Characteristics of non-randomized studies of pharmacologic treatment: a cross-sectional study

Sally Yaacoub, Raphaël Porcher, Anna Pellat, Hillary Bonnet, Viet-Thi Tran, Philippe Ravaud, Isabelle Boutron

SUPPLEMENTAL MATERIAL

Appendix 1. Search strategy for Ovid MEDLINE

1	exp Non-randomized controlled trials/ or (((Non random* or nonrandom*) adj3 (trial* or study or studies)) or NRSI).mp. or ((Non interven* or noninterven*) adj2 (trial* or study or studies)).mp. or ((cohort* or incidence) adj (study or studies or analys?s)).mp. or exp Control Groups/ or exp Matched-Pair Analysis/ or (case* adj2 (control* or comparison* or comparat* or compare* or referent* or compeer*)).mp. or ((match* or control*) adj (case* or group* or study or studies or pair* or control*)).mp. or (Interrupted Time Series or ITS study or ITS studies).mp. or ((CBA or Before after or "Before and after" or "pre and post" or pre post) adj (study or studies)).mp. or Comparative study/ or exp Epidemiologic studies/ or evaluation study/ or ((retrospective or prospective or longitudinal or follow up or followup or epidemiologic* or evaluation) adj1 (study or studies or analys?s or survey*)).mp. or ((comparat* or comparison* or continuing or observational) adj2 (study or studies or research or analys?s)).mp. or (population based adj1 (study or studies or analys?s)).mp. or (historic* adj2 (study or studies or analys?s)).mp. or Time factors/ or (time and factors).mp. or (Cross-section* or cross section* or Prevalence Studies or Prevalence study or prevalence analys?s or survey).mp. or ((emulat* or target or reference) adj2 (trial* or study or studies or experiment*)).mp. or exp Information Systems/ or exp Medical Records/ or Patient Discharge/ or Hospital Records/ or exp Health Services Research/ or exp insurance, health/ or exp Registries/ or (database* or registry or registries or register or registers or ehr* or emr* or secondary data* or big data).mp. or ((health or health care or healthcare or hospital* or patient* or physician* or medical or linked or surveillance or insurance or billing or admission or discharge or routine or routinely or claim* or administrative or registr* or real world or emergency department* or vigilance) adj2 (record* or claim* or data or file* or registr* or evidence or information system* or summar* or card* or study or studies)).mp.
2	exp drug therapy/ or drug therapy.fs. or (pharmacologic* or pharmacotherap* or pharmaco therap* or chemotherap* or chemo therap* or drug* or medication* or medicine* or dose* or dosing or intravenous* or oral or orally or subcutaneous* or subq or capsule* or tablet*or treatment* or pretreatment* or prescription* or agent* or regimen*).mp. or *pharmaceutical preparations/ or exp controlled substances/ or exp dosage forms/ or exp drugs, essential/ or exp drugs, generic/ or exp drugs, investigational/ or exp nonprescription drugs/ or exp prescription drugs/ or exp prodrugs/ or substandard drugs/ or synthetic drugs/ or exp designer drugs/ or exp "chemical actions and uses"/
3	1 and 2
4	exp Review/ or systematic review/ or Address/ or exp Biography/ or exp Bibliography/ or Case Reports/ or Clinical Conference/ or Comment/ or exp Congress/ or Editorial/ or Letter/ or exp Dictionary/ or Directory/ or exp Historical Article/ or exp Legal Case/ or exp Meta-Analysis/ or exp Guideline/ or News/ or Newspaper Article/ or Patient Education Handout/ or Legislation/ or Lecture/ or exp Video-Audio Media/ or Webcast/ or Portrait/ or Clinical Trial, Phase I/ or Clinical Trial, Phase ii/ or exp Randomized Controlled Trial/
5	exp animals/ not humans.sh.
6	3 not (4 or 5)
7	limit 6 to (english language and yr="2022")
8	limit 7 to dt=20220601-20220831

