tadalafil	58	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	227	supp	<5	supp
41-50	All patients	2,212	17,082.08	5	0.29 (0.10, 0.68)
	Patients treated with finasteride	328	supp	<5	supp
	Patients treated with dutasteride	105	supp	<5	supp
	Patients treated with alpha blockers	609	supp	<5	supp
	Patients treated with tadalafil	311	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	1,201	supp	<5	supp
51-60	All patients	11,681	85,017.60	13	0.15 (0.08, 0.26)
	Patients treated with finasteride	2,369	supp	<5	supp
	Patients treated with dutasteride	901	supp	<5	supp
	Patients treated with alpha blockers	4,013	supp	<5	supp
	Patients treated with tadalafil	1,159	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	6,416	40,515.51	6	0.15 (0.05, 0.32)
61-70	All patients	31,857	228,229.67	18	0.08 (0.05, 0.12)
	Patients treated with finasteride	8,179	supp	<5	supp
	Patients treated with dutasteride	2,854	supp	<5	supp
	Patients treated with alpha blockers	10,826	supp	<5	supp
	Patients treated with tadalafil	2,225	supp	<5	supp

	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	15,506	88,915.27	7	0.08 (0.03, 0.16)
71+	All patients	46,872	237,373.50	34	0.14 (0.10, 0.20)
	Patients treated with finasteride	14,626	supp	<5	supp
	Patients treated with dutasteride	4,450	supp	<5	supp
	Patients treated with alpha blockers	14,683	20,575.27	5	0.24 (0.08, 0.57)
	Patients treated with tadalafil	1,667	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	19,559	79,006.66	11	0.14 (0.07, 0.25)

* Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.
NC= No person counts
supp= If the number of participants or incident cases was <5; associated statistics have been suppressed to protect patients' confidentiality.

Appendix II. Table S 12. Incidence rates of composite suicidality outcome per 1,000 person- years in BPH patients by age group and by treatment in IPCI data source.

Age group	Cohorts*	Number of participants	Follow-up (person-years)	Number of incident cases (suicide related events)	Incidence Rate/1,000 PYs (95% CI)
18-30	All patients	11	supp	<5	supp
	Patients treated with finasteride	NC	NC	NC	NC
	Patients treated with dutasteride	NC	NC	NC	NC
	Patients treated with alpha blockers	5	supp	<5	supp
	Patients treated with tadalafil	<5	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	10	supp	<5	supp
31-40	All patients	31	supp	<5	supp

	Patients treated with finasteride	NC	NC	NC	NC
	Patients treated with dutasteride	<5	supp	<5	supp
	Patients treated with alpha blockers	18	supp	<5	supp
	Patients treated with tadalafil	<5	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	30	supp	<5	supp
41-50	All patients	645	supp	<5	supp
	Patients treated with finasteride	<5	supp	<5	supp
	Patients treated with dutasteride	27	supp	<5	supp
	Patients treated with alpha blockers	368	supp	<5	supp
	Patients treated with tadalafil	10	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	623	supp	<5	supp
51-60	All patients	3,346	15,868.98	8	0.50 (0.22, 0.99)
	Patients treated with finasteride	68	supp	<5	supp
	Patients treated with dutasteride	219	supp	<5	supp
	Patients treated with alpha blockers	1,879	supp	<5	supp
	Patients treated with tadalafil	75	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	3,123	13,121.57	7	0.53 (0.21, 1.10)
61-70	All patients	5,721	26,015.96	13	0.50 (0.27, 0.85)
	Patients treated with finasteride	181	supp	<5	supp
	Patients treated with dutasteride	511	supp	<5	supp
	Patients treated with alpha blockers	3,337	supp	<5	supp
	Patients treated with tadalafil	163	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC

	Non-treated	5,064	19,916.06	10	0.50 (0.24, 0.92)
71+	All patients	5,566	20,824.80	10	0.48 (0.23, 0.88)
	Patients treated with finasteride	314	supp	<5	supp
	Patients treated with dutasteride	704	supp	<5	supp
	Patients treated with alpha blockers	3,496	supp	<5	supp
	Patients treated with tadalafil	74	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	4,637	14,701.75	5	0.34 (0.11, 0.79)

* Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.
NC= No person counts
supp= If the number of participants or incident cases was <5; associated statistics have been suppressed to protect patients' confidentiality.

Appendix II. Table S 13. Incidence rates of composite suicidality outcome per 1,000 person- years in BPH patients by age group and by treatment in In-Gef RDB data source.

Age group	Cohorts*	Number of participants	Follow-up (person-years)	Number of incident cases (suicide related events)	Incidence Rate/1,000 PYs (95% CI)
18-30	All patients	86	supp	<5	supp
	Patients treated with finasteride	NC	NC	NC	NC
	Patients treated with dutasteride	NC	NC	NC	NC
	Patients treated with alpha blockers	22	supp	<5	supp
	Patients treated with tadalafil	NC	NC	NC	NC
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	85	supp	<5	supp
31-40	All patients	448	supp	<5	supp
	Patients treated with finasteride	NC	NC	NC	NC

	Patients treated with dutasteride	NC	NC	NC	NC
	Patients treated with alpha blockers	134	supp	<5	supp
	Patients treated with tadalafil	<5	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	444	supp	<5	supp
41-50	All patients	3,039	12,827.70	6	0.47 (0.17, 1.02)
	Patients treated with finasteride	NC	NC	NC	NC
	Patients treated with dutasteride	21	supp	<5	supp
	Patients treated with alpha blockers	1,44	supp	<5	supp
	Patients treated with tadalafil	41	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	2,910	11,873.98	6	0.51 (0.19, 1.10)
51-60	All patients	20,529	79,364.21	6	0.08 (0.03, 0.16)
	Patients treated with finasteride	NC	NC	NC	NC
	Patients treated with dutasteride	374	supp	<5	supp
	Patients treated with alpha blockers	10,885	supp	<5	supp
	Patients treated with tadalafil	230	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	18,523	68,259.19	8	0.12 (0.05, 0.23)
61-70	All patients	42,507	155,943.73	16	0.10 (0.06, 0.17)
	Patients treated with finasteride	NC	NC	NC	NC
	Patients treated with dutasteride	1,177	supp	<5	supp
	Patients treated with alpha blockers	24,407	59,202.21	9	0.15 (0.07, 0.29)
	Patients treated with tadalafil	323	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	36,374	124,249.56	16	0.13 (0.07, 0.21)

71+	All patients	95,622	293,803.45	39	0.13 (0.09, 0.18)
	Patients treated with finasteride	NC	NC	NC	NC
	Patients treated with dutasteride	3,368	supp	<5	supp
	Patients treated with alpha blockers	58,690	132,682.84	23	0.17 (0.11, 0.26)
	Patients treated with tadalafil	256	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	78,003	220,913.95	40	0.18 (0.13, 0.25)

* Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.
NC= No person counts
supp= If the number of participants or incident cases was <5; associated statistics have been suppressed to protect patients' confidentiality.

Appendix II. Table S 14. Incidence rates of composite suicidality outcome per 1,000 person- years in BPH patients by age group and by treatment in Croatian NAJS data source.

Age group	Cohorts*	Number of participants	Follow-up (person-years)	Number of incident cases (suicide related events)	Incidence Rate/1,000 PYs (95% CI)
18-30	All patients	1,713	7,619.53	9	1.18 (0.54, 2.24)
	Patients treated with finasteride	7	supp	<5	supp
	Patients treated with dutasteride	139	supp	<5	supp
	Patients treated with alpha blockers	302	supp	<5	supp
	Patients treated with tadalafil	NC	NC	NC	NC
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	1,584	7,026.30	9	1.28 (0.59, 2.43)
31-40	All patients	5,947	26,904.61	22	0.82 (0.51, 1.24)
	Patients treated with finasteride	<5	supp	<5	supp
	Patients treated with dutasteride	688	supp	<5	supp

	Patients treated with alpha blockers	1,462	supp	<5	supp
	Patients treated with tadalafil	NC	NC	NC	NC
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	5,374	23,569.30	17	0.72 (0.42, 1.15)
41-50	All patients	28,210	129,043.31	80	0.62 (0.49, 0.77)
	Patients treated with finasteride	87	supp	<5	supp
	Patients treated with dutasteride	4,113	supp	<5	supp
	Patients treated with alpha blockers	8,404	6,012.36	5	0.83 (0.27, 1.94)
	Patients treated with tadalafil	NC	NC	NC	NC
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	25,979	109,355.23	64	0.59 (0.45, 0.75)
51-60	All patients	73,650	347,852.52	224	0.64 (0.56, 0.73)
	Patients treated with finasteride	616	supp	<5	supp
	Patients treated with dutasteride	16,823	22,080.76	20	0.91 (0.55, 1.40)
	Patients treated with alpha blockers	33,777	30,960.44	23	0.74 (0.47, 1.11)
	Patients treated with tadalafil	NC	NC	NC	NC
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	67,449	269,828.82	166	0.62 (0.53, 0.72)
61-70	All patients	95,210	438,734.54	268	0.61 (0.54, 0.69)
	Patients treated with finasteride	2,294	supp	supp	supp
	Patients treated with dutasteride	31,147	45,246.02	30	0.66 (0.45, 0.95)
	Patients treated with alpha blockers	64,108	64,596.80	32	0.50 (0.34, 0.70)
	Patients treated with tadalafil	NC	NC	NC	NC
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	85,609	309,494.62	170	0.55 (0.47, 0.64)
71+	All patients	74,619	289,152.62	276	0.95 (0.85, 1.07)

	Patients treated with finasteride	4,679	7,364.45	11	1.49 (0.75, 2.67)
	Patients treated with dutasteride	30,144	41,953.24	45	1.07 (0.78, 1.44)
	Patients treated with alpha blockers	65,032	62,525.24	67	1.07 (0.83, 1.36)
	Patients treated with tadalafil	NC	NC	NC	NC
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	63,249	179,885.19	143	0.79 (0.67, 0.94)

* Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.
NC= No person counts
supp= If the number of participants or incident cases was <5; associated statistics have been suppressed to protect patients' confidentiality.

Appendix II. Table S 15. Incidence rates of composite suicidality outcome per 1,000 person- years in BPH patients by age group and by treatment in SIDIAP data source.

Age group	Cohorts*	Number of participants	Follow-up (person-years)	Number of incident cases (suicide related events)	Incidence Rate/1,000 PYs (95% CI)
18-30	All patients	236	supp	<5	supp
	Patients treated with finasteride	12	supp	<5	supp
	Patients treated with dutasteride	<5	supp	<5	supp
	Patients treated with alpha blockers	51	supp	<5	supp
	Patients treated with tadalafil	<5	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	218	supp	<5	supp
31-40	All patients	1,834	11,500.30	8	0.70 (0.30, 1.37)
	Patients treated with finasteride	21	supp	<5	supp
	Patients treated with dutasteride	26	supp	<5	supp
	Patients treated with alpha blockers	449	supp	<5	supp

	Patients treated with tadalafil	8	supp	<5	0.00 (0.00, 972.81)
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	1,754	11,008.24	7	0.64 (0.26, 1.31)
41-50	All patients	16,244	101,017.80	75	0.74 (0.58, 0.93)
	Patients treated with finasteride	202	supp	<5	supp
	Patients treated with dutasteride	375	supp	<5	supp
	Patients treated with alpha blockers	6,112	14,442.65	19	1.32 (0.79, 2.05)
	Patients treated with tadalafil	130	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	15,775	92,649.66	69	0.74 (0.58, 0.94)
51-60	All patients	65,063	420,004.53	174	0.41 (0.36, 0.48)
	Patients treated with finasteride	1,887	supp	<5	supp
	Patients treated with dutasteride	4,402	supp	<5	supp
	Patients treated with alpha blockers	30,520	82,173.60	38	0.46 (0.33, 0.63)
	Patients treated with tadalafil	952	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	61,093	348,773.72	148	0.42 (0.36, 0.50)
61-70	All patients	103,482	672,158.08	205	0.30 (0.26, 0.35)
	Patients treated with finasteride	5,080	14,463.33	5	0.35 (0.11, 0.81)
	Patients treated with dutasteride	12,437	31,879.94	9	0.28 (0.13, 0.54)
	Patients treated with alpha blockers	56,448	166,578.64	54	0.32 (0.24, 0.42)
	Patients treated with tadalafil	1,735	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC

	Non-treated	92,327	504,905.21	156	0.31 (0.26, 0.36)
71+	All patients	126,936	633,819.10	305	0.48 (0.43, 0.54)
	Patients treated with finasteride	8,386	22,967.74	15	0.65 (0.37, 1.08)
	Patients treated with dutasteride	18,920	45,972.63	17	0.37 (0.22, 0.59)
	Patients treated with alpha blockers	69,644	184,469.01	97	0.53 (0.43, 0.64)
	Patients treated with tadalafil	833	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	99,681	419,228.80	207	0.49 (0.43, 0.57)

* Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.
NC= No person counts
supp= If the number of participants or incident cases was <5; associated statistics have been suppressed to protect patients' confidentiality.

Appendix II. Table S 16. Incidence rates of composite suicidality outcome per 1,000 person- years in androgenetic alopecia and BPH patients by history of psychiatric disorders and by treatment in BIFAP data source.

history of psychiatric disorders	Cohorts	Number of participants	Follow-up (person-years)	Number of incident cases (suicide related events)	Incidence Rate/1,000 PYs (95% CI)
Yes	**General adult male population**	512,636	4,931,348.90	6,089	1.23 (1.20, 1.27)
No	**General adult male population**	8,108,584	69,361,603.62	25,146	0.36 (0.36, 0.37)
Yes	**Androgenetic alopecia**				
	All patients	1,662	5,135.10	9	1.75 (0.80, 3.33)
	Patients treated with finasteride	228	supp	<5	supp
	Patients treated with dutasteride	42	supp	<5	supp
	Patients treated with topical minoxidil	NC	NC	NC	NC
	Non-treated	1,600	4,267.02	8	1.87 (0.81, 3.69)

No	**Androgenetic alopecia**				
	All patients	7,618	29,453.07	8	0.27 (0.12, 0.54)
	Patients treated with finasteride	911	supp	<5	supp
	Patients treated with dutasteride	174	supp	<5	supp
	Patients treated with topical minoxidil	<5	supp	<5	supp
	Non-treated	7,330	25,880.15	7	0.27 (0.11, 0.56)
Yes	**BPH**				
	All patients	81,833	355,122.71	521	1.47 (1.34, 1.60)
	Patients treated with finasteride	575	supp	<5	supp
	Patients treated with dutasteride	17,326	38,793.86	49	1.26 (0.93, 1.67)
	Patients treated with alpha blockers	29,961	30,955.44	32	1.03 (0.71, 1.46)
	Patients treated with tadalafil	1,195	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	63,231	237,404.54	353	1.49 (1.34, 1.65)
No	**BPH**				
	All patients	362,962	1,853,858.77	712	0.38 (0.36, 0.41)
	Patients treated with finasteride	2,628	6,662.31	8	1.20 (0.52, 2.37)
	Patients treated with dutasteride	74,248	198,841.63	76	0.38 (0.30, 0.48)
	Patients treated with alpha blockers	128,909	144,231.36	42	0.29 (0.21, 0.39)
	Patients treated with tadalafil	3,223	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	285,287	1,220,707.04	457	0.37 (0.34, 0.41)

* Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.
NC= No person counts
supp= If the number of participants or incident cases was <5; associated statistics have been suppressed to protect patients' confidentiality.

Appendix II. Table S 17. Incidence rates of composite suicidality outcome per 1,000 person- years in androgenetic alopecia and BPH patients by history of psychiatric disorders and by treatment in CPRD-Gold data source.

history of psychiatric disorders	Cohorts	Number of participants	Follow-up (person-years)	Number of incident cases (suicide related events)	Incidence Rate/1,000 PYs (95% CI)
Yes	**General adult male population**	469,397	2,764,685.22	12,442	4.50 (4.42, 4.58)
No	**General adult male population**	3,866,927	22,869,319.37	25,331	1.11 (1.09, 1.12)
Yes	**Androgenetic alopecia**				
	All patients	151	supp	<5	supp
	Patients treated with finasteride	40	supp	<5	supp
	Patients treated with dutasteride	<5	supp	<5	supp
	Patients treated with topical minoxidil	<5	supp	<5	supp
	Non-treated	109	supp	<5	supp
No	**Androgenetic alopecia**				
	All patients	478	supp	<5	supp
	Patients treated with finasteride	108	supp	<5	supp
	Patients treated with dutasteride	<5	supp	<5	supp
	Patients treated with topical minoxidil	24	supp	<5	supp
	Non-treated	360	supp	<5	supp
Yes	**BPH**				
	All patients	15,038	68,170.05	185	2.71 (2.34, 3.13)
	Patients treated with finasteride	3,063	7,472.56	15	2.01 (1.12, 3.31)
	Patients treated with dutasteride	754	supp	<5	supp
	Patients treated with alpha blockers	9,065	17,433.43	59	3.38 (2.58, 4.37)
	Patients treated with tadalafil	439	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC

	Non-treated	11,591	41,314.88	115	2.78 (2.30, 3.34)
No	**BPH**				
	All patients	59,520	294,942.38	133	0.45 (0.38, 0.53)
	Patients treated with finasteride	12,806	37,170.58	16	0.43 (0.25, 0.70)
	Patients treated with dutasteride	2,578	supp	<5	supp
	Patients treated with alpha blockers	36,993	77,430.37	43	0.56 (0.40, 0.75)
	Patients treated with tadalafil	1,191	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	46,353	176,128.64	85	0.48 (0.39, 0.60)

* Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.
NC= No person counts
supp= If the number of participants or incident cases was <5; associated statistics have been suppressed to protect patients' confidentiality.

Appendix II. Table S 18. Incidence rates of composite suicidality outcome per 1,000 person- years in androgenetic alopecia and BPH patients by history of psychiatric disorders and by treatment in Danish DK-DHR data source.

History of psychiatric disorders	Cohorts	Number of participants	Follow-up (person-years)	Number of incident cases (suicide related events)	Incidence Rate/1,000 PYs (95% CI)
Yes	**General adult male population**	269,642	2,989,105.08	2,226	0.74 (0.71, 0.78)
No	**General adult male population**	2,652,695	29,365,122.48	3,675	0.13 (0.12, 0.13)
Yes	**Androgenetic alopecia**				
	All patients	60	supp	<5	supp
	Patients treated with finasteride	8	supp	<5	supp
	Patients treated with dutasteride	NC	NC	NC	NC
	Patients treated with topical minoxidil	<5	supp	<5	supp
	Non-treated	43	supp	<5	supp

No	**Androgenetic alopecia**				
	All patients	389	supp	<5	supp
	Patients treated with finasteride	62	supp	<5	supp
	Patients treated with dutasteride	<5	supp	<5	supp
	Patients treated with topical minoxidil	9	supp	<5	supp
	Non-treated	320	supp	<5	supp
Yes	**BPH**				
	All patients	17,067	92,208.60	43	0.47 (0.34, 0.63)
	Patients treated with finasteride	4,563	supp	<5	supp
	Patients treated with dutasteride	1,407	supp	<5	supp
	Patients treated with alpha blockers	5,284	supp	<5	supp
	Patients treated with tadalafil	1,080	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	7,094	33,048.60	20	0.61 (0.37, 0.93)
No	**BPH**				
	All patients	76,212	480,509.07	34	0.07 (0.05, 0.10)
	Patients treated with finasteride	21,028	supp	<5	supp
	Patients treated with dutasteride	6,909	supp	<5	supp
	Patients treated with alpha blockers	24,944	supp	<5	supp
	Patients treated with tadalafil	4,369	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	35,878	187,359.98	12	0.06 (0.03, 0.11)

* Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.
NC= No person counts
supp= If the number of participants or incident cases was <5; associated statistics have been suppressed to protect patients' confidentiality.