Appendix 2. Data extraction instruction sheet

Item	Explanation	Answer options
General characteristics		
Study ID		
Authors	Name of the first author	Open-ended
Title	Title of the article	Open-ended
Journal	Type of journal. E.g., General medical journal: The Lancet Specialized medical journal: The Lancet Oncology	1. General medical journal 2. Specialized medical journal 3. Non-medical journal
Region	Region of country of study	1. North America 2. Latin America and Caribbean 3. Middle East and North Africa 4. Sub-Saharan Africa 5. Europe 6. South Asia (Afghanistan, Pakistan, India, Nepal, Bangladesh, Sri Lanka) 7. Central and East Asia and Pacific 8. More than one: Specify
Setting	Healthcare setting of the study	1. Primary (Outpatient/Community), 2. Secondary (Inpatient/General hospital(s)), 3. Tertiary (Inpatient/Specialized or university hospital(s)), 4. Other: Specify 5. More than one: Specify 6. Not reported
Number of centers	Number of centers included in the study. In cases where the data is a regional/national registry, then it would not be applicable.	• [Continuous number] • Not reported • Not applicable
Sampling of centers or population	Is the sample representative of the population? i.e., there is a structured manner to sample the centers to obtain a representative sample of the population or the data source is representative of the population e.g., using a nationwide database of all health centers.	1. Yes: Specify 2. No

Medical area	Medical area in which the treatment is being evaluated based on the included population	1. Cardiology 2. Endocrinology 3. Infectious Disease 4. Obstetrics 5. Rheumatology 6. Oncology 7. Psychiatry/Psychology 8. Neurology 9. Respiratory 10. Hematology 11. Surgery 12. Gastroenterology 13. Other: Specify
Study design as reported	Study design as reported in the article, including all labels and terms used to describe it	Open-ended
Study design as judged	Study design as judged by reviewer according to the algorithm available at the end	1. Cohort 2. Case-control 3. Other: Specify
Study design diagram	Use of diagram to illustrate the study design including timepoints for eligibility, treatment assignment and follow-up	1. Yes 2. No
Flow diagram timepoints	The flow diagram of participants, if applicable, reports the dates for the timepoints for eligibility, treatment assignment and follow-up i.e., one is able to identify from the timepoints of eligibility, treatment assignment and follow-up from the flow diagram. Not applicable: when there is no flow diagram of participants.	1. Yes 2. No 3. Not applicable
Objective(s)	List the main objective of the study	Open-ended
Objective other than assessing treatment effect is included	In addition to the main objective of assessing treatment effect, do the authors report another objective? Objectives related to treatment effects are NOT considered as 'another objective', e.g., If an objective is to assess the factors associated with treatment success, then it is NOT another objective.	1. Yes: specify 2. No
Complementary or exploratory evidence	Is the study conducted to complement findings from previous studies or to explore the effect of the treatment?	1. Complementary of RCTs 2. Complementary of RCTs and/or NRS 3. Exploratory 4. Unclear
Data used	Type of data used, regardless of the purpose of the data used, i.e., for recruitment, for treatment evaluation, etc.	1. Routinely collected data 2. Standardized data collection from an existing cohort

	Routinely collected data is data collected without any research purpose, whereas standardized data collection is data collected with a specific research purpose, either an existing one or for the purpose of this study.	3. Standardized data collection from a cohort for the purpose of the study 4. More than one: Specify 5. Not reported
Source(s) of routinely collected data	Type(s) of data sources for all routinely collected data	1. Registry 2. Administrative data (Health administration data, Health insurance claims data, Pharmacy data) 3. Electronic health record 4. Wearable biometric monitoring device data 5. Health records (non-electronic, not specified) 6. Other: Specify 7. More than one: Specify 8. Not applicable 9. Not reported
Statistician/Methodologist	Statistician or methodologist included in the research team, as reported in the manuscript or included as an author with affiliation to a statistics, epidemiology or public health department, or mentioned in the acknowledgement.	1. Yes: author affiliation 2. Yes: explicitly reported 3. No
Research question	Explicit statement of research question or well-defined objective(s), from which the research question is identifiable.	1. Yes 2. No
Participants		
Eligibility criteria for participants	Eligibility criteria for participants is reported	1. Yes 2. No
Post-baseline/treatment events in the inclusion criteria	Post-baseline/treatment events included in the inclusion criteria. For example, use of treatment (“include only individuals who ever used therapy during the follow-up”), having an event (“include only those who ever had a specific event during the follow-up period”, or no follow-up data ("include only individuals who remain under follow-up" or “follow-up was at least 2 years”).	1. Yes: Use of treatment during FU 2. Yes: Having an outcome during FU 3. Yes: Specific duration of FU 4. Yes: More than one, specify: 5. No
Eligibility to any arm	Authors explicitly state whether participants can be eligible to any treatment arm i.e., patients should not have contraindications to any of the treatment arms.	1. Yes 2. No

Number of participants excluded due to post-baseline events	The number of participants that were excluded based on post-baseline events in the eligibility criteria*	• [continuous number] • Not reported • Not applicable
Sources for selection of participants reported	Sources for selection of participants are reported	1. Yes 2. No
Use of validation studies	Any validation studies of the codes or algorithms used to select the population. 'Not applicable' is when the study does not use routinely collected data.	1. Yes: validation studies 2. No: previous studies 3. No: not reported 4. Not applicable
Period of recruitment	Period of recruitment of participants is reported, e.g., a registry including patients registered in the 1 January 2014 to 1 January 2020. Include the day, month, year for the start and end of recruitment.*	• [Open-ended] • Not reported
Duration of recruitment	Duration of recruitment of participants is reported, e.g., the duration is 6 years (6x12=72 months) for a registry including patients registered in the 1 January 2014 to 1 January 2020 in months.*	• [Continuous number] • Not reported
Population	Define the population in which the treatment is being assessed	1. Chronic disease 2. Acute disease in chronic patients 3. Acute disease in healthy patients
Treatment		
Description of treatment	A description of the allocated treatment is reported, including the dosage form, dosage, and frequency	1. Yes 2. No
Comparator(s)	What is the pharmacologic treatment compared to?	1. Usual care/No treatment 2. Other active treatment 3. Different regimen of (target) treatment 4. More than one: Specify
Effect of active comparator	Do the authors explicitly state that the active comparator is expected to have no effect on the outcome of interest?	1. Yes 2. No 3. Not applicable
Pharmacologic family [If active comparator(s)]	If active comparator(s), is/are the comparator(s) in the same pharmacologic family as the (target) treatment? For studies with more than one comparator, if at least one of the comparators is from the same pharmacologic family, then select 'Yes: some comparator(s)'.	1. Yes: all comparators 2. Yes: some comparator(s) 3. No 4. Not applicable

Definition of treatment arms	How are the treatment arms defined? e.g., according to prescriptions, dispensing, adherence? Data from electronic health records are considered as prescriptions, unless reported otherwise. Data from pharmacy claims data or insurance claims are considered as dispensations, unless reported otherwise.	1. Prescriptions 2. Dispensations 3. Adherence 4. Other: Specify 5. Not reported 6. Not applicable
Description of actual treatment	A description of the actual treatment is reported, including, dosage form, dosage, frequency, duration	1. Yes 2. No
Initiation or continuation	The comparison is to assess the initiation of a treatment or to assess the continuation of a treatment (i.e., patients are starting the treatment, being already on the treatment, or having a combination of those starting the treatment and those on the treatment).*	1. Initiation of treatment 2. Continuation of treatment 3. Combination of initiation and continuation of treatment 4. Unclear
Inclusion of treatment users	Are the treatment users incident/new users or prevalent users? Incident users are 'new users', whereas prevalent users are patients who are already on the treatment.	1. Incident/New users 2. Prevalent users 3. Unclear 4. Both
Comparison in question	What is the comparison in question? Treatment initiation is a one-time decision (i.e., treatment exposure is not based on follow-up data [ITT analogue]). Static treatment strategy is when the treatment is given for a specific period of time, and needs follow-up data to identify/classify patients (per-protocol analogue). Dynamic treatment strategy is similar to static treatment but 'dynamic' e.g., treat to target strategy in rheumatoid arthritis.	1. Treatment initiation 2. Static treatment 3. Dynamic treatment 4. Delay of treatment 5. Discontinuation of treatment 6. Treatment duration 7. More than one: Specify 8. Other: Specify
Treatment over time	Did the distribution of the treatment change over time during the study period? i.e., Is there a 'time-issue'? This can be due to change in clinical practice, approval of drug, long duration of recruitment 'Addressed' time-issue is when authors accounted for the time-issue in their analysis, for example through matching.*	1. Yes: addressed 2. Yes: not addressed 3. No 4. Unclear
Treatment deviations defined	Treatment deviations are defined, i.e., cross-over, stopping treatment, non-compliance	1. Yes 2. No
Treatment deviations reported	Treatment deviations are reported, i.e., there was a difference between planned treatment and actual treatment	1. Yes 2. No