Appendix II. Table S 19. Incidence rates of composite suicidality outcome per 1,000 person-years in androgenetic alopecia and BPH patients by history of psychiatric disorders and by treatment in IPCI data source.

history of psychiatric disorders	Cohorts	Number of participants	Follow-up (person-years)	Number of incident cases (suicide related events)	Incidence Rate/1,000 PYs (95% CI)
Yes	**General adult male population**	86,958	421,632.84	671	1.59 (1.47, 1.72)
No	**General adult male population**	913,678	4,614,829.80	1,78	0.39 (0.37, 0.40)
Yes	**Androgenetic alopecia**				
	All patients	613	supp	<5	supp
	Patients treated with finasteride	208	supp	<5	supp
	Patients treated with dutasteride	8	supp	<5	supp
	Patients treated with topical minoxidil	104	supp	<5	supp
	Non-treated	391	supp	<5	supp
No	**Androgenetic alopecia**				
	All patients	1,336	supp	<5	supp
	Patients treated with finasteride	397	supp	<5	supp
	Patients treated with dutasteride	7	supp	<5	supp
	Patients treated with topical minoxidil	200	supp	<5	supp
	Non-treated	924	supp	<5	supp
Yes	**BPH**				
	All patients	3,212	12,836.84	10	0.78 (0.37, 1.43)
	Patients treated with finasteride	143	supp	<5	supp
	Patients treated with dutasteride	302	supp	<5	supp
	Patients treated with alpha blockers	1,963	supp	<5	supp
	Patients treated with tadalafil	100	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC

	Non-treated	2,824	9,957.00	7	0.70 (0.28, 1.45)
No	**BPH**				
	All patients	12,108	53,485.30	23	0.43 (0.27, 0.65)
	Patients treated with finasteride	424	supp	<5	supp
	Patients treated with dutasteride	1,16	supp	<5	supp
	Patients treated with alpha blockers	7,140	supp	<5	supp
	Patients treated with tadalafil	224	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	10,663	40,960.23	17	0.42 (0.24, 0.66)

* Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.
NC= No person counts
supp= If the number of participants or incident cases was <5; associated statistics have been suppressed to protect patients' confidentiality.

Appendix II. Table S 20. Incidence rates of composite suicidality outcome per 1,000 person-years in androgenetic alopecia and BPH patients by history of psychiatric disorders and by treatment in InGef RDB data source.

history of psychiatric disorders	Cohorts	Number of participants	Follow-up (person-years)	Number of incident cases (suicide related events)	Incidence Rate/1,000 PYs (95% CI)
Yes	**General adult male population**	68,615	407,939.51	349	0.86 (0.77, 0.95)
No	**General adult male population**	3,994,614	25,374,000.36	1,446	0.06 (0.05, 0.06)
Yes	**Androgenetic alopecia**				
	All patients	27	supp	<5	supp
	Patients treated with finasteride	588	supp	<5	supp
	Patients treated with dutasteride	NC	NC	NC	NC
	Patients treated with topical minoxidil	NC	NC	NC	NC
	Non-treated	28	supp	<5	supp

No	**Androgenetic alopecia**				
	All patients	208	supp	<5	supp
	Patients treated with finasteride	<5	supp	<5	supp
	Patients treated with dutasteride	NC	NC	NC	NC
	Patients treated with topical minoxidil	NC	NC	NC	NC
	Non-treated	201	supp	<5	supp
Yes	**BPH**				
	All patients	16,800	48,712.59	23	0.47 (0.30, 0.71)
	Patients treated with finasteride	NC	NC	NC	NC
	Patients treated with dutasteride	612	supp	<5	supp
	Patients treated with alpha blockers	11,681	24,178.22	15	0.62 (0.35, 1.02)
	Patients treated with tadalafil	136	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	14,752	40,310.46	28	0.69 (0.46, 1.00)
No	**BPH**				
	All patients	145,433	495,302.59	45	0.09 (0.07, 0.12)
	Patients treated with finasteride	4,633	supp	<5	supp
	Patients treated with dutasteride	4,328	supp	<5	supp
	Patients treated with alpha blockers	83,897	196,370.20	21	0.11 (0.07, 0.16)
	Patients treated with tadalafil	716	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	121,589	387,032.79	43	0.11 (0.08, 0.15)

* Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.
NC= No person counts
supp= If the number of participants or incident cases was <5; associated statistics have been suppressed to protect patients' confidentiality.

Appendix II. Table S 21. Incidence rates of composite suicidality outcome per 1,000 person-years in androgenetic alopecia and BPH patients by history of psychiatric disorders and by treatment in Croatian NAJS data source.

history of psychiatric disorders	Cohorts	Number of participants	Follow-up (person-years)	Number of incident cases (suicide related events)	Incidence Rate/1,000 PYs (95% CI)
Yes	**General adult male population**	213,510	1,530,725.96	2,609	1.70 (1.64, 1.77)
No	**General adult male population**	1,705,440	11,789,355.08	5,105	0.43 (0.42, 0.45)
Yes	**Androgenetic alopecia**				
	All patients	276	supp	<5	supp
	Patients treated with finasteride	<5	supp	<5	supp
	Patients treated with dutasteride	<5	supp	<5	supp
	Patients treated with topical minoxidil	NC	NC	NC	NC
	Non-treated	307	supp	<5	supp
No	**Androgenetic alopecia**				
	All patients	1,364	supp	<5	supp
	Patients treated with finasteride	11	supp	<5	supp
	Patients treated with dutasteride	<5	supp	<5	supp
	Patients treated with topical minoxidil	NC	NC	NC	NC
	Non-treated	1,398	supp	<5	supp
Yes	**BPH**				
	All patients	80,332	335,342.97	444	1.32 (1.20, 1.45)
	Patients treated with finasteride	2,071	3,019.38	9	2.98 (1.36, 5.66)
	Patients treated with dutasteride	27,971	37,098.19	55	1.48 (1.12, 1.93)
	Patients treated with alpha blockers	54,789	47,613.54	55	1.16 (0.87, 1.50)
	Patients treated with tadalafil	NC	NC	NC	NC

	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	71,200	242,287.28	290	1.20 (1.06, 1.34)
No	**BPH**				
	All patients	199,031	904,029.28	435	0.48 (0.44, 0.53)
	Patients treated with finasteride	5,616	9,108.82	6	0.66 (0.24, 1.43)
	Patients treated with dutasteride	55,084	77,097.35	44	0.57 (0.41, 0.77)
	Patients treated with alpha blockers	118,298	117,305.88	73	0.62 (0.49, 0.78)
	Patients treated with tadalafil	NC	NC	NC	NC
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	178,057	656,930.92	279	0.42 (0.38, 0.48)

* Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.
NC= No person counts
supp= If the number of participants or incident cases was <5; associated statistics have been suppressed to protect patients' confidentiality.

Appendix II. Table S 22. Incidence rates of composite suicidality outcome per 1,000 person-years in androgenetic alopecia and BPH patients by history of psychiatric disorders and by treatment in SIDIAP data source.

history of psychiatric disorders	Cohorts	Number of participants	Follow-up (person-years)	Number of incident cases (suicide related events)	Incidence Rate/1,000 PYs (95% CI)
Yes	**General adult male population**	211,03	2,107,713.62	2,654	1.26 (1.21, 1.31)
No	**General adult male population**	3,105,513	29,520,224.68	8,021	0.27 (0.27, 0.28)
Yes	**Androgenetic alopecia**				
	All patients	1,073	5,542.89	8	1.44 (0.62, 2.84)
	Patients treated with finasteride	39	supp	<5	supp
	Patients treated with dutasteride	34	supp	<5	supp
	Patients treated with topical minoxidil	109	supp	<5	supp

	Non-treated	910	supp	<5	supp
No	**Androgenetic alopecia**				
	All patients	4,192	26,588.04	7	0.26 (0.11, 0.54)
	Patients treated with finasteride	142	supp	<5	supp
	Patients treated with dutasteride	63	supp	<5	supp
	Patients treated with topical minoxidil	357	supp	<5	supp
	Non-treated	3,663	23,712.38	6	0.25 (0.09, 0.55)
Yes	**BPH**				
	All patients	60,162	296,016.90	356	1.20 (1.08, 1.33)
	Patients treated with finasteride	3,321	7,957.58	8	1.01 (0.43, 1.98)
	Patients treated with dutasteride	7,729	16,204.32	11	0.68 (0.34, 1.21)
	Patients treated with alpha blockers	34,211	82,674.34	108	1.31 (1.07, 1.58)
	Patients treated with tadalafil	1,200	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	52,374	229,736.67	290	1.26 (1.12, 1.42)
No	**BPH**				
	All patients	253,635	1,543,902.53	412	0.27 (0.24, 0.29)
	Patients treated with finasteride	12,267	34,606.60	15	0.43 (0.24, 0.71)
	Patients treated with dutasteride	28,435	72,805.87	19	0.26 (0.16, 0.41)
	Patients treated with alpha blockers	129,014	365,850.14	100	0.27 (0.22, 0.33)
	Patients treated with tadalafil	2,459	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	218,476	1,148,156.98	298	0.26 (0.23, 0.29)

* Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.
NC= No person counts
supp= If the number of participants or incident cases was <5; associated statistics have been suppressed to protect patients' confidentiality.

Appendix II. Table S 23. Incidence rates of composite suicidality outcome per 1,000 person-years in androgenetic alopecia and BPH patients by prior sexual dysfunction and by treatment in BIFAP data source.

history of sexual dysfunction	Cohorts	Number of participants	Follow-up (person-years)	Number of incident cases (suicide related events)	Incidence Rate/1,000 PYs (95% CI)
Yes	**General adult male population**	49,264	533,771.82	324	0.61 (0.54, 0.68)
No	**General adult male population**	8,571,956	73,759,180.70	30,911	0.42 (0.41, 0.42)
Yes	**Androgenetic alopecia**				
	All patients	185	supp	<5	supp
	Patients treated with finasteride	13	supp	<5	supp
	Patients treated with dutasteride	7	supp	<5	supp
	Patients treated with topical minoxidil	<5	supp	<5	supp
	Non-treated	178	supp	<5	supp
No	**Androgenetic alopecia**				
	All patients	9,095	34,137.38	15	0.44 (0.25, 0.72)
	Patients treated with finasteride	1,126	supp	<5	supp
	Patients treated with dutasteride	209	supp	<5	supp
	Patients treated with topical minoxidil	<5	supp	<5	supp
	Non-treated	8,752	29,744.91	13	0.44 (0.23, 0.75)
Yes	**BPH**				
	All patients	18,925	82,512.74	67	0.81 (0.63, 1.03)
	Patients treated with finasteride	81	supp	<5	supp
	Patients treated with dutasteride	4,291	supp	<5	supp
	Patients treated with alpha blockers	7,423	supp	<5	supp
	Patients treated with tadalafil	1,455	supp	<5	supp

	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	14,618	54,371.62	46	0.85 (0.62, 1.13)
No	**BPH**				
	All patients	425,87	2,126,468.74	1,166	0.55 (0.52, 0.58)
	Patients treated with finasteride	3,122	7,722.76	10	1.29 (0.62, 2.38)
	Patients treated with dutasteride	87,283	228,496.20	121	0.53 (0.44, 0.63)
	Patients treated with alpha blockers	151,447	167,649.99	72	0.43 (0.34, 0.54)
	Patients treated with tadalafil	2,963	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	333,900	1,403,739.95	764	0.54 (0.51, 0.58)

* Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.
NC= No person counts
supp= If the number of participants or incident cases was <5; associated statistics have been suppressed to protect patients' confidentiality.

Appendix II. Table S 24. Incidence rates of composite suicidality outcome per 1,000 person-years in androgenetic alopecia and BPH patients by prior sexual dysfunction and by treatment in CPRD-Gold data source.

history of sexual dysfunction	Cohorts	Number of participants	Follow-up (person-years)	Number of incident cases (suicide related events)	Incidence Rate/1,000 PYs (95% CI)
Yes	**General adult male population**	158,423	996,018.47	1,396	1.40 (1.33, 1.48)
No	**General adult male population**	4,177,901	24,637,986.12	36,377	1.48 (1.46, 1.49)
Yes	**Androgenetic alopecia**				
	All patients	26	supp	<5	supp
	Patients treated with finasteride	5	supp	<5	supp
	Patients treated with dutasteride	NC	NC	NC	NC
	Patients treated with topical minoxidil	<5	supp	<5	supp

	Non-treated	22	supp	<5	supp
No	**Androgenetic alopecia**				
	All patients	603	2,799.89	5	1.79 (0.58, 4.17)
	Patients treated with finasteride	143	supp	<5	supp
	Patients treated with dutasteride	supp	supp	<5	supp
	Patients treated with topical minoxidil	26	supp	<5	supp
	Non-treated	447	supp	<5	supp
Yes	**BPH**				
	All patients	12,965	58,299.78	68	1.17 (0.91, 1.48)
	Patients treated with finasteride	2,234	5,484.93	6	1.09 (0.40, 2.38)
	Patients treated with dutasteride	449	supp	<5	supp
	Patients treated with alpha blockers	6,187	11,722.38	17	1.45 (0.84, 2.32)
	Patients treated with tadalafil	1,079	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	7,606	25,954.14	29	1.12 (0.75, 1.60)
No	**BPH**				
	All patients	61,593	304,812.65	250	0.82 (0.72, 0.93)
	Patients treated with finasteride	13,635	39,158.21	25	0.64 (0.41, 0.94)
	Patients treated with dutasteride	2,883	supp	<5	supp
	Patients treated with alpha blockers	39,871	83,141.41	85	1.02 (0.82, 1.26)
	Patients treated with tadalafil	551	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	50,338	191,489.39	171	0.89 (0.76, 1.04)

* Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.
NC= No person counts
supp= If the number of participants or incident cases was <5; associated statistics have been suppressed to protect patients' confidentiality.

Appendix II. Table S 25. Incidence rates of composite suicidality outcome per 1,000 person-years in androgenetic alopecia and BPH patients by prior sexual dysfunction and by treatment in DK-DHR data source.

history of sexual dysfunction	Cohorts	Number of participants	Follow-up (person-years)	Number of incident cases (suicide related events)	Incidence Rate/1,000 PYs (95% CI)
Yes	**General adult male population**	140,355	1,678,719.13	389	0.23 (0.21, 0.26)
No	**General adult male population**	2,778,467	30,675,508.43	5,512	0.18 (0.17, 0.18)
Yes	**Androgenetic alopecia**				
	All patients	46	supp	<5	supp
	Patients treated with finasteride	10	supp	<5	supp
	Patients treated with dutasteride	NC	NC	NC	NC
	Patients treated with topical minoxidil	<5	supp	<5	supp
	Non-treated	36	supp	<5	supp
No	**Androgenetic alopecia**				
	All patients	403	supp	<5	supp
	Patients treated with finasteride	60	supp	<5	supp
	Patients treated with dutasteride	<5	supp	<5	supp
	Patients treated with topical minoxidil	9	supp	<5	supp
	Non-treated	327	supp	<5	supp
Yes	**BPH**				
	All patients	23,971	133,102.97	25	0.19 (0.12, 0.28)
	Patients treated with finasteride	4,408	supp	<5	supp
	Patients treated with dutasteride	1,328	supp	<5	supp
	Patients treated with alpha blockers	4,955	supp	<5	supp
	Patients treated with tadalafil	2,999	supp	<5	supp

	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	6,024	26,228.36	6	0.23 (0.08, 0.50)
No	**BPH**				
	All patients	69,308	439,614.70	52	0.12 (0.09, 0.16)
	Patients treated with finasteride	21,183	supp	<5	supp
	Patients treated with dutasteride	6,988	supp	<5	supp
	Patients treated with alpha blockers	25,273	supp	<5	supp
	Patients treated with tadalafil	2,450	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	36,948	194,180.22	26	0.13 (0.09, 0.20)

* Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.
NC= No person counts
supp= If the number of participants or incident cases was <5; associated statistics have been suppressed to protect patients' confidentiality.

Appendix II. Table S 26. Incidence rates of composite suicidality outcome per 1,000 person-years in androgenetic alopecia and BPH patients by prior sexual dysfunction and by treatment in IPCI data source.

history of sexual dysfunction	Cohorts	Number of participants	Follow-up (person-years)	Number of incident cases (suicide related events)	Incidence Rate/1,000 PYs (95% CI)
Yes	**General adult male population**	10,368	57,986.13	43	0.74 (0.54, 1.00)
No	**General adult male population**	990,268	4,978,476.51	2,408	0.48 (0.46, 0.50)
Yes	**Androgenetic alopecia**				
	All patients	50	supp	<5	supp
	Patients treated with finasteride	14	supp	<5	supp
	Patients treated with dutasteride	NC	NC	NC	NC
	Patients treated with topical minoxidil	9	supp	<5	supp

	Non-treated	33	supp	<5	supp
No	**Androgenetic alopecia**				
	All patients	1,899	supp	<5	supp
	Patients treated with finasteride	591	supp	<5	supp
	Patients treated with dutasteride	15	supp	<5	supp
	Patients treated with topical minoxidil	295	supp	<5	supp
	Non-treated	1,282	supp	<5	supp
Yes	**BPH**				
	All patients	1,097	supp	<5	supp
	Patients treated with finasteride	27	supp	<5	supp
	Patients treated with dutasteride	75	supp	<5	supp
	Patients treated with alpha blockers	464	supp	<5	supp
	Patients treated with tadalafil	187	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	670	supp	<5	supp
No	**BPH**				
	All patients	14,223	61,710.75	31	0.50 (0.34, 0.71)
	Patients treated with finasteride	540	supp	<5	supp
	Patients treated with dutasteride	1,387	supp	<5	supp
	Patients treated with alpha blockers	8,639	supp	<5	supp
	Patients treated with tadalafil	137	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	12,817	48,665.12	23	0.47 (0.30, 0.71)

* Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.
NC= No person counts
supp= If the number of participants or incident cases was <5; associated statistics have been suppressed to protect patients' confidentiality.

Appendix II. Table S 27. Incidence rates of composite suicidality outcome per 1,000 person-years in androgenetic alopecia and BPH patients by prior sexual dysfunction and by treatment in InGef RDB data source.

history of sexual dysfunction	Cohorts	Number of participants	Follow-up (person-years)	Number of incident cases (suicide related events)	Incidence Rate/1,000 PYs (95% CI)
Yes	**General adult male population**	305	supp	<5	supp
No	**General adult male population**	4,062,924	25,779,928.30	1,794	0.07 (0.07, 0.07)
Yes	**Androgenetic alopecia**				
	All patients	NC	NC	NC	NC
	Patients treated with finasteride	NC	NC	NC	NC
	Patients treated with dutasteride	NC	NC	NC	NC
	Patients treated with topical minoxidil	NC	NC	NC	NC
	Non-treated	NC	NC	NC	NC
No	**Androgenetic alopecia**				
	All patients	235	supp	<5	supp
	Patients treated with finasteride	<5	supp	<5	supp
	Patients treated with dutasteride	NC	NC	NC	NC
	Patients treated with topical minoxidil	NC	NC	NC	NC
	Non-treated	229	supp	<5	supp
Yes	**BPH**				
	All patients	131	supp	<5	supp
	Patients treated with finasteride	<5	supp	<5	supp
	Patients treated with dutasteride	5	supp	<5	supp
	Patients treated with alpha blockers	80	supp	<5	supp
	Patients treated with tadalafil	10	supp	<5	supp

	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	114	supp	<5	supp
No	**BPH**				
	All patients	162,102	543,541.42	68	0.13 (0.10, 0.16)
	Patients treated with finasteride	5,219	supp	<5	supp
	Patients treated with dutasteride	4,935	supp	<5	supp
	Patients treated with alpha blockers	95,498	220,407.78	36	0.16 (0.11, 0.23)
	Patients treated with tadalafil	842	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	136,227	426,950.82	71	0.17 (0.13, 0.21)

* Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.
NC= No person counts
supp= If the number of participants or incident cases was <5; associated statistics have been suppressed to protect patients' confidentiality.