Addressing treatment deviations	Method for addressing treatment deviations	1. Excluded 2. Censored 3. Included in the allocated arm 4. Included in the treated arm 5. Other: Specify
Drug approval	When was the drug molecule approved? This is not dependent on the dosing regimen or indication. It is specific to the drug molecule.	1. Approved from a long time 2. Recently approved 3. Unapproved
Treatment assignment		
Grace period to start treatment or active comparator	A time window/delay to initiate the treatment (i.e., grace period) is reported	1. Yes 2. No
Grace period	If there is a grace period, specify period (with time unit) to initiate treatment or active comparator e.g., 7 days. If the grace period is a range, then report the upper end of the period e.g., the grace period reported in the study is 4-8 weeks, then the extracted grace period is 8 weeks.	Continuous number
Difference in grace period	Difference in the grace period to initiate treatment and to initiate active comparator is reported	1. There is a difference 2. There is NO difference 3. Not applicable 4. Not reported
Data during grace period	If the data during the grace period is available and aligned with sampling	1. Yes 2. No 3. Not applicable
Point-exposure or time-varying treatment	Treatment is at point-exposure (clearly defined irrespective of time), i.e., only chance to decide if treatment or not, for example, one administration of a treatment, e.g., injection) or treatment is time-varying (i.e., deciding to give a treatment or not based on time-varying factors e.g., (a) the treatment of interest is static but patients' treatment status may vary in the available observational data; or (b) the intervention of interest involves a strategy to vary treatment over time (time-varying treatment strategy).*	1. Point-exposure 2. Time-varying treatment 3. Unclear

Method to address time-varying treatment or point-exposure treatment	How did the authors address time-varying treatment?*	1. Randomly assign the individual to one of the strategies 2. Clone exact copies of individuals and assign each clone to one of strategies then censor clone when strategies are deviated from 3. Time-varying Cox model 4. Marginal structural model (MSM) 5. Structural nested mean models (SNMMs) 6. Other: Specify 7. Not reported
Statistical considerations		
Outcomes		
Primary outcome(s)	Authors first identify the primary outcomes, (i.e., list them), then define them, i.e., provide a detailed definition including details on method of assessment or on prespecified time point of primary interest, when relevant.	1. Identified only, not defined 2. Identified and defined 3. Not identified
Type of research question	The type of research question the study is addressing: efficacy, safety or both according to the *objective* and the *outcomes* reported in the *Methods section.* Mortality can be considered an efficacy and/or a safety outcome depending on the context. Adverse events are safety outcomes.	1. Effectiveness 2. Safety 3. Both
Confounders		
Confounders/Covariates reported	Confounders/confounders were clearly identified e.g., a list of confounders is reported	1. Yes 2. No
Identifying confounders/covariates	How were the confounders/covariates identified?	1. Literature 2. Statistical methods 3. Confounders/covariates are ONLY listed with no justification 4. Other: Specify 5. Not reported
Method of identifying confounders/covariates *[if they were identified through statistical methods]*	Method of identifying confounders/covariates through analysis. For example, authors use the backward or forward approach in the model, or they use a specific p-value cut-off. 'Not applicable' is when confounders/covariates where identified through methods other than 'analysis'	1. Select variables that are statistically significant in univariate analysis (p-value<0.05) 2. Select variables that have a p-value less than the chosen cut-off in the univariate analysis (other than 0.05) 3. Backward approach in the model