Appendix II. Table S 28. Incidence rates of composite suicidality outcome per 1,000 person-years in androgenetic alopecia and BPH patients by prior sexual dysfunction and by treatment in Croatian NAJS data source.

history of sexual dysfunction	Cohorts	Number of participants	Follow-up (person-years)	Number of incident cases (suicide related events)	Incidence Rate/1,000 PYs (95% CI)
Yes	**General adult male population**	1,712	12,659.61	14	1.11 (0.60, 1.86)
No	**General adult male population**	1,917,238	13,307,421.42	7,700	0.58 (0.57, 0.59)
Yes	**Androgenetic alopecia**				
	All patients	5	supp	<5	supp
	Patients treated with finasteride	<5	supp	<5	supp
	Patients treated with dutasteride	NC	NC	NC	NC

	Patients treated with topical minoxidil	NC	NC	NC	NC
	Non-treated	9	supp	<5	supp
No	**Androgenetic alopecia**				
	All patients	1,635	supp	<5	supp
	Patients treated with finasteride	11	supp	<5	supp
	Patients treated with dutasteride	7	supp	<5	supp
	Patients treated with topical minoxidil	NC	NC	NC	NC
	Non-treated	1,696	supp	<5	supp
Yes	**BPH**				
	All patients	1,574	5,925.86	10	1.69 (0.81, 3.10)
	Patients treated with finasteride	22	supp	<5	supp
	Patients treated with dutasteride	623	supp	<5	supp
	Patients treated with alpha blockers	1,111	supp	<5	supp
	Patients treated with tadalafil	NC	NC	NC	NC
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	1,395	4,552.34	7	1.54 (0.62, 3.17)
No	**BPH**				
	All patients	277,789	1,233,446.39	869	0.70 (0.66, 0.75)
	Patients treated with finasteride	7,665	12,101.89	15	1.24 (0.69, 2.04)
	Patients treated with dutasteride	82,432	113,457.37	98	0.86 (0.70, 1.05)
	Patients treated with alpha blockers	171,976	164,091.67	127	0.77 (0.65, 0.92)
	Patients treated with tadalafil	NC	NC	NC	NC
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	247,862	894,665.85	562	0.63 (0.58, 0.68)

* Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.
NC= No person counts

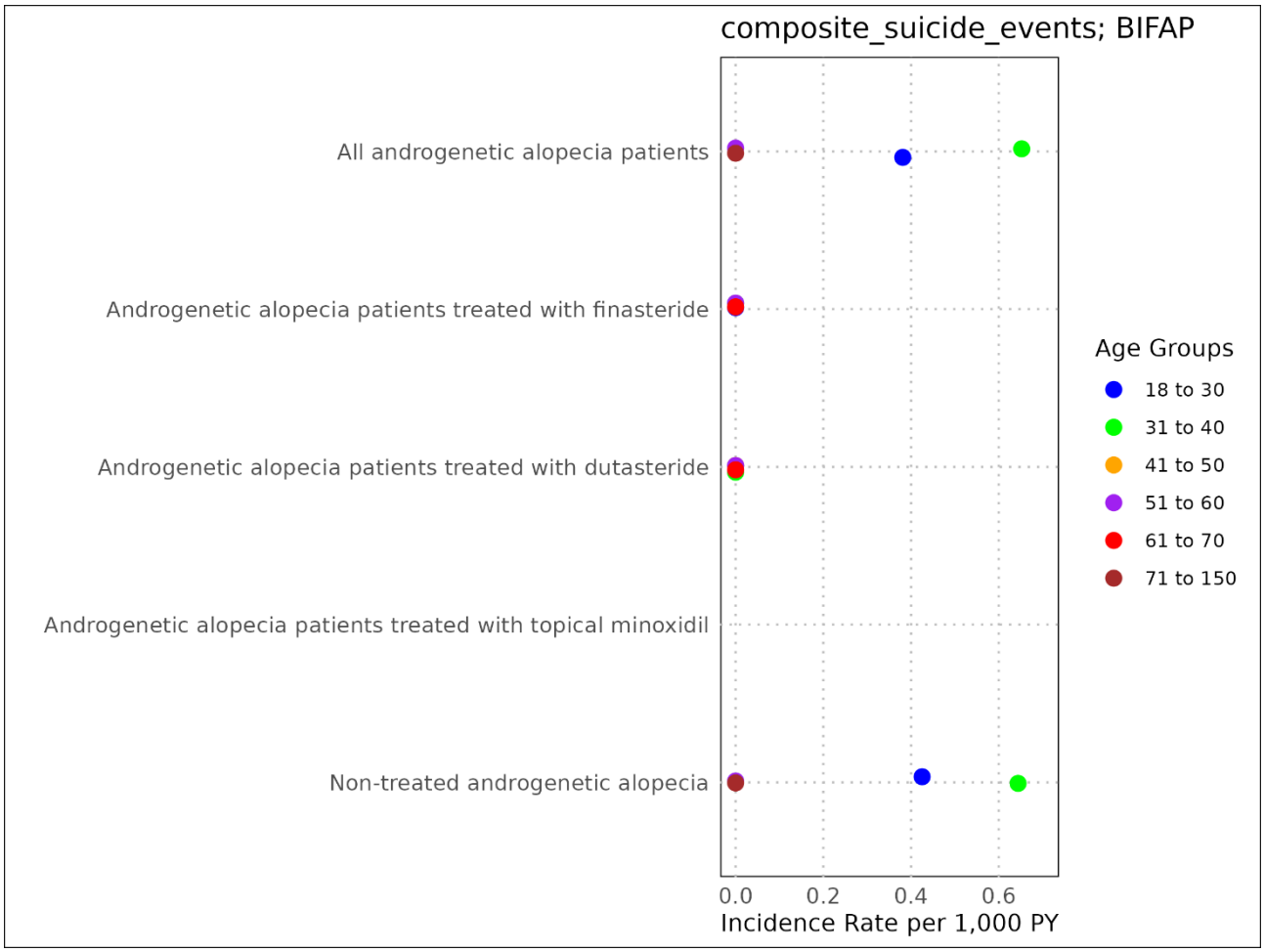
supp= If the number of participants or incident cases was <5; associated statistics have been suppressed to protect patients' confidentiality.

Appendix II. Table S 29. Incidence rates of composite suicidality outcome per 1,000 person-years in androgenetic alopecia and BPH patients by prior sexual dysfunction in SIDIAP data source.

history of sexual dysfunction	Cohorts	Number of participants	Follow-up (person-years)	Number of incident cases (suicide related events)	Incidence Rate/1,000 PYs (95% CI)
Yes	**General adult male population**	18,943	197,698.58	98	0.50 (0.40, 0.60)
No	**General adult male population**	3,297,600	31,430,239.73	10,577	0.34 (0.33, 0.34)
Yes	**Androgenetic alopecia**				
	All patients	145	supp	<5	supp
	Patients treated with finasteride	<5	supp	<5	supp
	Patients treated with dutasteride	5	supp	<5	supp
	Patients treated with topical minoxidil	12	supp	<5	supp
	Non-treated	129	supp	<5	supp
No	**Androgenetic alopecia**				
	All patients	5,120	31,396.48	14	0.45 (0.24, 0.75)
	Patients treated with finasteride	179	supp	<5	supp
	Patients treated with dutasteride	92	supp	<5	supp
	Patients treated with topical minoxidil	454	supp	<5	supp
	Non-treated	4,444	27,833.74	9	0.32 (0.15, 0.61)
Yes	**BPH**				
	All patients	19,017	90,885.97	53	0.58 (0.44, 0.76)
	Patients treated with finasteride	1,134	supp	<5	supp
	Patients treated with dutasteride	2,583	supp	<5	supp

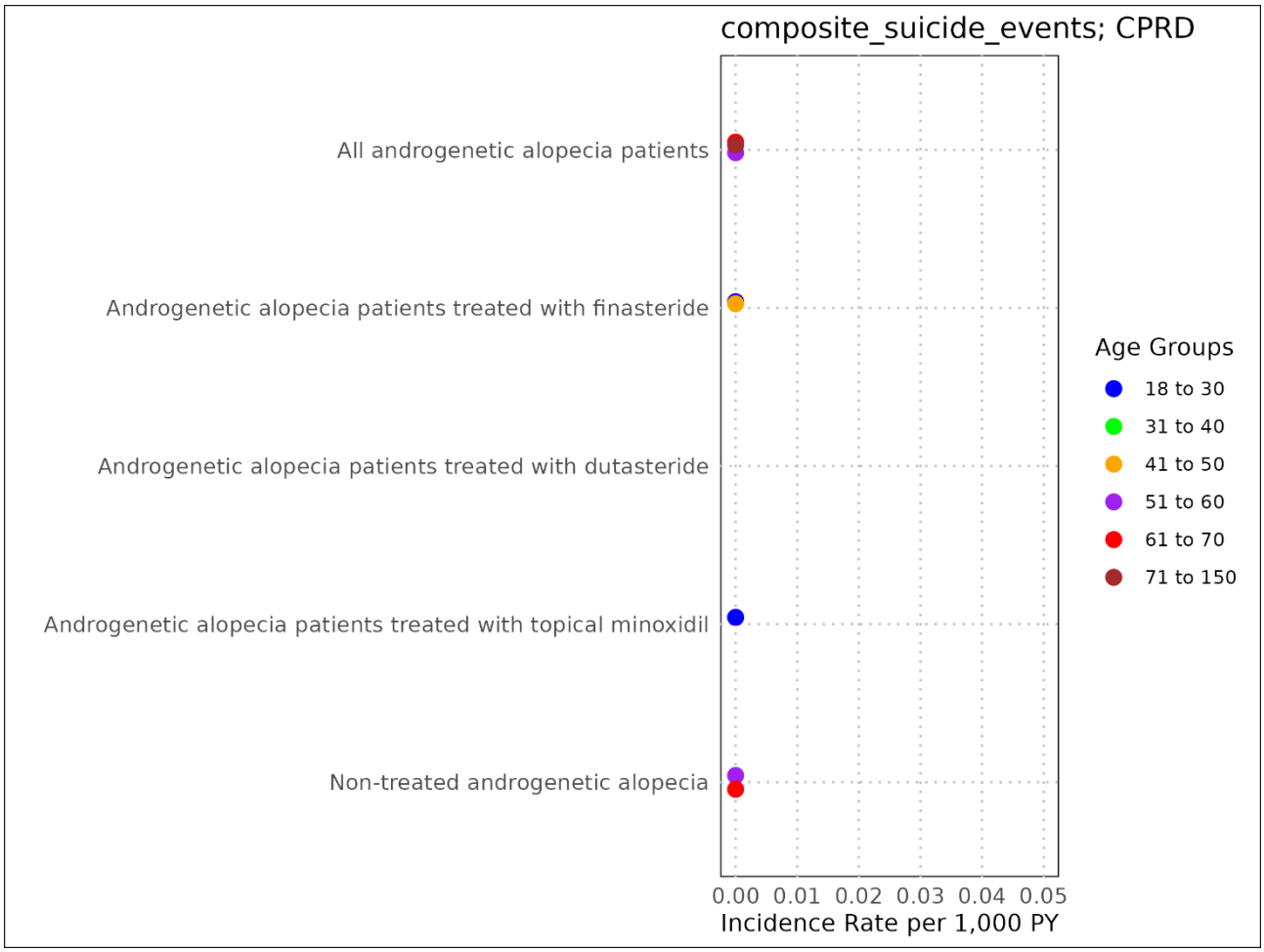
	Patients treated with alpha blockers	11,143	26,594.24	20	0.75 (0.46, 1.16)
	Patients treated with tadalafil	2,035	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	16,209	69,609.20	40	0.57 (0.41, 0.78)
No	**BPH**				
	All patients	294,780	1,749,033.47	715	0.41 (0.38, 0.44)
	Patients treated with finasteride	14,454	39,933.45	19	0.48 (0.29, 0.74)
	Patients treated with dutasteride	33,581	83,819.58	29	0.35 (0.23, 0.50)
	Patients treated with alpha blockers	152,082	421,930.24	188	0.45 (0.38, 0.51)
	Patients treated with tadalafil	1,624	supp	<5	supp
	Patients treated with tadalafil + finasteride/dutasteride	NC	NC	NC	NC
	Non-treated	254,641	1,308,284.45	548	0.42 (0.38, 0.46)

* Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.
NC= No person counts
supp= If the number of participants or incident cases was <5; associated statistics have been suppressed to protect patients' confidentiality.



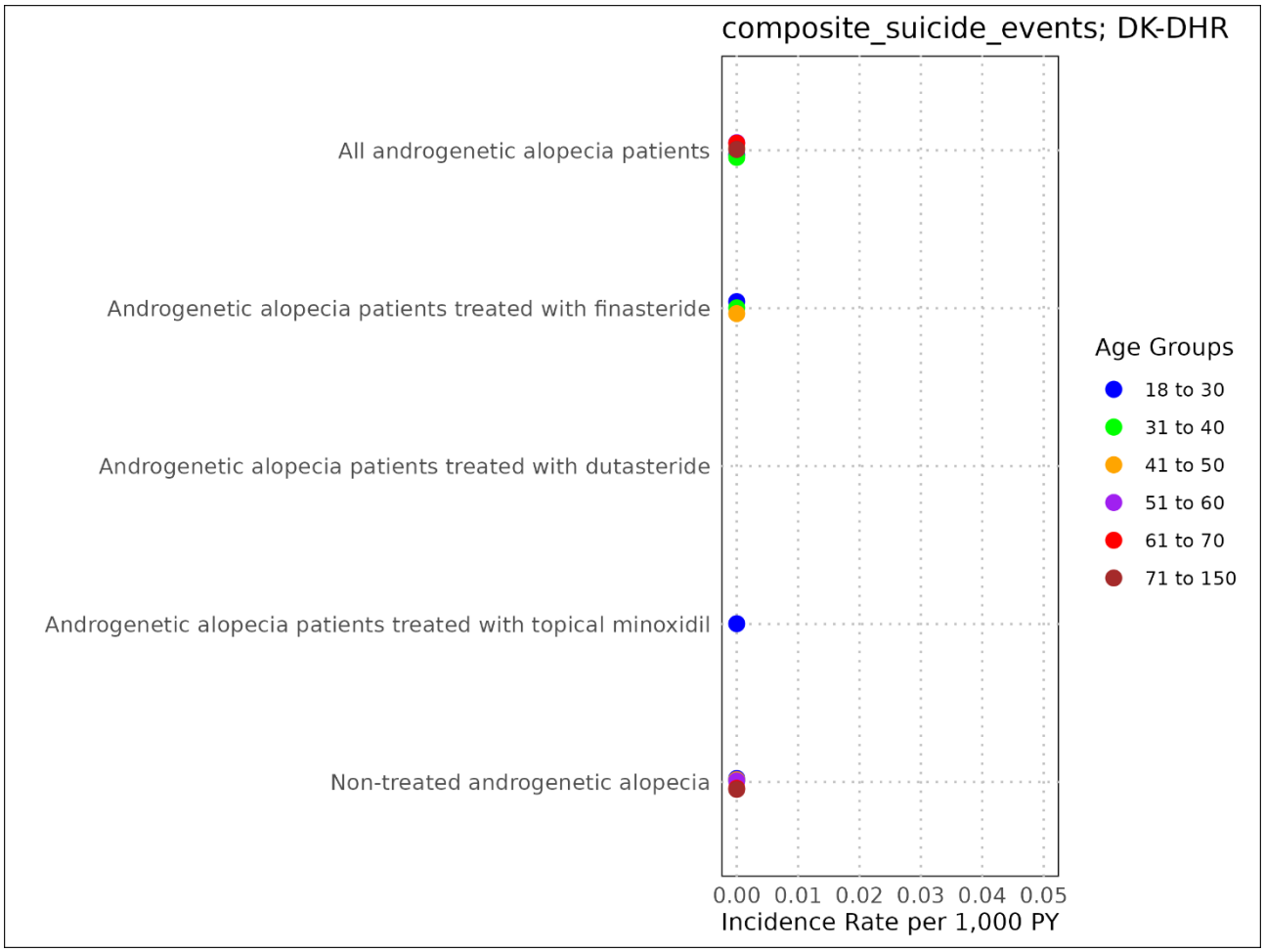
Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.

Appendix II. Figure S 1. Incidence rates of composite suicidality outcome per 1,000 person- years in androgenetic alopecia patients by age group and by treatment in BIFAP data source.



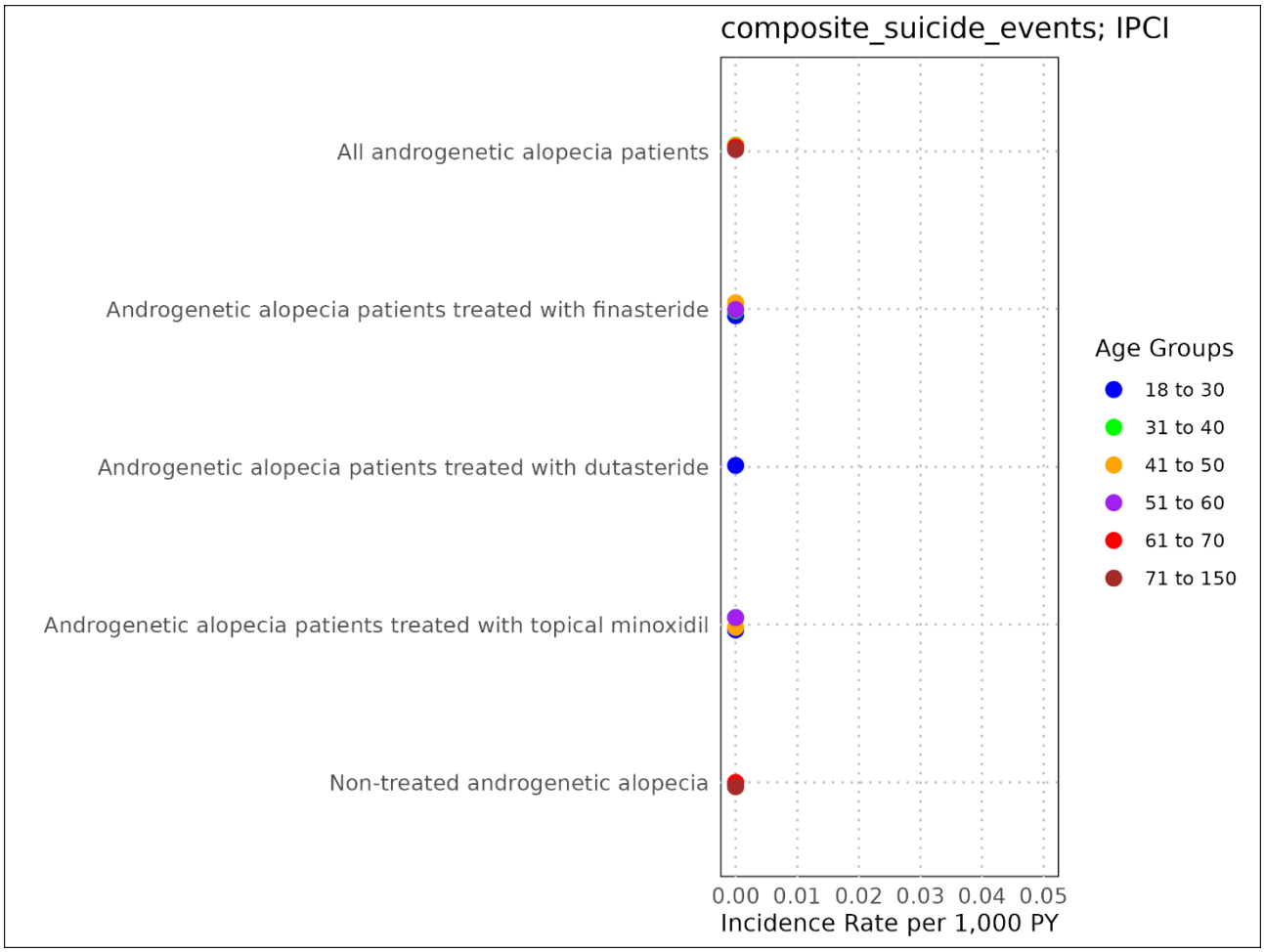
Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.