		4. Forward approach in the model 5. Other: Specify 6. Not applicable
Accounting for confounding	Method for accounting for confounding factors. G-computation is also referred to as parametric g-formula or g-standardization or regression-imputation	1. Matching 2. Stratification or regression 3. Inverse probability weighting 4. Standardization 5. Cloning and censoring 6. G-computation (i.e. regression-imputation) 7. Other: Specify 8. Not reported
Description of method to account for confounding	Describe the method used to account for confounding (e.g. regression with imputation, linear regression, logistic regression, time-varying cox model, etc)	[Open-ended]
Propensity score	Propensity score is used	1. Yes 2. No
E-value reported	E-value is reported. E-value is a new standardized approach for sensitivity analyses on confounding in observational studies. It is the minimum magnitude of association that an unmeasured confounder needs to have with both the exposure and the outcome to fully explain away the observed exposure-outcome association, conditional on the measured covariates.	1. Yes 2. No
Use of negative control reported	Use of negative control outcomes or exposures. A negative control outcome (NCO) is a variable known not to be causally affected by the treatment of interest. Likewise, a negative control exposure (NCE) is a variable known not to causally affect the outcome of interest. In prior literature, NCO has been referred to as falsification outcome/endpoint, control outcome, secondary outcome, supplementary response, and unaffected outcome. NCE has been referred to as control exposure and residual confounding	1. Negative control outcome(s) 2. Negative control exposure(s) 3. Not reported

	indicator. Both NCO and NCE have been referred to as proxies of unmeasured confounder.	
Patients included once or multiple times	Patients were allowed to enter the study population once or multiple times (i.e., new user study design)*	1. Once 2. Multiple times
Addressing multiple time zeros	Method to address having multiple eligibility timepoints*	1. Choose one of the multiple times 2. Take all eligibility times (sequence nested trials) 3. Choose eligible times and match person-time 4. No solution described 5. Not applicable
Study size		
Sample size determination	How was sample size determined is reported? Post-hoc power calculations are not relevant.	1. Yes: Specify 2. No
Participants considered eligible	Total number of participants considered eligible. If there are multiple cohorts in the study, report the number of participants of the largest one. If there are multiple analysis (ITT and PP), report the number of participants of the main analysis or ITT analysis if not specified. If there are different number of participants for different outcomes, report the one for the primary outcome. If there is more than one observation per patient, report the number of participants and not the number of observations. If there is matching or weighting, report the number of eligible participants before matching or weighting.	Continuous number
Participants analyzed	Total number of participants analyzed If there is matching or weighting, report the number of eligible participants after matching or weighting.	Continuous number
Analysis		
Analysis/Causal contrast of interest planned	Analysis or causal contrast of interest that is planned as reported	1. Per-protocol 2. Intention-to-treat 3. Both 4. Not reported
Analysis/Causal contrast of interest conducted	Analysis or causal contrast of interest that is conducted/done as judged by reviewer*	1. Per-protocol 2. Intention-to-treat 3. Both 4. Other: Specify
Follow-up		

Longest follow-up reported for an outcome (in months)	Longest follow-up time reported for an outcome (specifying the unit), e.g., median or mean of FU time reported or a specified time period e.g., 2-year mortality. If the outcome measured in unit of time e.g., 'length of stay', then report the median or mean for this outcome.	Continuous number
Target trial emulation		
Target trial	Did the author(s) specify a target trial?	1. Yes 2. No
Time points are clearly reported	Are the three timepoints clearly reported? The three timepoints are: 1. Eligibility: Time point of patients meeting complete eligibility criteria reported 2. Assignment: Time point of treatment initiation reported (treatment assignment) 3. Follow-up: Time point of the start of follow-up reported (baseline, time zero, T0)	1. Yes 2. No
Possible to identify the three time points *[If the three timepoints are not clearly reported]*	Is it possible to identify the three time points?	1. Yes 2. No 3. Not applicable
Key time points reported or identified are synchronized *[If the three timepoints are reported or identified]*	Are all three time points reported or identified are synchronized (i.e., eligibility, treatment assignment and start of follow-up)? 'Not applicable' is when NOT all of the three timepoints are reported	1. Yes 2. No 3. Unclear 4. Not applicable
Bias		
Relevant reported bias	Do the authors report presence of bias(es) (either accounted for or not) in the Methods or Discussion sections? Specify the bias reported, e.g., confounding bias, selection bias, etc	1. Yes: Specify 2. No
Bias due to inclusion of prevalent users	Was there a risk of bias due to inclusion of prevalent users as judged by reviewers? When (1) follow-up starts after eligibility criteria completion and treatment assignment OR (2) Follow-up starts at eligibility but after treatment assignment.	1. Yes 2. No 3. Unable to assess

	E.g., including individuals who initiated one of the treatment strategies of interest some time before the start of follow-up and who continue to follow the same strategy during the follow-up. Patients who experience early outcomes after starting the treatment are not captured.	
Bias in selection of participants due to post-treatment/baseline eligibility	Was there a risk of bias in selection in selection of participants due to post-treatment/baseline eligibility as judged by reviewers? When (2) follow-up starts at eligibility but after treatment assignment OR (3) Follow-up starts before treatment assignment and eligibility. E.g., including individuals to meet some eligibility criteria after treatment assignment (post-treatment criteria) In a target trial, there were several sequential eligibility criteria: having a diagnosis of colon cancer, undergoing surgery for colon cancer, surviving 1 month after surgery. Individuals who die between the times of first and last eligibility criterion –between colon cancer diagnosis and 1 month after surgery – were not included in the trial because they never complete eligibility into the study. Because treatment assignment predates eligibility, selection bias may arise. The same bias would arise if 'surviving 1 month after surgery' was instead, for example, 'receiving at least 2 consecutive prescriptions of treatment' where those who stopped the treatment after 1 prescription are excluded.	1. Yes 2. No 3. Unable to assess
Bias due to immortal time period	Was there a risk of bias due to immortal time period as judged by reviewers? When (3) follow-up starts before treatment assignment and eligibility OR (4) follow-up starts at eligibility but treatment is assigned later. E.g., taking the same example as the one before, immortal time bias exists because by definition nobody would die between treatment assignment and the completion of the eligibility criteria (surviving 1 month after surgery). Similarly, taking the other example 'receiving at least 2 consecutive prescriptions', patients who have an outcome between prescription 1 and prescription 2 are excluded from the analysis. Having a grace period would also lead to bias due to immortal time period.	1. Yes 2. No 3. Unable to assess

Bias in classification of treatment arms	Was there a risk of bias of classification of treatment arms as judged by reviewers? When (4) follow-up starts at eligibility but treatment is assigned later. When there is a grace period, assigning the treatment strategies based on a minimum or maximum number of prescriptions during a period after time zero (e.g., at least three prescriptions for active treatment and 0 prescriptions for no treatment) OR based on the mean number of treatment prescriptions after time zero. E.g., If there is a grace period where initiating treatment is within 6 days of diagnosis, if the patient has an outcome before day 6 without having started the treatment, it is uncertain whether to classify the patient in the treatment or no treatment arm. Assigning these patients to a single arm leads to bias due to classification of treatment arms.	1. Yes 2. No 3. Unable to assess
Strategy for addressing bias judged	What is the strategy to address the risk of bias identified by reviewers?	1. Selection of new users 2. An exact copy of the population was assigned to treatment and censored when deviation occurs 3. Exposure was considered as time-dependent variable in all analysis 4. Random assignment 5. Creating clone and assigning each clone to treatment arm 6. Series of analysis 7. Matching 8. Other: Specify 9. More than one: Specify 10. Not reported 11. Not applicable
Which bias was addressed	Specify which bias was addressed using the strategies specified in the previous question. If there is more than one strategy, then specify which strategy is used for which bias.	1. Prevalence user bias 2. Selection bias 3. Immortal time bias 4. Misclassification bias 5. More than one: Specify 6. Not applicable