Appendix II. Figure S 2. Incidence rates of composite suicidality outcome per 1,000 person- years in androgenetic alopecia patients by age group and by treatment in CPRD-Gold data source.



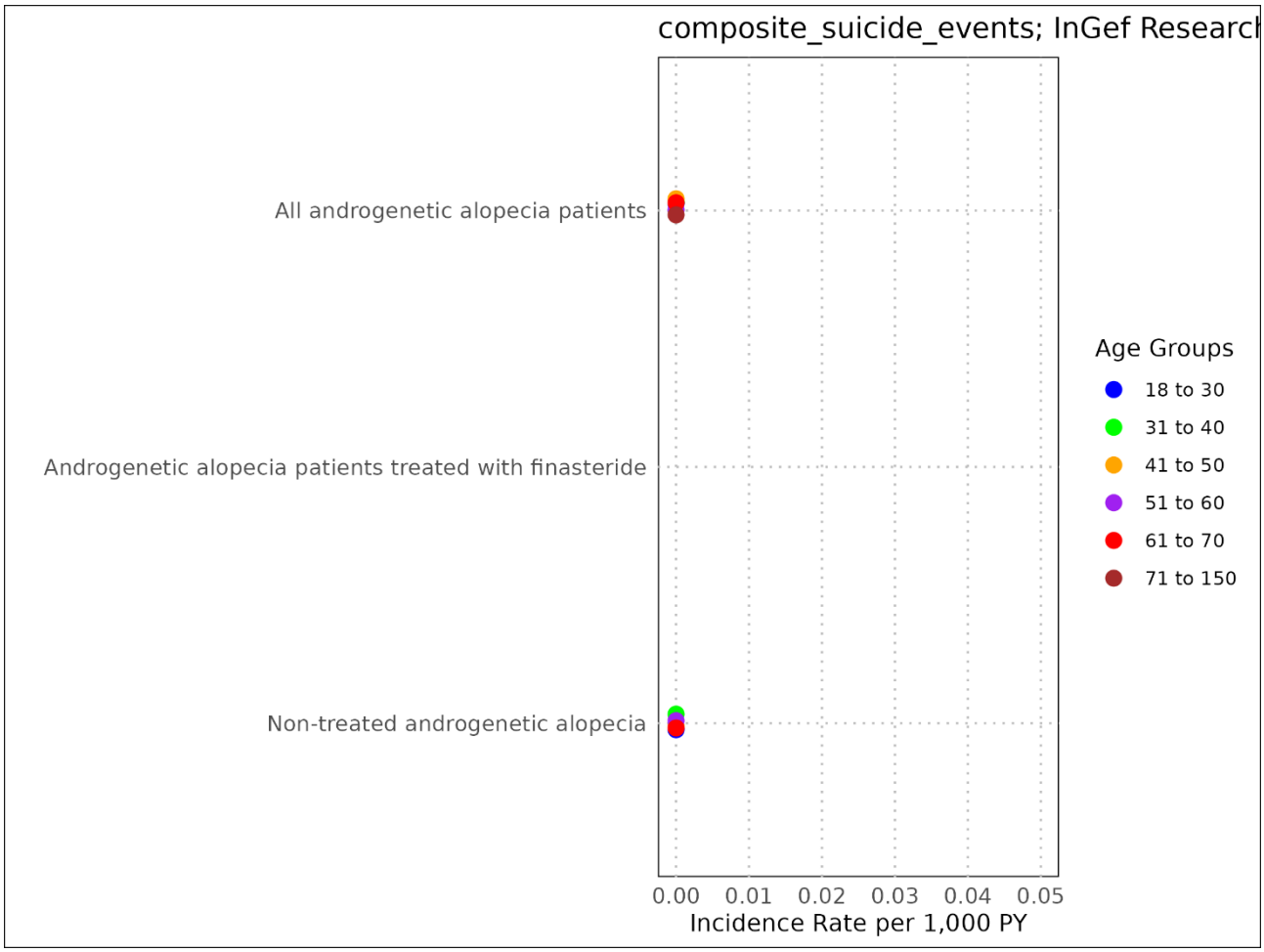
Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.

Appendix II. Figure S 3. Incidence rates of composite suicidality outcome per 1,000 person- years in androgenetic alopecia patients by age group and by treatment in DK-DHR data source.



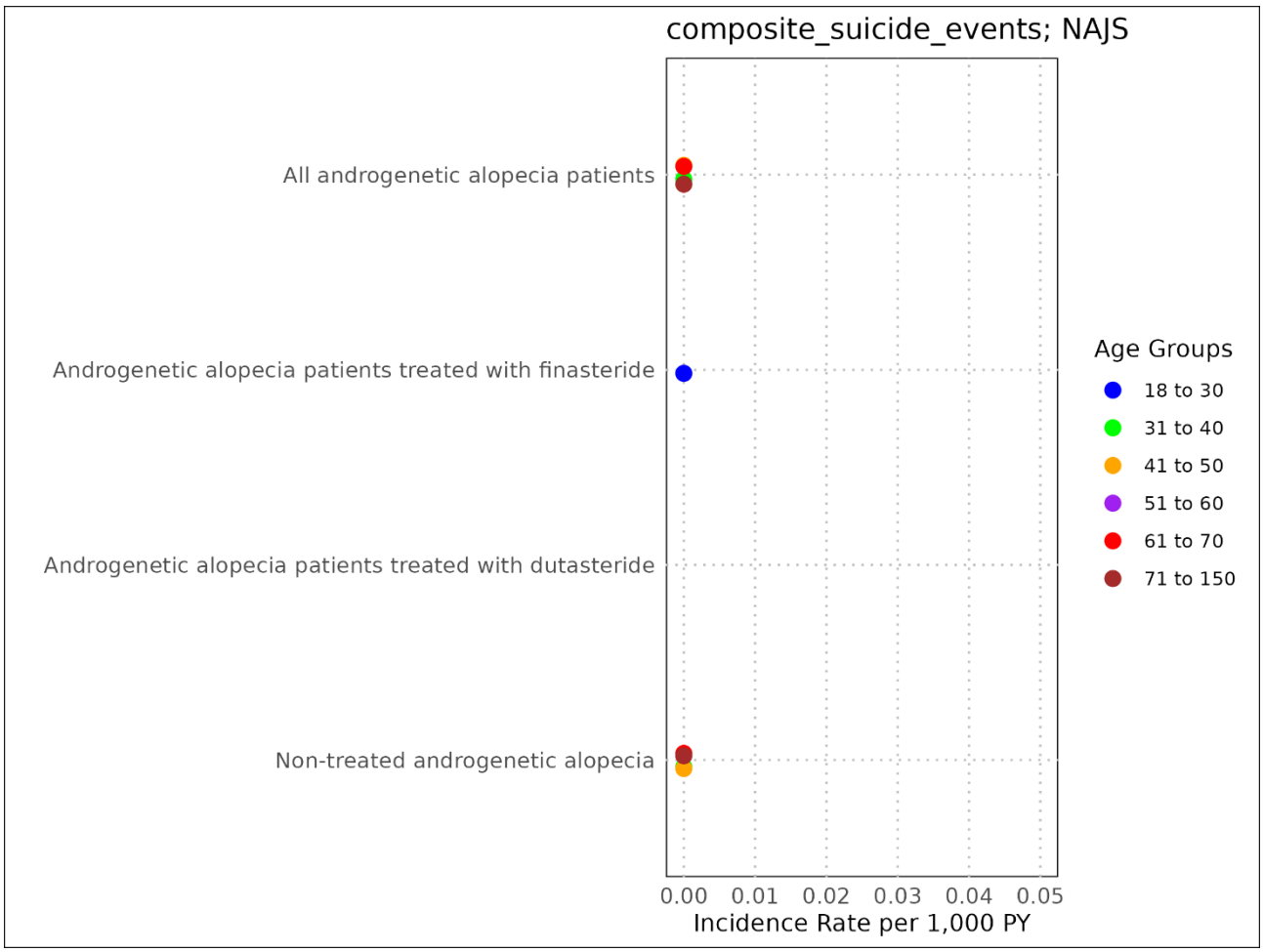
Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.

Appendix II. Figure S 4. Incidence rates of composite suicidality outcome per 1,000 person-years in androgenetic alopecia patients by age group and by treatment in IPCI data source.



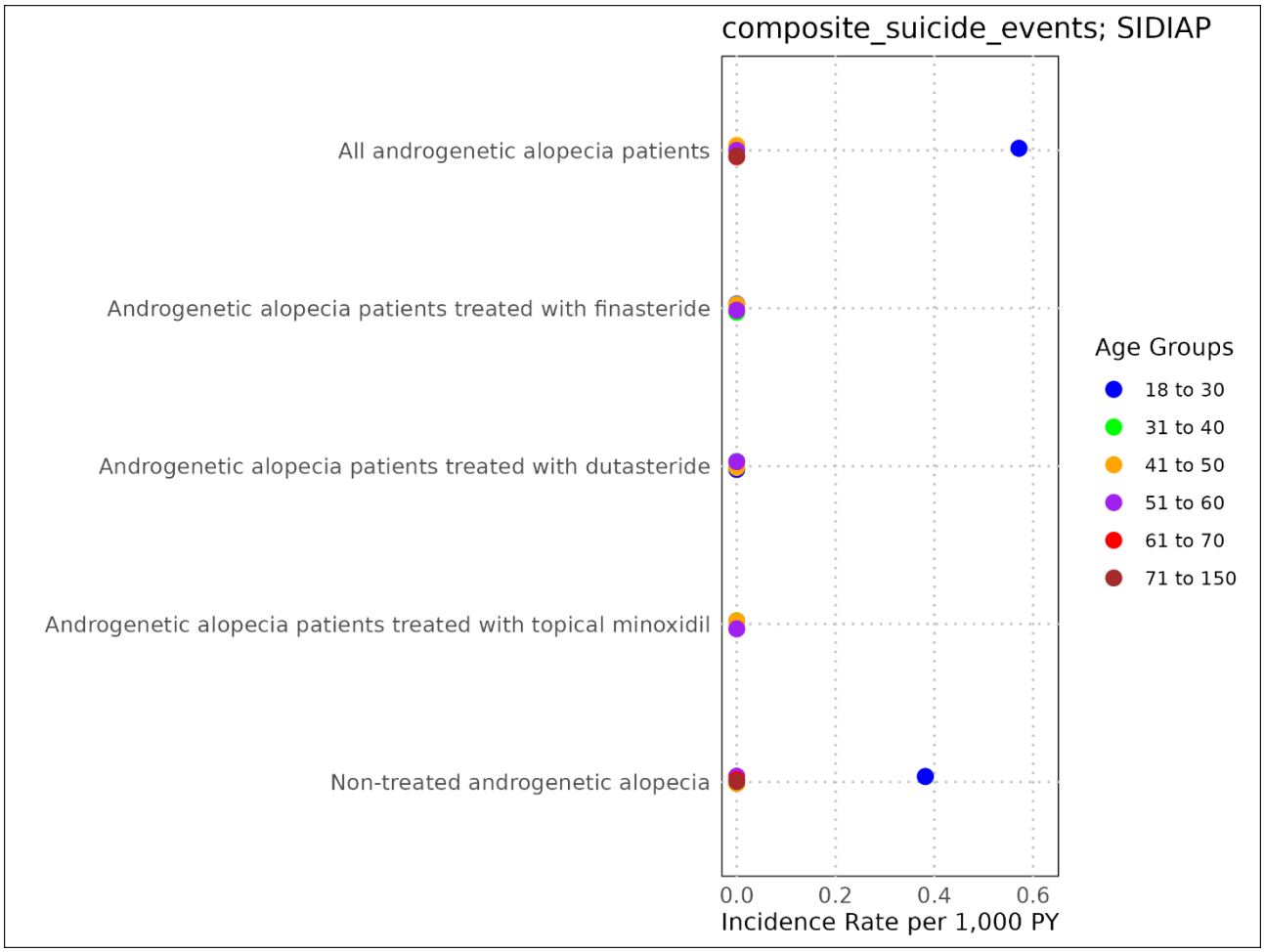
Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.

Appendix II. Figure S 5. Incidence rates of composite suicidality outcome per 1,000 person-years in androgenetic alopecia patients by age group and by treatment in InGef RDB data source.



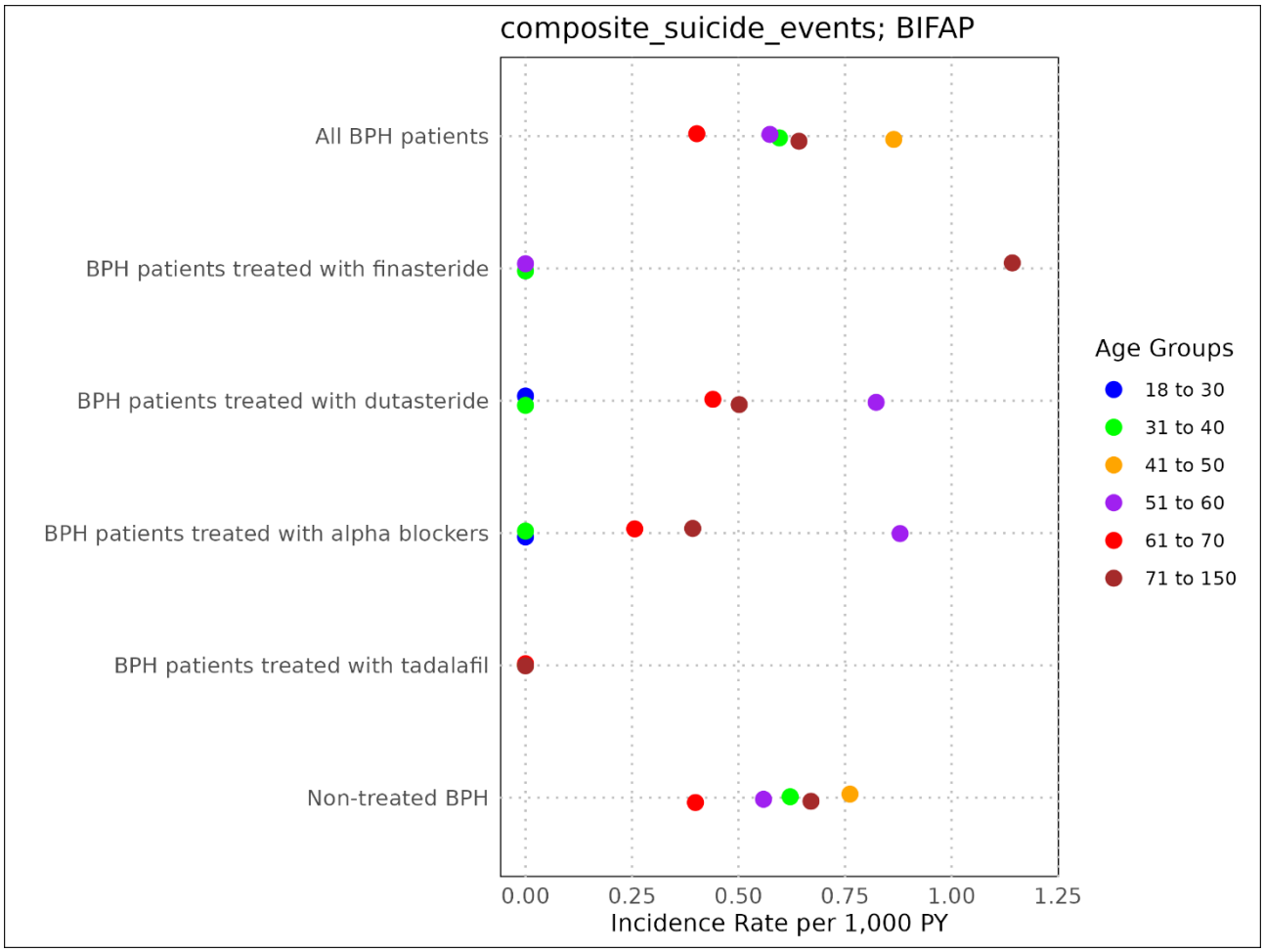
Non-treated refers to patients with no recorded prescription for the study treatments during the follow up time for each condition of interest.

Appendix II. Figure S 6. Incidence rates of composite suicidality outcome per 1,000 person-years in androgenetic alopecia patients by age group and by treatment in NAJS data source.



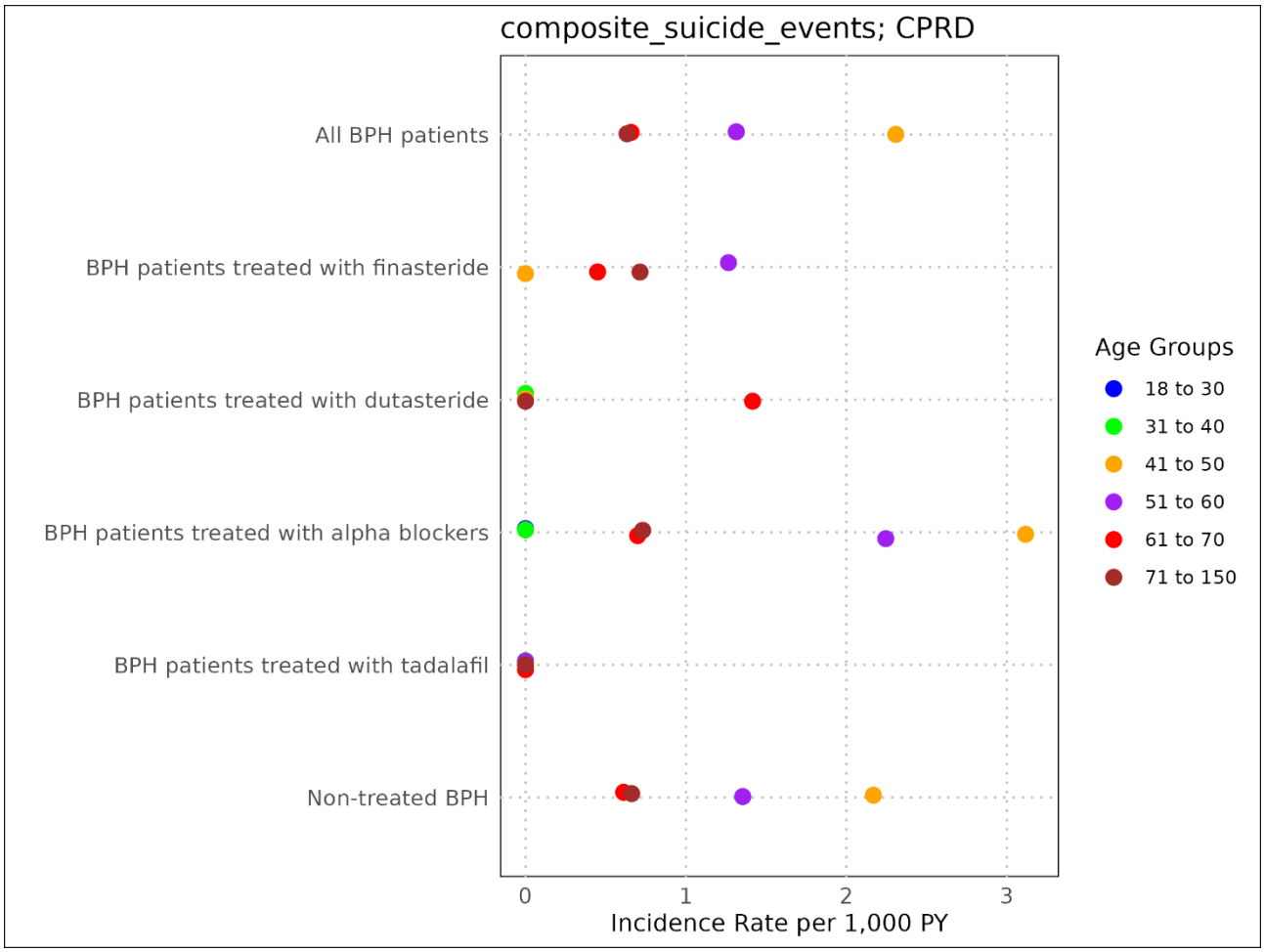
Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.