Addressed bias due to inclusion of prevalent users	Was the bias due to inclusion of prevalent users addressed? Not applicable: When there is no bias	1. Yes 2. No 3. Not applicable
Addressed bias in selection of participants due to post-treatment/baseline eligibility	Was the bias in selection of participants due to post-treatment/baseline eligibility addressed? Not applicable: When there is no bias	1. Yes 2. No 3. Not applicable
Addressed bias due to immortal time periods	Was the bias due to immortal time periods addressed? Not applicable: When there is no bias	1. Yes 2. No 3. Not applicable
Addressed bias in classification of treatment arms	Was the bias in classification of treatment arms? Not applicable: When there is no bias	1. Yes 2. No 3. Not applicable
Open Science indicators		
Registration	Registration of the study in study registry	1. Yes 2. No
Protocol	Availability of (or accessibility to) the study protocol	1. Yes (open-access) 2. Yes (not open-access) 3. No
Changes reported	Important changes to protocol or statistical analysis plan with reasons are reported, e.g., the manuscript has a section on 'changes to protocol'	1. Yes 2. No
Data sharing statement	Data sharing statement	1. Data available in a public, open access repository 2. Data are available upon reasonable request 3. Data may be obtained from a third party and are not publicly available 4. All data relevant to the study are included in the article or uploaded as supplementary information 5. Data sharing not applicable as no datasets generated and/or analyzed for this study 6. Not reported
Access to the coding and algorithms	Code and algorithm provided, either as supplementary material or an accessible link to classify exposure and/or outcome	1. Code and algorithm used to classify exposures provided 2. Code and algorithm to classify outcomes provided 3. Both 4. None 5. Available upon request
Funding source	Funding source	1. Internal funding 2. Governmental 3. Intergovernmental

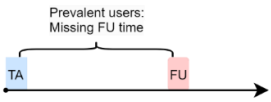
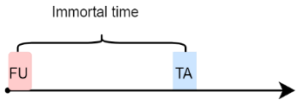
		4. Private-for-profit (companies/entities) 5. Private not-for-profit (organizations/philanthropies) 6. More than one: specify 7. Unclear 8. No funding 9. Not reported
Conflict of interest	Conflict of interests (COIs) of authors	1. None declared 2. Financial COI 3. Non-financial COI 4. Both types of COIs 5. Not reported
Ethical approval	Review of study by ethical/institutional review board	1. Approved 2. Waived 3. Not reviewed 4. Not reported
Adherence to reporting GL	Indication of adherence to reporting guideline	1. STROBE 2. RECORD 3. RECORD-PE 4. Other: Specify 5. Not reported
Use of causal language	Do authors conclude on the effect of the treatment using causal language in the **abstract.**	1. Yes 2. No
Conclusion in abstract	Authors' conclusion on the effect of the treatment is in favor, neutral or against the treatment in the **abstract.***	1. In favor of the treatment 2. Not in favor nor against the treatment (no clear preference) 3. Against the treatment 4. Unclear
Specific notes	Specific concepts, ideas, classifications to highlight for mapping of NRS	• Open-ended
General notes	General notes	• Open-ended

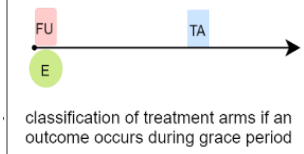
*Results are not presented.

Appendix 3. Study design

We considered the study as case-control when the participants were selected according to the outcome and then the treatment exposure was assessed. We considered the study design as cohort when the participants were selected according to the treatment exposure and the outcome was subsequently assessed.