Appendix II. Figure S 7. Incidence rates of composite suicidality outcome per 1,000 person-years in androgenetic alopecia patients by age group and by treatment in SIDIAP data source.



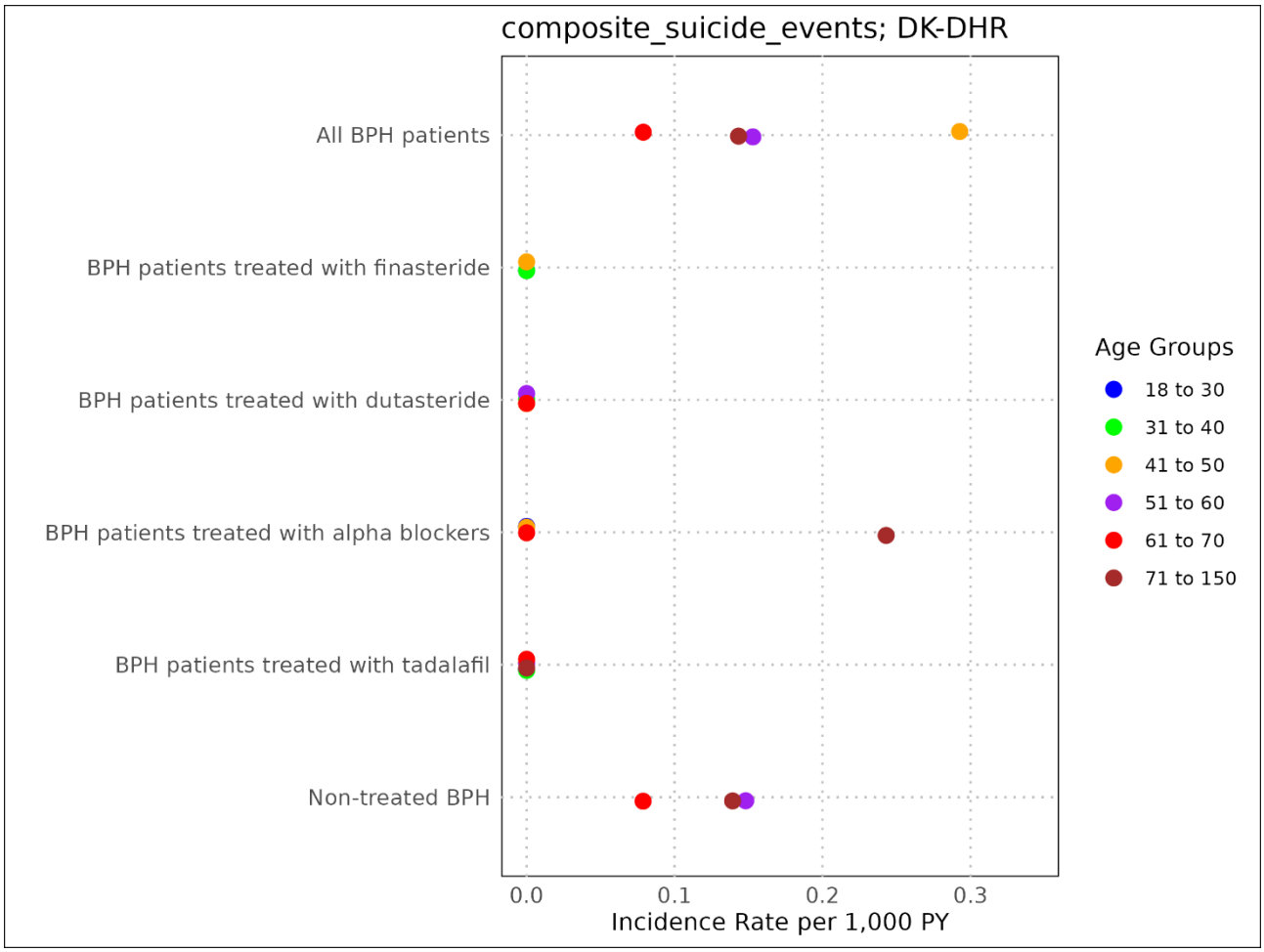
Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.

Appendix II. Figure S 8. Incidence rates of composite suicidality outcome per 1,000 person-years in BPH patients by age group and by treatment in BIFAP data source.



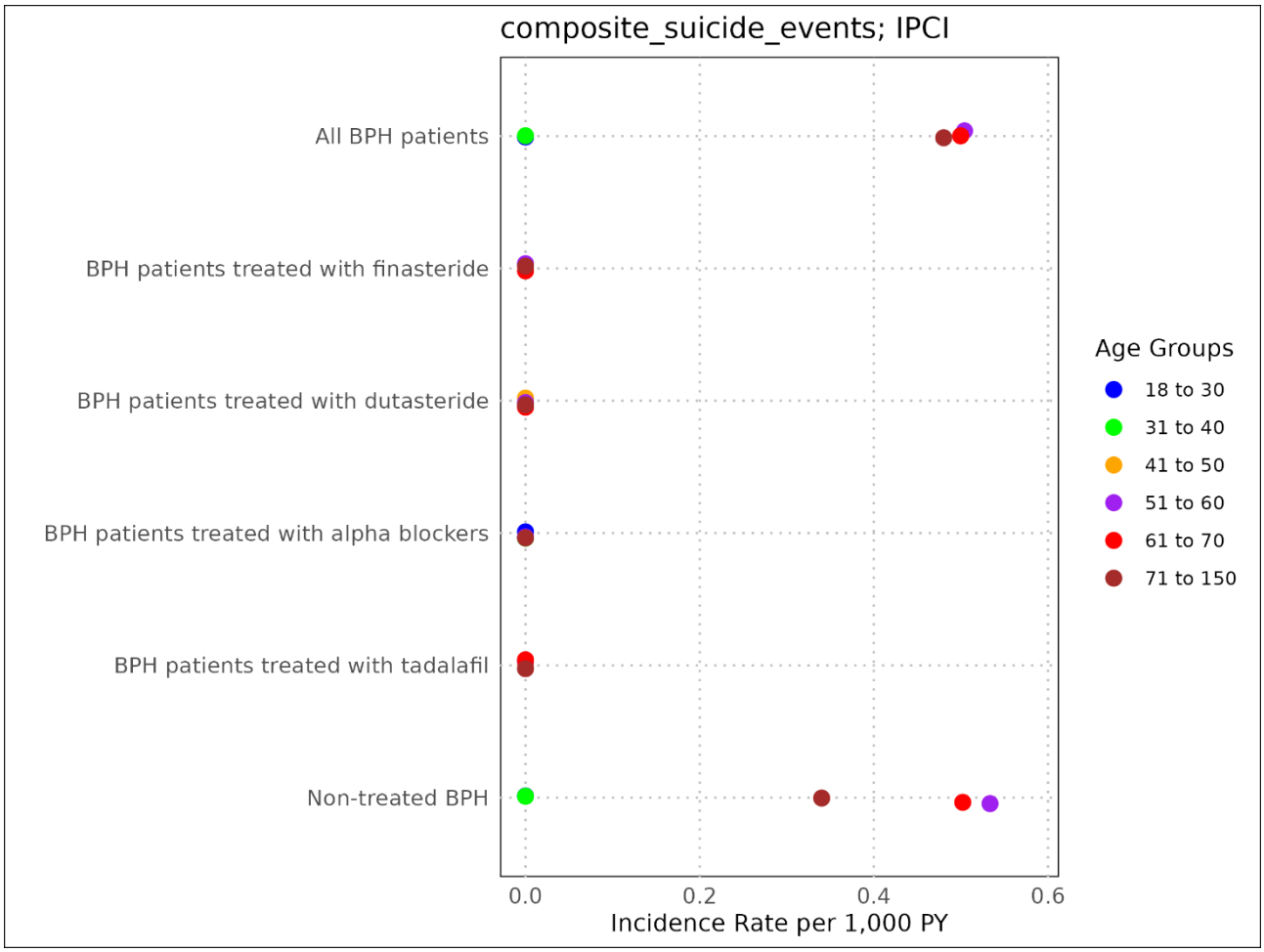
Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.

Appendix II. Figure S 9. Incidence rates of composite suicidality outcome per 1,000 person-years in BPH patients by age group and by treatment in CPRD-Gold data source.



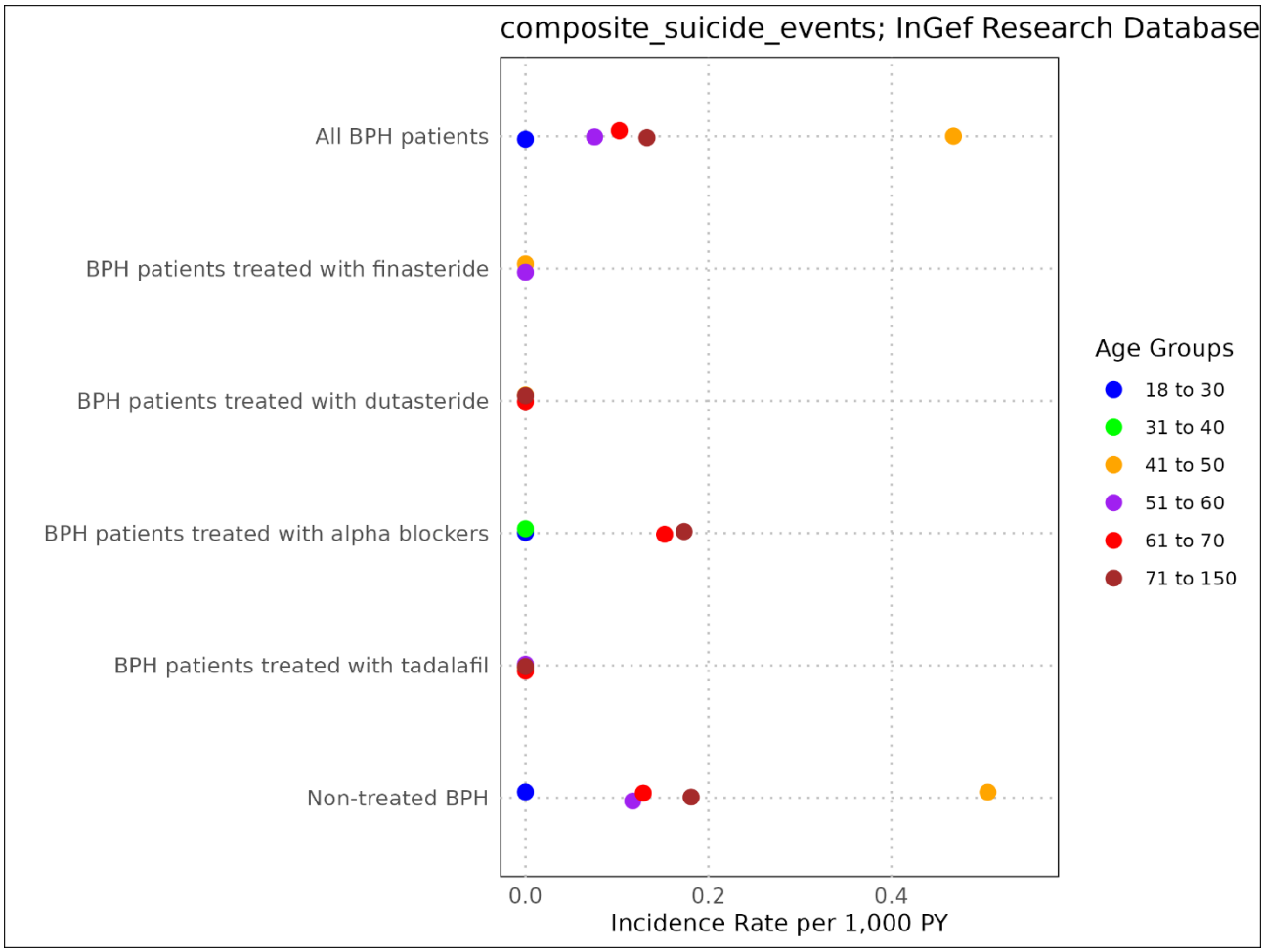
Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.

Appendix II. Figure S 10. Incidence rates of composite suicidality outcome per 1,000 person-years in BPH patients by age group and by treatment in DK-DHR data source.



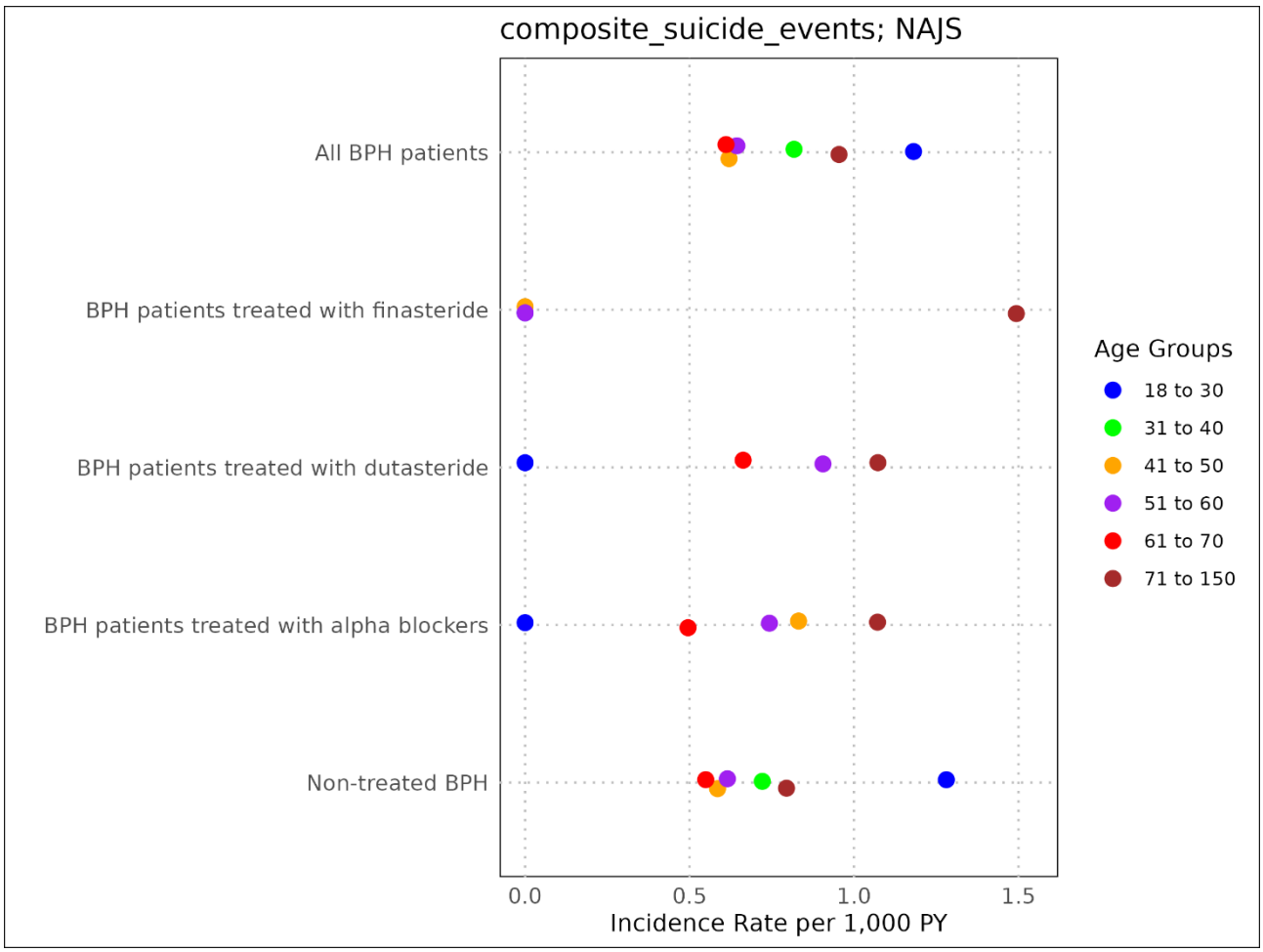
Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.

Appendix II. Figure S 11. Incidence rates of composite suicidality outcome per 1,000 person-years in BPH patients by age group and by treatment in IPCI data source.



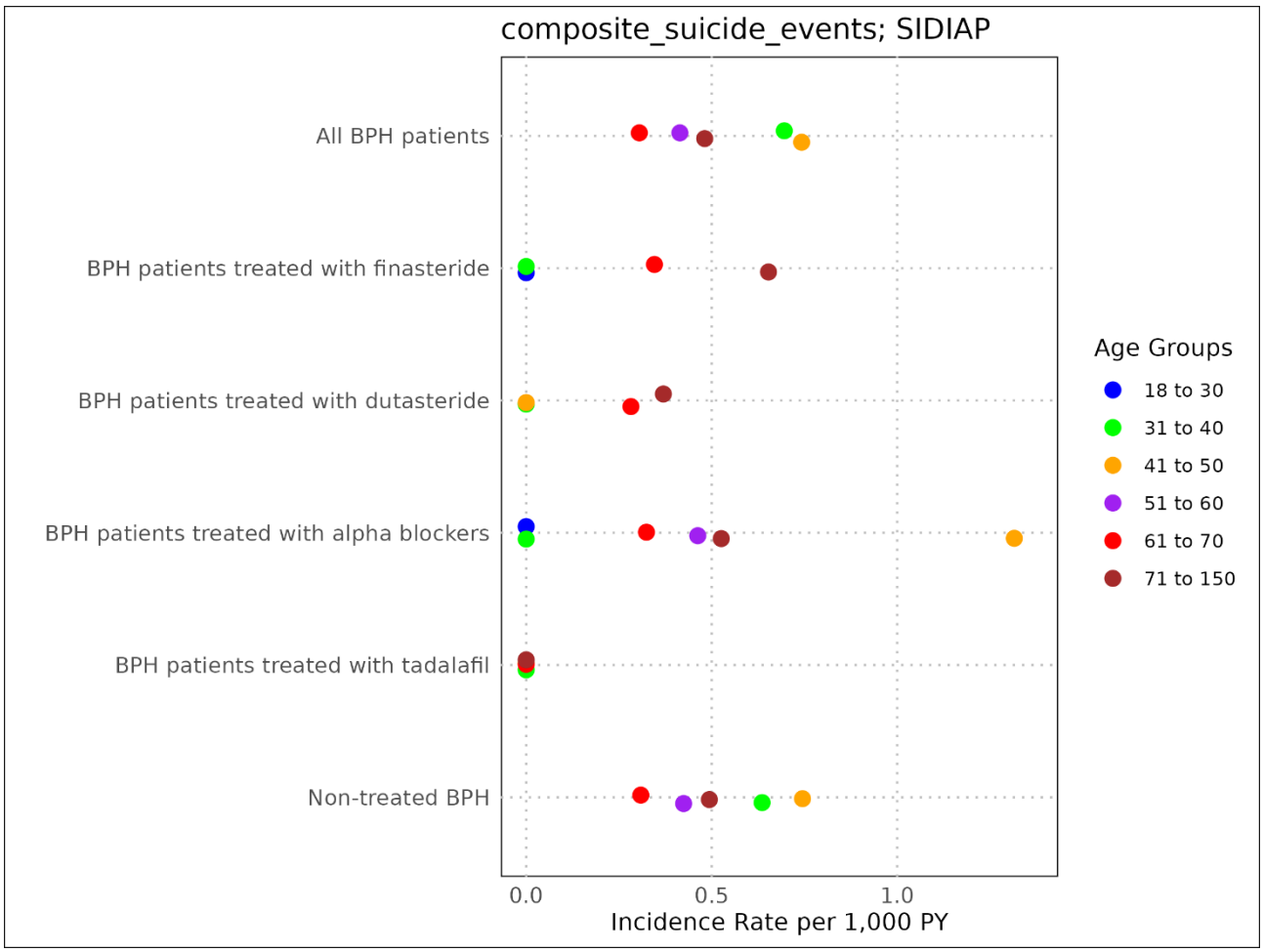
Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.

Appendix II. Figure S 12. Incidence rates of composite suicidality outcome per 1,000 person-years in BPH patients by age group and by treatment in InGef RDB data source.



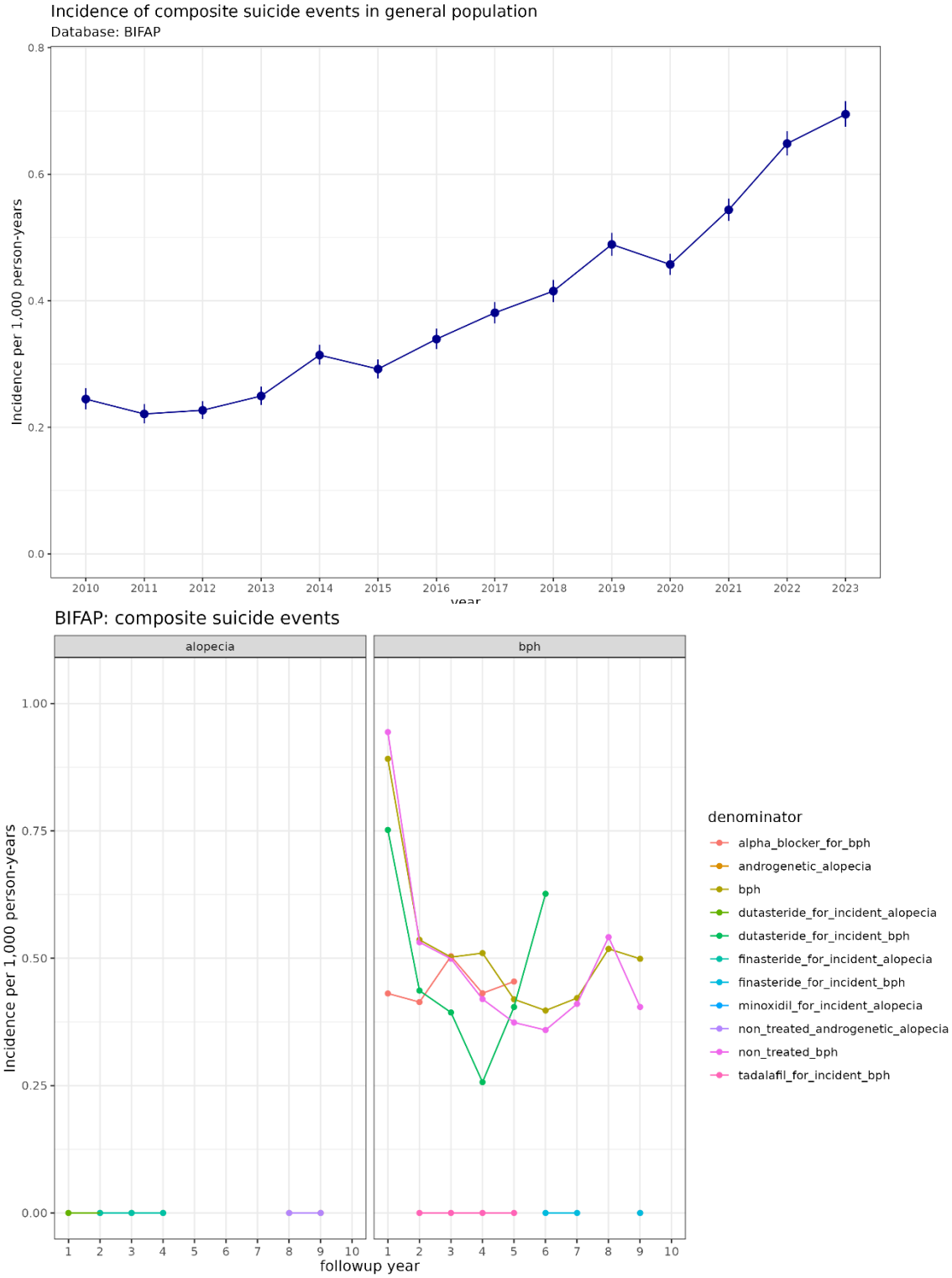
Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.

Appendix II. Figure S 13. Incidence rates of composite suicidality outcome per 1,000 person-years in BPH patients by age group and by treatment in NAJS data source.

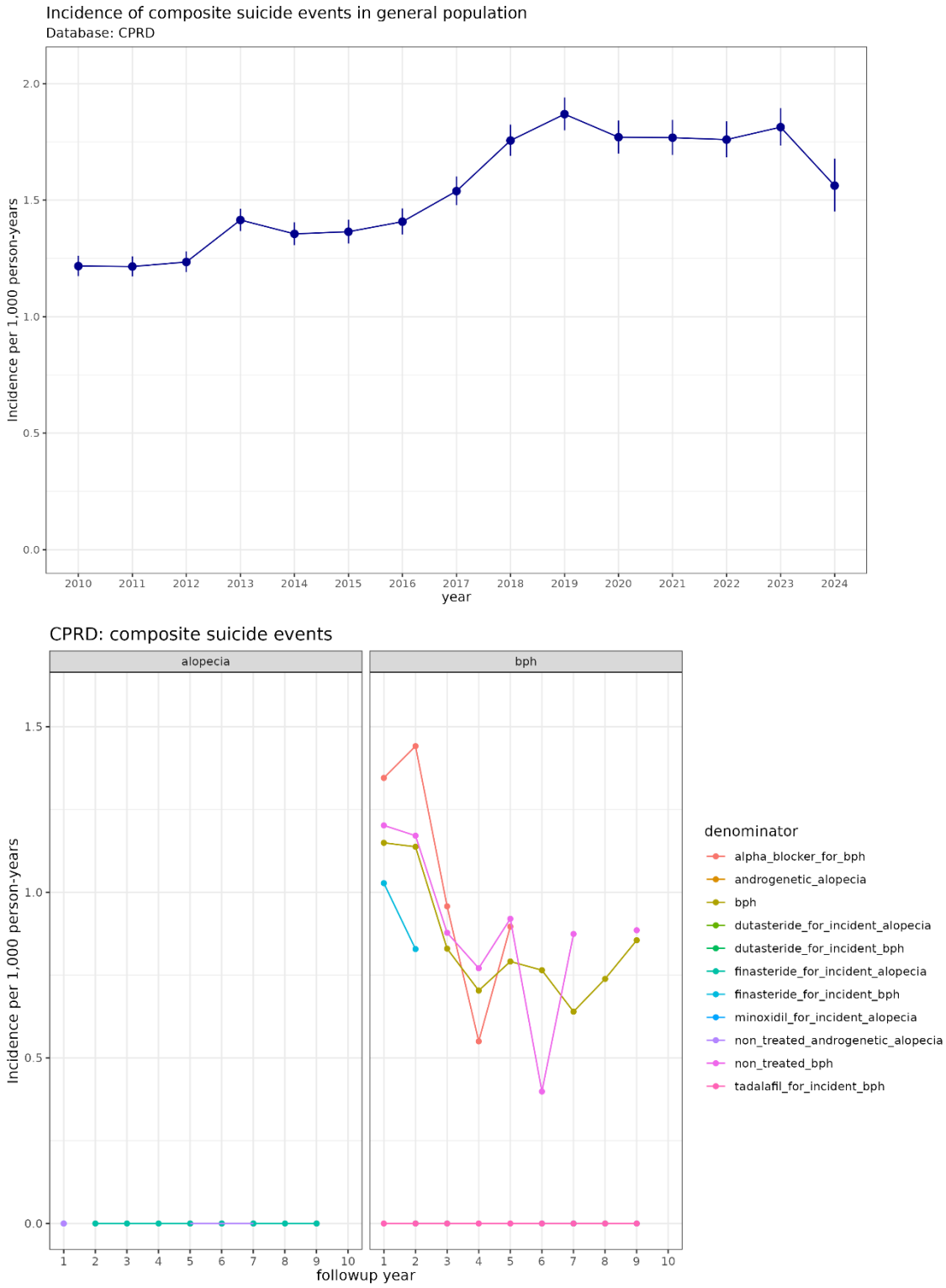


Non-treated refers to patients with no recorded prescription for the study treatments for each condition of interest.

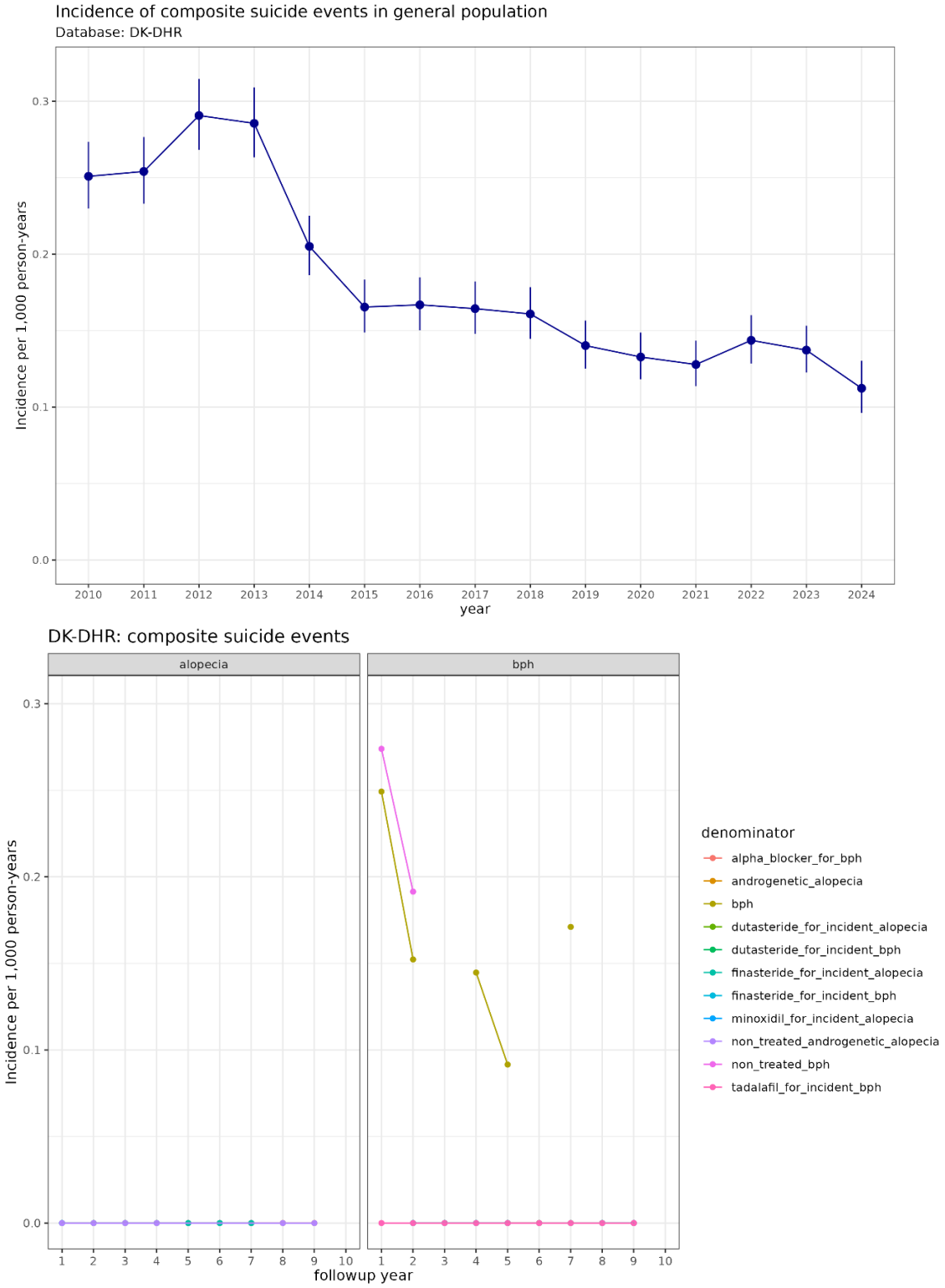
Appendix II. Figure S 14. Incidence rates of composite suicidality outcome per 1,000 person-years in BPH patients by age group and by treatment in SIDIAP data source.



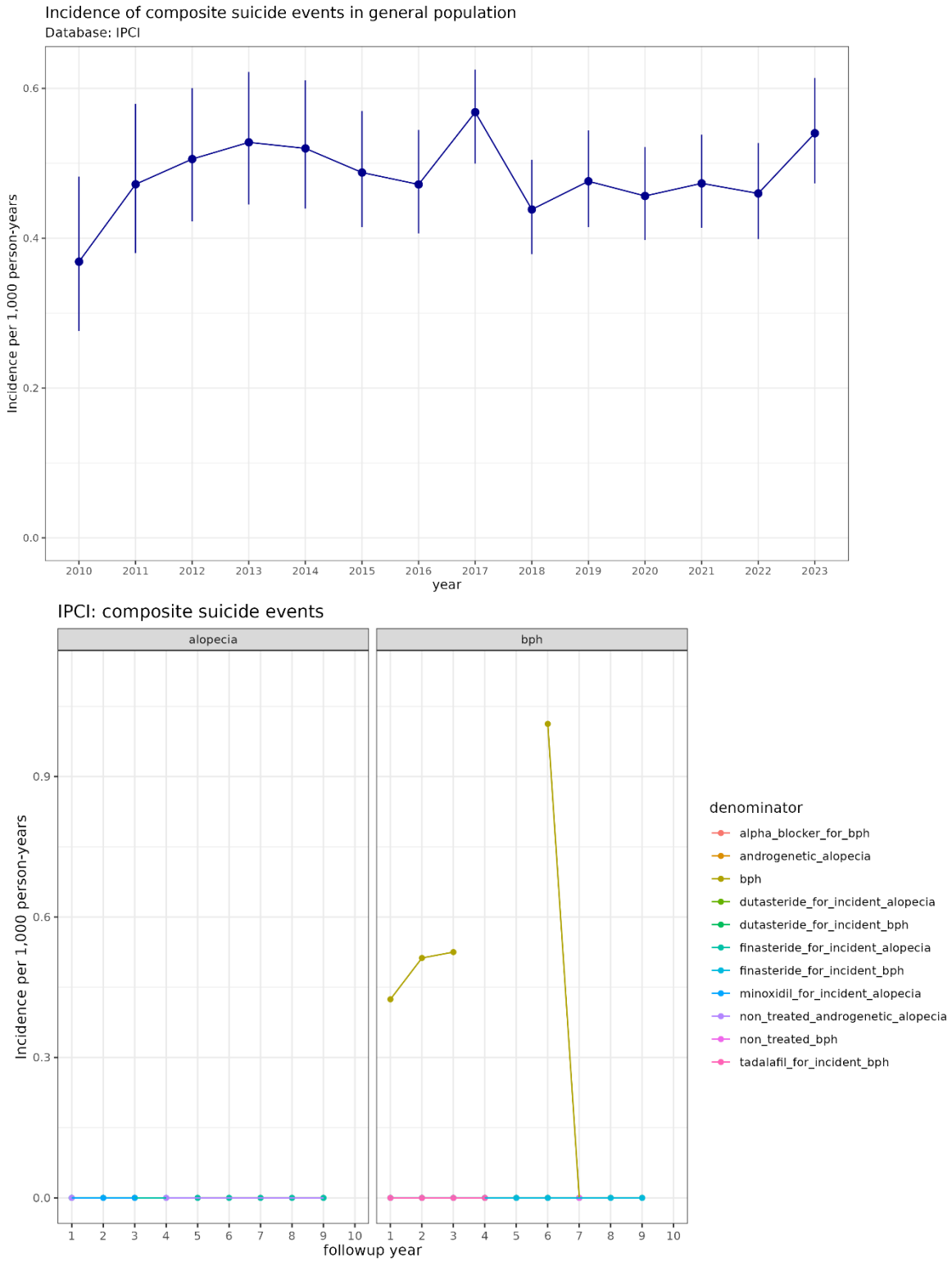
Appendix II. Figure S 15. Incidence rates of composite suicidality outcome per 1,000 person-years over calendar years/follow up years in the general population, androgenetic alopecia, BPH patients, and treatment initiators in BIFAP data source.



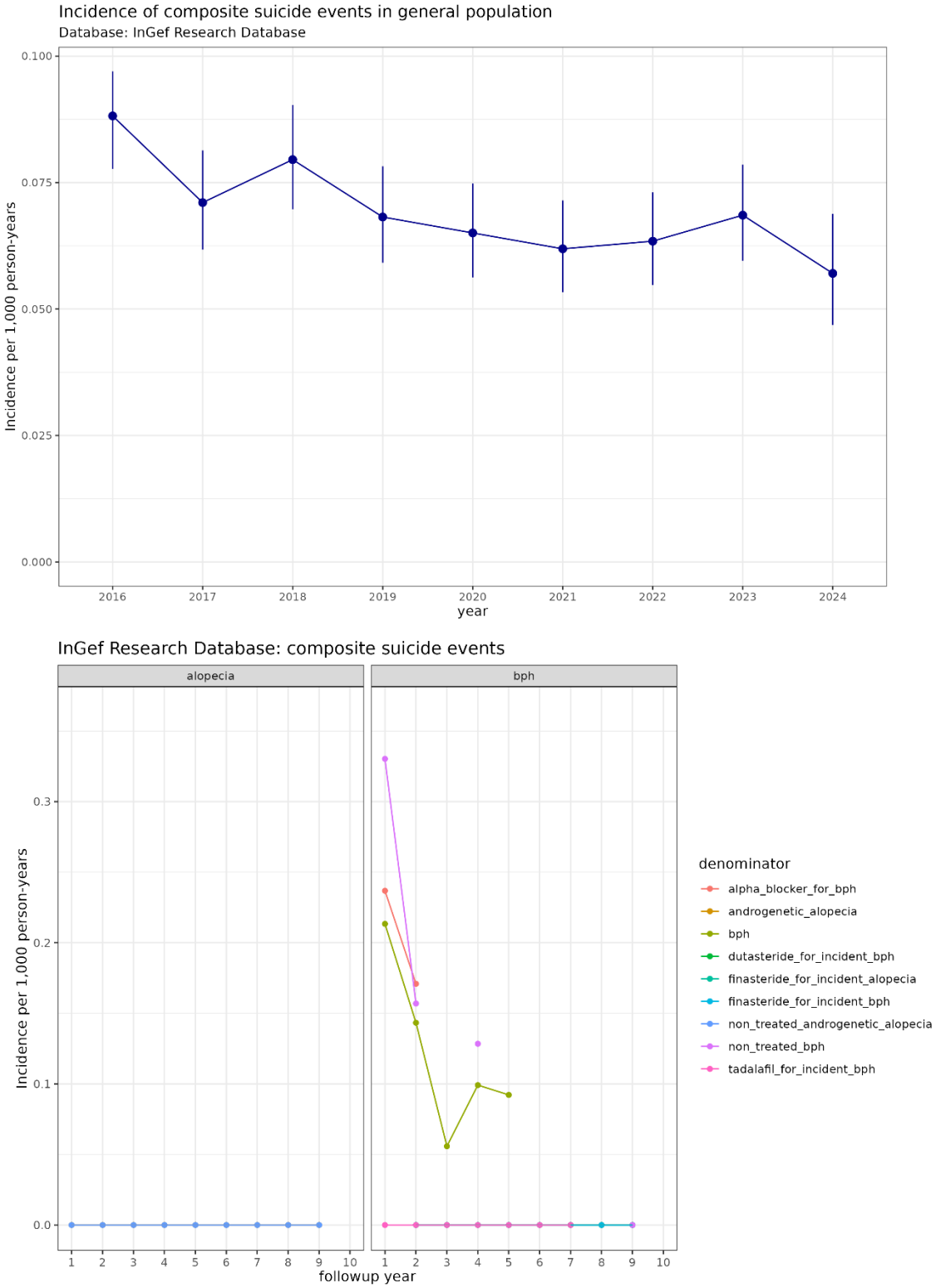
Appendix II. Figure S 16. Incidence rates of composite suicidality outcome per 1,000 person-years over calendar years/follow up years in the general population, androgenetic alopecia, BPH patients, and treatment initiators in CPRD-Gold data source.



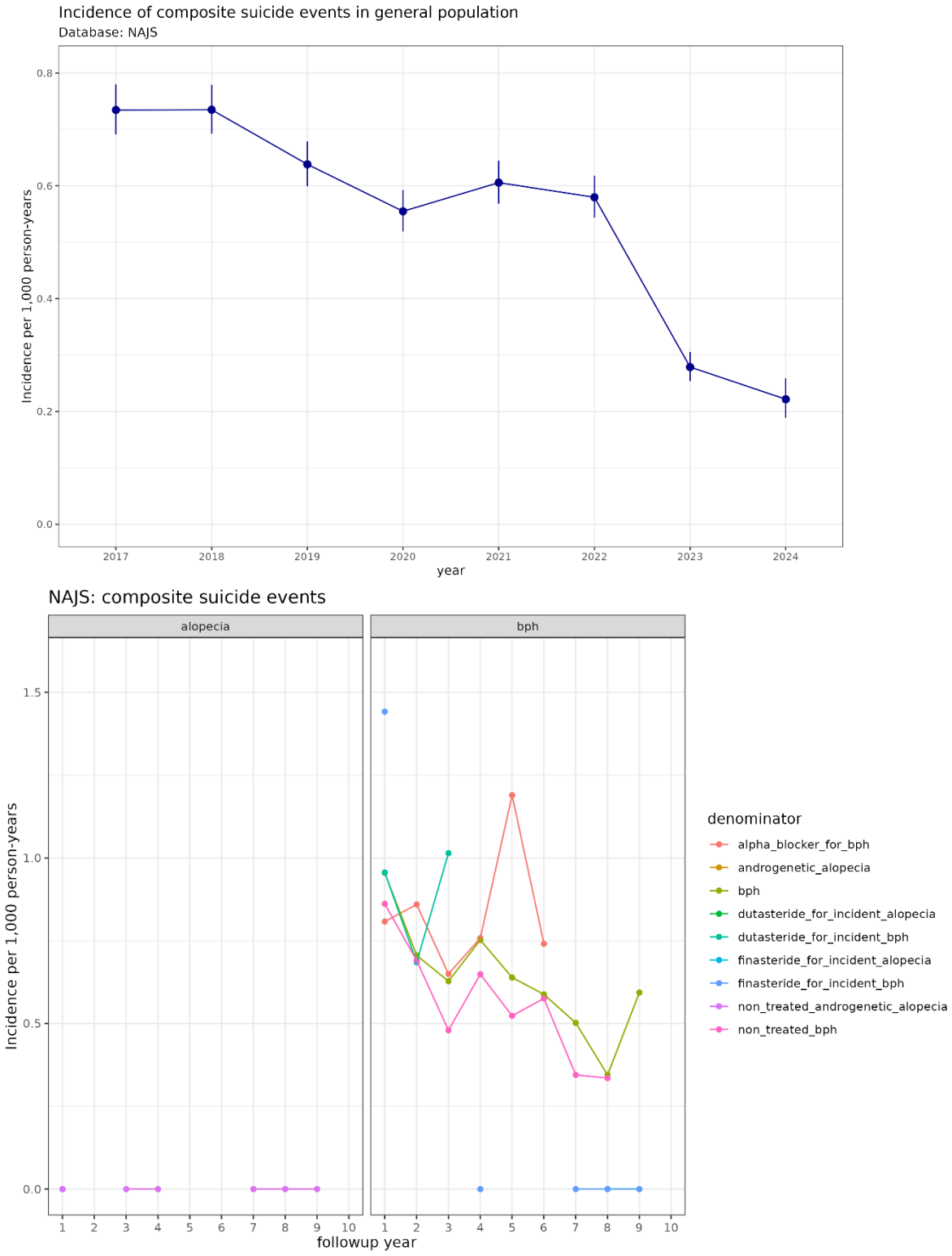
Appendix II. Figure S 17. Incidence rates of composite suicidality outcome per 1,000 person-years over calendar years/follow up years in the general population, androgenetic alopecia, BPH patients, and treatment initiators in DK-DHR data source.



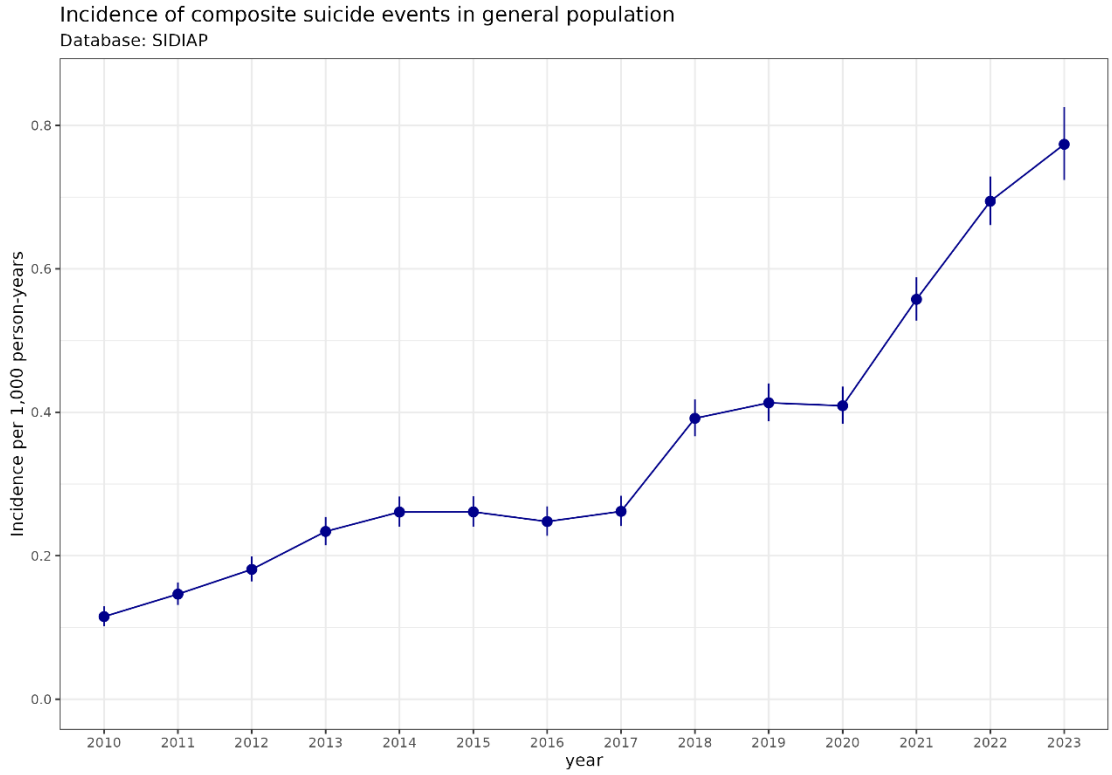
Appendix II. Figure S 18. Incidence rates of composite suicidality outcome per 1,000 person-years over calendar years/follow up years in the general population, androgenetic alopecia, BPH patients, and treatment initiators in IPCI data source.

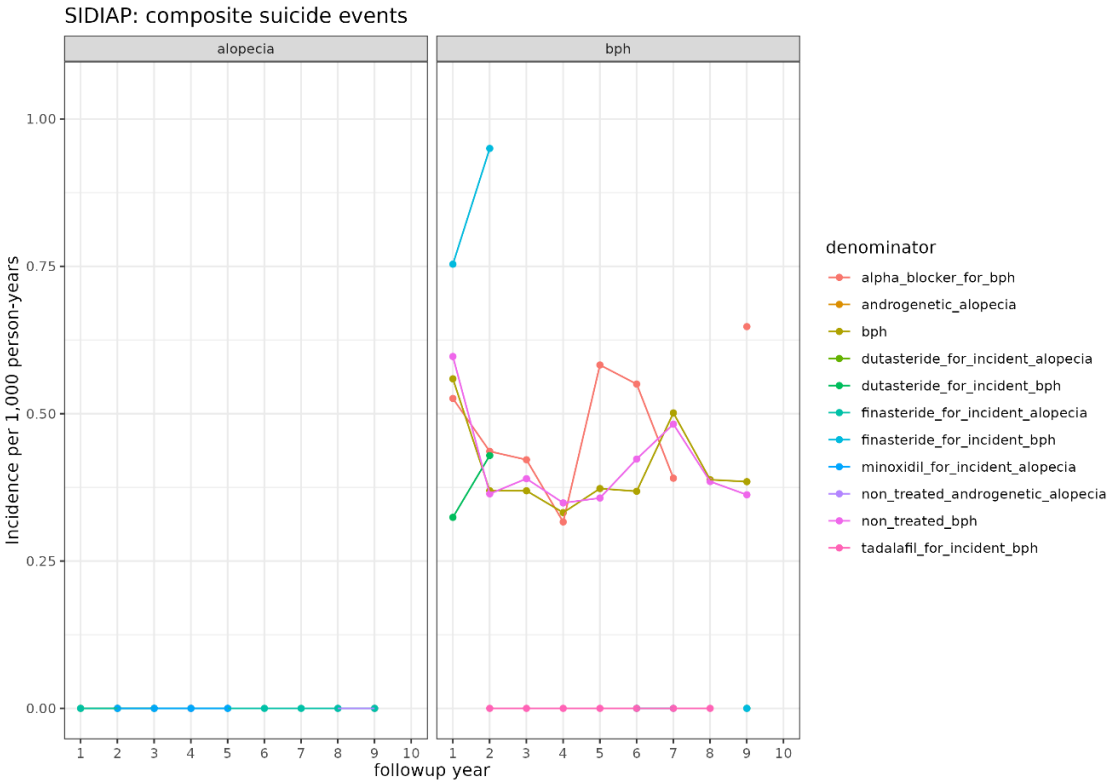


Appendix II. Figure S 19. Incidence rates of composite suicidality outcome per 1,000 person-years over calendar years/follow up years in the general population, androgenetic alopecia, BPH patients, and treatment initiators in InGef RDB data source.



Appendix II. Figure S 20. Incidence rates of composite suicidality outcome per 1,000 person-years over calendar years/follow up years in the general population, androgenetic alopecia, BPH patients, and treatment initiators in Croatian NAJS data source.





Appendix II. Figure S 21. Incidence rates of composite suicidality outcome per 1,000 person-years over calendar years/follow up years in the general population, androgenetic alopecia, BPH patients, and treatment initiators in SIDIAP data source.

Appendix II. Table S 30. Contribution of individual suicide related events to the composite suicidality outcome.

Database	Cohorts	Composite suicide N	Completed suicide N (%)	Attempted suicide N (%)	Suicidal ideation N (%)	Intentional self-harm N (%)
BIFAP	General adult male population	31,235	1,613 (5.16)	8,749 (28.01)	26,385 (84.47)	6,059 (19.40)
	Androgenetic alopecia	17	0 (0.00)	6 (35.29)	15 (88.24)	supp
	BPH	1,233	74 (6.00)	454 (36.82)	950 (77.05)	340 (27.58)
CPRD	General adult male population	37,773	86 (0.23)	10,952 (28.99)	23,614 (62.52)	15,392 (40.75)
	Androgenetic alopecia	6	0 (0.00)	supp	supp	6 (100.00)
	BPH	318	0 (0.00)	69 (21.70)	213 (66.98)	116 (36.48)
DK-DHR	General adult male population	5,956	0 (0.00)	5,521 (92.70)	0 (0.00)	4,796 (80.52)
	Androgenetic alopecia	0	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
	BPH	77	0 (0.00)	74 (96.10)	0 (0.00)	61 (79.22)
IPCI	General adult male population	2,451	418 (17.05)	2,091 (85.31)	0 (0.00)	0 (0.00)
	Androgenetic alopecia	<5	supp	supp	0 (0.00)	0 (0.00)
	BPH	33	6 (18.18)	27 (81.82)	0 (0.00)	0 (0.00)
In-Gef RDB	General adult male population	1,807	0 (0.00)	0 (0.00)	0 (0.00)	1,807 (100.00)
	Androgenetic alopecia	0	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
	BPH	69	0 (0.00)	0 (0.00)	0 (0.00)	69 (100.00)
Croatian NAJS	General adult male population	7,714	3,061 (39.68)	7,508 (97.33)	0 (0.00)	2,970 (38.50)
	Androgenetic alopecia	supp	0 (0.00)	supp	0 (0.00)	supp
	BPH	879	412 (46.87)	858 (97.61)	0 (0.00)	289 (32.88)
SIDIAP	General adult male population	10,675	0 (0.00)	5,967 (55.90)	3,600 (33.72)	2,993 (28.04)
	Androgenetic alopecia	15	0 (0.00)	6 (40.00)	10 (66.67)	supp
	BPH	768	0 (0.00)	401 (52.21)	311 (40.49)	209 (27.21)

Appendix II. Table S 31. Study attrition of individuals included in each cohort in BIFAP data source.

Cohorts	Reason	Number of subjects	Number of excluded subjects
General adult male population			
	Starting population	22,580,036	-
	Missing year of birth	22,580,036	0
	Missing sex	22,580,036	0
	Cannot satisfy age criteria during the study period based on year of birth	19,703,465	2,876,571
	No observation time available during study period	19,069,360	634,105
	Doesn't satisfy age criteria during the study period	19,069,360	0
	Prior history requirement not fulfilled during study period	18,138,611	930,749
	Not Male	8,741,881	9,396,730
	No observation time available after applying age, prior observation and, if applicable, target criteria	8,628,238	113,643
	Has history of outcomes of interest	8,621,220	7,018
Androgenetic alopecia			
	Qualifying initial records	19,491	0
	Age>=18	19,146	345
	Male	9,414	9,732
	No history of outcome of interest	9,384	30
	No history of androgenetic alopecia	9,384	0
	No history of BPH	9,280	104
Androgenetic alopecia patients treated with finasteride			
	Qualifying initial records	1,479	0
	Age>=18	1,479	0
	Male	1,199	280
	No history of treatment for androgenetic alopecia	1,146	53
	No prior history of outcome of interest	1,144	-
	No history of BPH	1,139	5
Androgenetic alopecia patients treated with dutasteride			
	Qualifying initial records	581	0
	Age>=18	581	0
	Male	294	287
	No history of treatment for androgenetic alopecia	236	58
	No prior history of outcome of interest	233	-
	No history of BPH	216	17

Androgenetic alopecia patients treated with topical minoxidil			
	Qualifying initial records	8	0
	Age>=18	8	0
	Male	5	-
	No history of treatment for androgenetic alopecia	5	0
	No prior history of outcome of interest	-	-
	No history of BPH	-	0
No recorded prescription for the androgenetic alopecia treatments			
	Qualifying initial records	19,491	0
	Age>=18	9,640	9,851
	Male	9,414	226
	No history of outcome of interest	9,384	30
	No history of androgenetic alopecia	8,930	454
	No history of BPH	8,930	0
BPH			
	Qualifying initial records	446,754	0
	Age>=18	446,707	47
	Male	445,994	713
	No history of BPH outside observation period	445,994	0
	No history of outcome of interest	444,885	1,109
	No history of androgenetic alopecia	444,795	90
BPH patients treated with finasteride			
	Qualifying initial records	8,960	0
	Age>=18	8,960	0
	Male	8,956	-
	No history of treatment for BPH	3,218	5,738
	No history of outcome of interest	3,208	10
	No history of androgenetic alopecia	3,203	5
BPH patients treated with dutasteride			
	Qualifying initial records	141,351	0
	Age>=18	141,351	0
	Male	141,280	71
	No history of treatment for BPH	91,812	49,468
	No history of outcome of interest	91,594	218
	No history of androgenetic alopecia	91,574	20
BPH patients treated with alpha blockers			

	Qualifying initial records	221,566	0
	Age>=18	221,566	0
	Male	221,437	129
	No history of outcome of interest	220,849	588
	No history of treatment for BPH	158,897	61,952
	No history of androgenetic alopecia	158,870	27
BPH patients treated with tadalafil			
	Qualifying initial records	6,544	0
	Age>=18	6,544	0
	Male	6,544	0
	No history of treatment for BPH	4,437	2,107
	No history of outcome of interest	4,421	16
	No history of androgenetic alopecia	4,418	-
BPH patients treated with tadalafil + finasteride/dutasteride			
	Qualifying initial records	0	0
	Age>=18	0	0
	Male	0	0
	No history of treatment for BPH	0	0
	No history of outcome of interest	0	0
	No history of androgenetic alopecia	0	0
No recorded prescription for the BPH treatments			
	Qualifying initial records	446,754	0
	Age>=18	446,707	47
	Male	445,994	713
	No history of outcome of interest	444,923	1,071
	No history of treatment for BPH	348,518	96,405
	No history of androgenetic alopecia	348,518	0

Appendix II. Table S 32. Study attrition of individuals included in each cohort in CPRD-Gold data source.

Cohorts	Reason	Number of subjects	Number of excluded subjects
General adult male population			
	Starting population	17,521,504	-
	Missing year of birth	17,521,504	0
	Missing sex	17,521,504	0

	Cannot satisfy age criteria during the study period based on year of birth	15,965,595	1,555,909
	No observation time available during study period	10,504,523	5,461,072
	Doesn't satisfy age criteria during the study period	10,504,523	0
	Prior history requirement not fulfilled during study period	9,523,944	980,579
	Not Male	4,671,118	4,852,826
	No observation time available after applying age, prior observation and, if applicable, target criteria	4,366,305	304,813
	Has history of outcomes of interest	4,336,324	29,981
Androgenetic alopecia			
	Qualifying initial records	931	0
	Age>=18	892	39
	Male	642	250
	No history of outcome of interest	631	11
	No history of androgenetic alopecia	631	0
	No history of BPH	629	-
Androgenetic alopecia patients treated with finasteride			
	Qualifying initial records	177	0
	Age>=18	177	0
	Male	172	5
	No history of treatment for androgenetic alopecia	149	23
	No prior history of outcome of interest	148	-
	No history of BPH	148	0
Androgenetic alopecia patients treated with dutasteride			
	Qualifying initial records	6	0
	Age>=18	6	0
	Male	6	0
	No history of treatment for androgenetic alopecia	-	-
	No prior history of outcome of interest	-	0
	No history of BPH	-	0
Androgenetic alopecia patients treated with topical minoxidil			
	Qualifying initial records	57	0
	Age>=18	57	0
	Male	30	27
	No history of treatment for androgenetic alopecia	27	-
	No prior history of outcome of interest	29	-
	No history of BPH	27	0

No recorded prescription for the androgenetic alopecia treatments			
	Qualifying initial records	931	0
	Age>=18	678	253
	Male	642	36
	No history of outcome of interest	631	11
	No history of treatment for androgenetic alopecia	469	162
	No history of BPH	469	0
BPH			
	Qualifying initial records	75,232	0
	Age>=18	75,225	7
	Male	75,187	38
	No history of BPH outside observation period	75,187	0
	No history of outcome of interest	74,566	621
	No history of androgenetic alopecia	74,558	8
BPH patients treated with finasteride			
	Qualifying initial records	22,521	0
	Age>=18	22,521	0
	Male	22,517	-
	No history of treatment for BPH	15,991	6,526
	No history of outcome of interest	15,870	121
	No history of androgenetic alopecia	15,869	-
BPH patients treated with dutasteride			
	Qualifying initial records	5,342	0
	Age>=18	5,342	0
	Male	5,340	-
	No history of treatment for BPH	3,362	1,978
	No history of outcome of interest	3,332	30
	No history of androgenetic alopecia	3,332	0
BPH patients treated with alpha blockers			
	Qualifying initial records	59,204	0
	Age>=18	59,204	0
	Male	59,192	12
	No history of outcome of interest	58,699	493
	No history of treatment for BPH	46,061	12,638
	No history of androgenetic alopecia	46,058	-
BPH patients treated with tadalafil			
	Qualifying initial records	3,934	0

	Age>=18	3,934	0
	Male	3,934	0
	No history of treatment for BPH	1,650	2,284
	No history of outcome of interest	1,630	20
	No history of androgenetic alopecia	1,630	0
BPH patients treated with tadalafil + finasteride/dutasteride			
	Qualifying initial records	0	0
	Age>=18	0	0
	Male	0	0
	No history of treatment for BPH	0	0
	No history of outcome of interest	0	0
	No history of androgenetic alopecia	0	0
No recorded prescription for the BPH treatments			
	Qualifying initial records	75,232	0
	Age>=18	75,225	7
	Male	75,187	38
	No history of outcome of interest	74,566	621
	No history of treatment for BPH	57,944	16,622
	No history of androgenetic alopecia	57,944	0

Appendix II. Table S 33. Study attrition of individuals included in each cohort in DK-DHR data source.

Cohorts	Reason	Number of subjects	Number of excluded subjects
General adult male population			
	Starting population	8,593,356	-
	Missing year of birth	8,593,356	0
	Missing sex	8,593,356	0
	Cannot satisfy age criteria during the study period based on year of birth	7,375,360	1,217,996
	No observation time available during study period	6,194,097	1,181,263
	Doesn't satisfy age criteria during the study period	6,194,097	0
	Prior history requirement not fulfilled during study period	5,885,980	308,117
	Not Male	2,927,048	2,958,932
	No observation time available after applying age, prior observation and, if applicable, target criteria	2,920,859	6,189
	Has history of outcomes of interest	2,916,174	4,685
Androgenetic alopecia			

	Qualifying initial records	1,071	0
	Age>=18	1,032	39
	Male	459	573
	No history of outcome of interest	457	-
	No history of androgenetic alopecia	457	0
	No history of BPH	452	5
Androgenetic alopecia patients treated with finasteride			
	Qualifying initial records	146	0
	Age>=18	146	0
	Male	117	29
	No history of treatment for androgenetic alopecia	71	46
	No prior history of outcome of interest	71	0
	No history of BPH	71	0
Androgenetic alopecia patients treated with dutasteride			
	Qualifying initial records	10	0
	Age>=18	10	0
	Male	8	-
	No history of treatment for androgenetic alopecia	5	-
	No prior history of outcome of interest	5	0
	No history of BPH	-	-
Androgenetic alopecia patients treated with topical minoxidil			
	Qualifying initial records	82	0
	Age>=18	82	0
	Male	15	67
	No history of treatment for androgenetic alopecia	15	0
	No prior history of outcome of interest	12	-
	No history of BPH	12	0
No recorded prescription for the androgenetic alopecia treatments			
	Qualifying initial records	1,071	0
	Age>=18	478	593
	Male	459	19
	No history of outcome of interest	457	-
	No history of androgenetic alopecia	366	91
	No history of BPH	366	0
BPH			

	Qualifying initial records	94,157	0
	Age>=18	94,121	36
	Male	94,088	33
	No history of BPH outside observation period	94,088	0
	No history of outcome of interest	93,930	158
	No history of androgenetic alopecia	93,919	11
BPH patients treated with finasteride			
	Qualifying initial records	37,217	0
	Age>=18	37,217	0
	Male	37,204	13
	No history of treatment for BPH	25,779	11,425
	No history of outcome of interest	25,739	40
	No history of androgenetic alopecia	25,738	-
BPH patients treated with dutasteride			
	Qualifying initial records	13,743	0
	Age>=18	13,743	0
	Male	13,737	6
	No history of treatment for BPH	8,358	5,379
	No history of outcome of interest	8,350	8
	No history of androgenetic alopecia	8,350	0
BPH patients treated with alpha blockers			
	Qualifying initial records	56,453	0
	Age>=18	56,453	0
	Male	56,447	6
	No history of outcome of interest	56,354	93
	No history of treatment for BPH	30,374	25,980
	No history of androgenetic alopecia	30,372	-
BPH patients treated with tadalafil			
	Qualifying initial records	13,001	0
	Age>=18	13,001	0
	Male	12,997	-
	No history of treatment for BPH	5,581	7,416
	No history of outcome of interest	5,560	21
	No history of androgenetic alopecia	5,559	-
BPH patients treated with tadalafil + finasteride/dutasteride			
	Qualifying initial records	0	0
	Age>=18	0	0
	Male	0	0

	No history of treatment for BPH	0	0
	No history of outcome of interest	0	0
	No history of androgenetic alopecia	0	0
No recorded prescription for the BPH treatments			
	Qualifying initial records	94,157	0
	Age>=18	94,121	36
	Male	94,088	33
	No history of outcome of interest	93,930	158
	No history of treatment for BPH	43,233	50,697
	No history of androgenetic alopecia	43,233	0

Appendix II. Table S 34. Study attrition of individuals included in each cohort in IPCI data source.

Cohorts	Reason	Number of subjects	Number of excluded subjects
General adult male population			
	Starting population	2,870,221	-
	Missing year of birth	2,870,221	0
	Missing sex	2,870,221	0
	Cannot satisfy age criteria during the study period based on year of birth	2,454,655	415,566
	No observation time available during study period	2,419,701	34,954
	Doesn't satisfy age criteria during the study period	2,419,701	0
	Prior history requirement not fulfilled during study period	2,164,663	255,038
	Not Male	1,050,161	1,114,502
	No observation time available after applying age, prior observation and, if applicable, target criteria	1,001,336	48,825
	Has history of outcomes of interest	1,000,636	700
Androgenetic alopecia			
	Qualifying initial records	4,153	0
	Age>=18	4,034	119
	Male	1,978	2,056
	No history of outcome of interest	1,971	7
	No history of androgenetic alopecia	1,971	0
	No history of BPH	1,949	22
Androgenetic alopecia patients treated with finasteride			
	Qualifying initial records	685	0
	Age>=18	685	0

	Male	666	19
	No history of treatment for androgenetic alopecia	607	59
	No prior history of outcome of interest	606	-
	No history of BPH	605	-
Androgenetic alopecia patients treated with dutasteride			
	Qualifying initial records	48	0
	Age>=18	48	0
	Male	36	12
	No history of treatment for androgenetic alopecia	18	18
	No prior history of outcome of interest	18	0
	No history of BPH	15	-
Androgenetic alopecia patients treated with topical minoxidil			
	Qualifying initial records	682	0
	Age>=18	682	0
	Male	337	345
	No history of treatment for androgenetic alopecia	336	-
	No prior history of outcome of interest	305	31
	No history of BPH	304	-
No recorded prescription for the androgenetic alopecia treatments			
	Qualifying initial records	4,153	0
	Age>=18	2,065	2,088
	Male	1,978	87
	No history of outcome of interest	1,971	7
	No history of androgenetic alopecia	1,315	656
	No history of BPH	1,315	0
BPH			
	Qualifying initial records	15,433	0
	Age>=18	15,432	-
	Male	15,426	6
	No history of BPH outside observation period	15,426	0
	No history of outcome of interest	15,350	76
	No history of androgenetic alopecia	15,320	30
BPH patients treated with finasteride			
	Qualifying initial records	937	0
	Age>=18	937	0
	Male	936	-

	No history of treatment for BPH	569	367
	No history of outcome of interest	568	-
	No history of androgenetic alopecia	567	-
BPH patients treated with dutasteride			
	Qualifying initial records	2,090	0
	Age>=18	2,090	0
	Male	2,089	-
	No history of treatment for BPH	1,470	619
	No history of outcome of interest	1,462	8
	No history of androgenetic alopecia	1,462	0
BPH patients treated with alpha blockers			
	Qualifying initial records	11,120	0
	Age>=18	11,120	0
	Male	11,118	-
	No history of outcome of interest	11,050	68
	No history of treatment for BPH	9,111	1,939
	No history of androgenetic alopecia	9,103	8
BPH patients treated with tadalafil			
	Qualifying initial records	630	0
	Age>=18	630	0
	Male	630	0
	No history of treatment for BPH	324	306
	No history of outcome of interest	324	0
	No history of androgenetic alopecia	324	0
BPH patients treated with tadalafil + finasteride/dutasteride			
	Qualifying initial records	0	0
	Age>=18	0	0
	Male	0	0
	No history of treatment for BPH	0	0
	No history of outcome of interest	0	0
	No history of androgenetic alopecia	0	0
No recorded prescription for the BPH treatments			
	Qualifying initial records	15,433	0
	Age>=18	15,432	-
	Male	15,426	6
	No history of outcome of interest	15,350	76
	No history of treatment for BPH	13,487	1,863

	No history of androgenetic alopecia	13,487	0

Appendix II. Table S 35. Study attrition of individuals included in each cohort in InGef data source.

Cohorts	Reason	Number of subjects	Number of excluded subjects
General adult male population			
	Starting population	10,512,855	-
	Missing year of birth	10,512,855	0
	Missing sex	10,512,855	0
	Cannot satisfy age criteria during the study period based on year of birth	8,936,212	1,576,643
	No observation time available during study period	8,936,212	0
	Doesn't satisfy age criteria during the study period	8,936,212	0
	Prior history requirement not fulfilled during study period	8,209,349	726,863
	Not Male	4,114,401	4,094,948
	No observation time available after applying age, prior observation and, if applicable, target criteria	4,063,949	50,452
	Has history of outcomes of interest	4,063,229	720
Androgenetic alopecia			
	Qualifying initial records	1,207	0
	Age>=18	1,150	57
	Male	249	901
	No history of outcome of interest	249	0
	No history of androgenetic alopecia	249	0
	No history of BPH	236	13
Androgenetic alopecia patients treated with finasteride			
	Qualifying initial records	16	0
	Age>=18	16	0
	Male	16	0
	No history of treatment for androgenetic alopecia	-	14
	No prior history of outcome of interest	-	0
	No history of BPH	-	0
Androgenetic alopecia patients treated with dutasteride			
	Qualifying initial records	-	0
	Age>=18	-	0
	Male	-	-
	No history of treatment for androgenetic alopecia	0	-

	No prior history of outcome of interest	0	0
	No history of BPH	0	0
Androgenetic alopecia patients treated with topical minoxidil			
	Qualifying initial records	0	0
	Age>=18	0	0
	Male	0	0
	No history of treatment for androgenetic alopecia	0	0
	No prior history of outcome of interest	0	0
	No history of BPH	0	0
No recorded prescription for the androgenetic alopecia treatments			
	Qualifying initial records	1,207	0
	Age>=18	276	931
	Male	249	27
	No history of outcome of interest	249	0
	No history of androgenetic alopecia	230	19
	No history of BPH	230	0
BPH			
	Qualifying initial records	163,563	0
	Age>=18	163,556	7
	Male	163,364	192
	No history of BPH outside observation period	163,364	0
	No history of outcome of interest	163,284	80
	No history of androgenetic alopecia	163,278	6
BPH patients treated with finasteride			
	Qualifying initial records	14,400	0
	Age>=18	14,400	0
	Male	14,400	0
	No history of treatment for BPH	5,257	9,143
	No history of outcome of interest	5,256	-
	No history of androgenetic alopecia	5,256	0
BPH patients treated with dutasteride			
	Qualifying initial records	11,282	0
	Age>=18	11,282	0
	Male	11,282	0
	No history of treatment for BPH	5,002	6,280
	No history of outcome of interest	4,998	-
	No history of androgenetic alopecia	4,998	0

BPH patients treated with alpha blockers			
	Qualifying initial records	114,789	0
	Age>=18	114,789	0
	Male	114,750	39
	No history of outcome of interest	114,688	62
	No history of treatment for BPH	96,200	18,488
	No history of androgenetic alopecia	96,199	-
BPH patients treated with tadalafil			
	Qualifying initial records	1,493	0
	Age>=18	1,493	0
	Male	1,493	0
	No history of treatment for BPH	870	623
	No history of outcome of interest	869	-
	No history of androgenetic alopecia	869	0
BPH patients treated with tadalafil + finasteride/dutasteride			
	Qualifying initial records	0	0
	Age>=18	0	0
	Male	0	0
	No history of treatment for BPH	0	0
	No history of outcome of interest	0	0
	No history of androgenetic alopecia	0	0
No recorded prescription for the BPH treatments			
	Qualifying initial records	163,563	0
	Age>=18	163,556	7
	Male	163,364	192
	No history of outcome of interest	163,298	66
	No history of treatment for BPH	137,195	26,103
	No history of androgenetic alopecia	137,195	0

Appendix II. Table S 36. Study attrition of individuals included in each cohort in Croatian NAJS data source.

Cohorts	Reason	Number of subjects	Number of excluded subjects
General adult male population			
	Starting population	5,448,809	-

	Missing year of birth	5,448,809	0
	Missing sex	5,448,808	-
	Cannot satisfy age criteria during the study period based on year of birth	4,745,452	703,356
	No observation time available during study period	4,062,968	682,484
	Doesn't satisfy age criteria during the study period	4,062,968	0
	Prior history requirement not fulfilled during study period	3,971,778	91,190
	Not Male	1,925,292	2,046,486
	No observation time available after applying age, prior observation and, if applicable, target criteria	1,920,070	5,222
	Has history of outcomes of interest	1,918,950	1,120
Androgenetic alopecia			
	Qualifying initial records	5,343	0
	Age>=18	5,065	278
	Male	1,762	3,303
	No history of outcome of interest	1,760	-
	No history of androgenetic alopecia	1,760	0
	No history of BPH	1,640	120
Androgenetic alopecia patients treated with finasteride			
	Qualifying initial records	32	0
	Age>=18	32	0
	Male	22	10
	No history of treatment for androgenetic alopecia	15	7
	No prior history of outcome of interest	15	0
	No history of BPH	12	-
Androgenetic alopecia patients treated with dutasteride			
	Qualifying initial records	61	0
	Age>=18	61	0
	Male	53	8
	No history of treatment for androgenetic alopecia	27	26
	No prior history of outcome of interest	26	-
	No history of BPH	7	19
Androgenetic alopecia patients treated with topical minoxidil			
	Qualifying initial records	0	0
	Age>=18	0	0
	Male	0	0
	No history of treatment for androgenetic alopecia	0	0
	No prior history of outcome of interest	0	0

	No history of BPH	0	0
No recorded prescription for the androgenetic alopecia treatments			
	Qualifying initial records	5,343	0
	Age>=18	1,914	3,429
	Male	1,762	152
	No history of outcome of interest	1,760	-
	No history of androgenetic alopecia treatment	1,705	55
	No history of BPH	1,705	0
BPH			
	Qualifying initial records	283,322	0
	Age>=18	283,075	247
	Male	279,863	3,212
	No history of BPH outside observation period	279,863	0
	No history of outcome of interest	279,449	414
	No history of androgenetic alopecia	279,363	86
BPH patients treated with finasteride			
	Qualifying initial records	11,856	0
	Age>=18	11,856	0
	Male	11,840	16
	No history of treatment for BPH	7,698	4,142
	No history of outcome of interest	7,689	9
	No history of androgenetic alopecia	7,687	-
BPH patients treated with dutasteride			
	Qualifying initial records	89,879	0
	Age>=18	89,879	0
	Male	89,826	53
	No history of treatment for BPH	83,250	6,576
	No history of outcome of interest	83,082	168
	No history of androgenetic alopecia	83,055	27
BPH patients treated with alpha blockers			
	Qualifying initial records	226,416	0
	Age>=18	226,416	0
	Male	226,310	106
	No history of outcome of interest	225,995	315
	No history of treatment for BPH	173,132	52,863
	No history of androgenetic alopecia	173,087	45
BPH patients treated with tadalafil			

	Qualifying initial records	0	0
	Age>=18	0	0
	Male	0	0
	No history of treatment for BPH	0	0
	No history of outcome of interest	0	0
	No history of androgenetic alopecia	0	0
BPH patients treated with tadalafil + finasteride/dutasteride			
	Qualifying initial records	0	0
	Age>=18	0	0
	Male	0	0
	No history of treatment for BPH	0	0
	No history of outcome of interest	0	0
	No history of androgenetic alopecia	0	0
No recorded prescription for the BPH treatments			
	Qualifying initial records	283,322	0
	Age>=18	283,075	247
	Male	279,863	3,212
	No history of outcome of interest	279,452	411
	No history of treatment for BPH	249,257	30,195
	No history of androgenetic alopecia	249,257	0

Appendix II. Table S 37. Study attrition of individuals included in each cohort in SIDIAP data source.

Cohorts	Reason	Number of subjects	Number of excluded subjects
General adult male population			
	Starting population	8,553,325	-
	Missing year of birth	8,553,325	0
	Missing sex	8,553,325	0
	Cannot satisfy age criteria during the study period based on year of birth	7,493,483	1,059,842
	No observation time available during study period	7,091,491	401,992
	Doesn't satisfy age criteria during the study period	7,091,491	0
	Prior history requirement not fulfilled during study period	6,868,226	223,265
	Not Male	3,408,528	3,459,698
	No observation time available after applying age, prior observation and, if applicable, target criteria	3,317,611	90,917
	Has history of outcomes of interest	3,316,543	1,068

Androgenetic alopecia			
	Qualifying initial records	12,605	0
	Age>=18	12,375	230
	Male	5,373	7,002
	No history of outcome of interest	5,363	10
	No history of androgenetic alopecia	5,363	0
	No history of BPH	5,265	98
Androgenetic alopecia patients treated with finasteride			
	Qualifying initial records	757	0
	Age>=18	757	0
	Male	334	423
	No history of treatment for androgenetic alopecia	188	146
	No prior history of outcome of interest	187	-
	No history of BPH	181	6
Androgenetic alopecia patients treated with dutasteride			
	Qualifying initial records	449	0
	Age>=18	449	0
	Male	221	228
	No history of treatment for androgenetic alopecia	120	101
	No prior history of outcome of interest	120	0
	No history of BPH	97	23
Androgenetic alopecia patients treated with topical minoxidil			
	Qualifying initial records	1,263	0
	Age>=18	1,263	0
	Male	500	763
	No history of treatment for androgenetic alopecia	498	-
	No prior history of outcome of interest	477	21
	No history of BPH	466	11
No recorded prescription for the androgenetic alopecia treatments			
	Qualifying initial records	12,605	0
	Age>=18	5,508	7,097
	Male	5,373	135
	No history of outcome of interest	5,363	10
	No history of androgenetic alopecia	4,573	790
	No history of BPH	4,573	0

BPH			
	Qualifying initial records	314,592	0
	Age>=18	314,582	10
	Male	314,443	139
	No history of BPH outside observation period	314,443	0
	No history of outcome of interest	313,951	492
	No history of androgenetic alopecia	313,797	154
BPH patients treated with finasteride			
	Qualifying initial records	31,726	0
	Age>=18	31,726	0
	Male	31,719	7
	No history of treatment for BPH	15,632	16,087
	No history of outcome of interest	15,595	37
	No history of androgenetic alopecia	15,588	7
BPH patients treated with dutasteride			
	Qualifying initial records	60,027	0
	Age>=18	60,027	0
	Male	60,017	10
	No history of treatment for BPH	36,251	23,766
	No history of outcome of interest	36,177	74
	No history of androgenetic alopecia	36,164	13
BPH patients treated with alpha blockers			
	Qualifying initial records	196,618	0
	Age>=18	196,618	0
	Male	196,578	40
	No history of outcome of interest	196,191	387
	No history of treatment for BPH	163,294	32,897
	No history of androgenetic alopecia	163,225	69
BPH patients treated with tadalafil			
	Qualifying initial records	4,987	0
	Age>=18	4,987	0
	Male	4,987	0
	No history of treatment for BPH	3,681	1,306
	No history of outcome of interest	3,665	16
	No history of androgenetic alopecia	3,659	6
BPH patients treated with tadalafil + finasteride/dutasteride			
	Qualifying initial records	0	0
	Age>=18	0	0

	Male	0	0
	No history of treatment for BPH	0	0
	No history of outcome of interest	0	0
	No history of androgenetic alopecia	0	0
No recorded prescription for the BPH treatments			
	Qualifying initial records	314,592	0
	Age>=18	314,582	10
	Male	314,443	139
	No history of outcome of interest	313,964	479
	No history of treatment for BPH	270,850	43,114
	No history of androgenetic alopecia	270,850	0