Appendix 4. Summary table of possible biases related to time point misalignment

Bias	Illustration*	Explanation	Example	Methods to address it
Bias due to inclusion of prevalent users	 Time point of eligibility can be at treatment assignment or follow-up.	This occurs when follow-up starts after treatment initiation, therefore individuals who experience early outcomes after starting the treatment will not be included (if the outcome is death) or the outcome data may not be captured (if the outcome is different than death).	Hospitalized patients may already be taking DOACs prior to hospitalization although the follow-up in the study starts at hospitalization (eligibility). Individuals who die in the time-period between initiating DOACs and meeting eligibility (hospitalization)/start of follow-up will not be included in the study, or data on outcomes that occur during that time period will not be captured.	Only include new users
Bias due to post-treatment eligibility	 Time point of follow-up can be at treatment assignment or eligibility.	This occurs when eligibility is based on criteria that occurred after treatment initiation (e.g., specific duration of follow-up or having an event during follow-up).	1) Specific duration of follow-up: Only hospitalized patients who were followed up for one week would be included. 2) Having an event during follow-up: Hospitalized patients taking DOACs should have a specific level of international normalised ratio (INR) to be eligible, otherwise they would be excluded. Another example is if hospitalized patients on treatment with DOACs are excluded if major bleeding occurs, before the start of follow-up (i.e., follow-up start after treatment assignment).	Do not include participants based on post-treatment eligibility criteria
Bias due to immortal time periods	 The time point of eligibility can be at treatment assignment or at follow-up.	This occurs when treatment initiation is after the start of follow-up. There is 'immortal time', i.e., participants must survive long enough to receive the treatment being studied (they cannot experience the outcome during some period of follow-up time).	1) Sequential eligibility: to be included, patients should be hospitalized and survive for one week in hospitalization. Those who die in the first week will be excluded since they never fulfill the eligibility criteria. 2) Use of treatment during follow-up: Eligible hospitalized patients need to have at least two prescriptions to be assigned to the DOACs group. If they have received the two prescriptions, it implicitly means that they have survived through the two prescriptions.	- Clone exact copies of participants and assign each clone to one of strategies then censor the clone when strategies are deviated from - Randomly assign participants to one of the treatment strategies - Conducting a sequence of nested trial emulations where study eligibility criteria are applied and

			3) Grace period[a]: if eligible hospitalized patients can initiate DOACs within one week of hospitalization, it means that patients who initiate treatment at day 7 have survived an entire week.	treatment status is defined at different time points - Consider the exposure as a time-dependent variable
Bias due to classification of treatment arms	 classification of treatment arms if an outcome occurs during grace period	This occurs when there is uncertainty to which treatment arm the participant should be assigned to.	Eligible hospitalized patients can initiate DOACs within one week of hospitalization (i.e., 7-day grace period) and a major bleeding occurred at day 6 in patients who were not receiving DOACs, it is uncertain whether to classify the patient in the DOAC group or no prophylaxis group.	- Clone exact copies of participants and assign each clone to one of strategies then censor the clone when strategies are deviated from - Randomly assign participants to one of the treatment strategies

Abbreviations: FU: time point for start of follow-up, E: time point for eligibility, DOAC: direct oral anticoagulants, VTE: venous thromboembolism

[a]Grace period: a period between when participants meet eligibility to when they initiate the treatment. If not adequately addressed in the analysis, the presence of a grace period would impose risk of bias due to immortal time period and due to classification of treatment.

Appendix 5. Methods to address bias due to immortal time period and due to classification of treatment arms

- Clone-censor-weight approach (1): This method consists of cloning exact copies of participants and assigning each clone to one of strategies, then censoring the clone when strategies are deviated from, followed by using inverse-probability-of-censoring weights, where uncensored observations are up-weighted to represent censored observations with similar characteristics (n=1) [a,b]
- Randomly assigning participants to one of the treatment strategies (2-4): participants would be randomly assigned to one treatment strategy (n=2) [a]
- Conducting a sequence of nested trial emulations (2-4): several trial emulations are conducted where study eligibility criteria are applied and treatment status is defined at different time points (n=3)
- Consider the treatment as a time-dependent variable (2-4) and use an approach to address time-dependent confounding factors (n=10) [a]
- Landmark analysis (5): landmark time is selected and any participant who were lost to follow-up prior to that time is excluded from further analysis, while remaining participants who remain are classified based on their response at the landmark time (n=1) [c]

[a] More than one method was used in two reports: 1) clone-censor-weight approach with considering the treatment as time-dependent variable; and 2) randomly assigning participants with considering the treatment as time-dependent variable.

[b] The grace period introduced from clone-censor-weight approach was labeled as 'presence of grace period', but was considered as 'addressed' i.e., did not induce bias.

[c] May introduce prevalent user bias

1. Maringe C, Benitez Majano S, Exarchakou A, Smith M, Rachet B, Belot A, et al. Reflection on modern methods: trial emulation in the presence of immortal-time bias. Assessing the benefit of major surgery for elderly lung cancer patients using observational data. International journal of epidemiology. 2020;49(5):1719-29.

2. Hernán MA, Wang W, Leaf DE. Target Trial Emulation: A Framework for Causal Inference From Observational Data. Jama. 2022;328(24):2446-7.

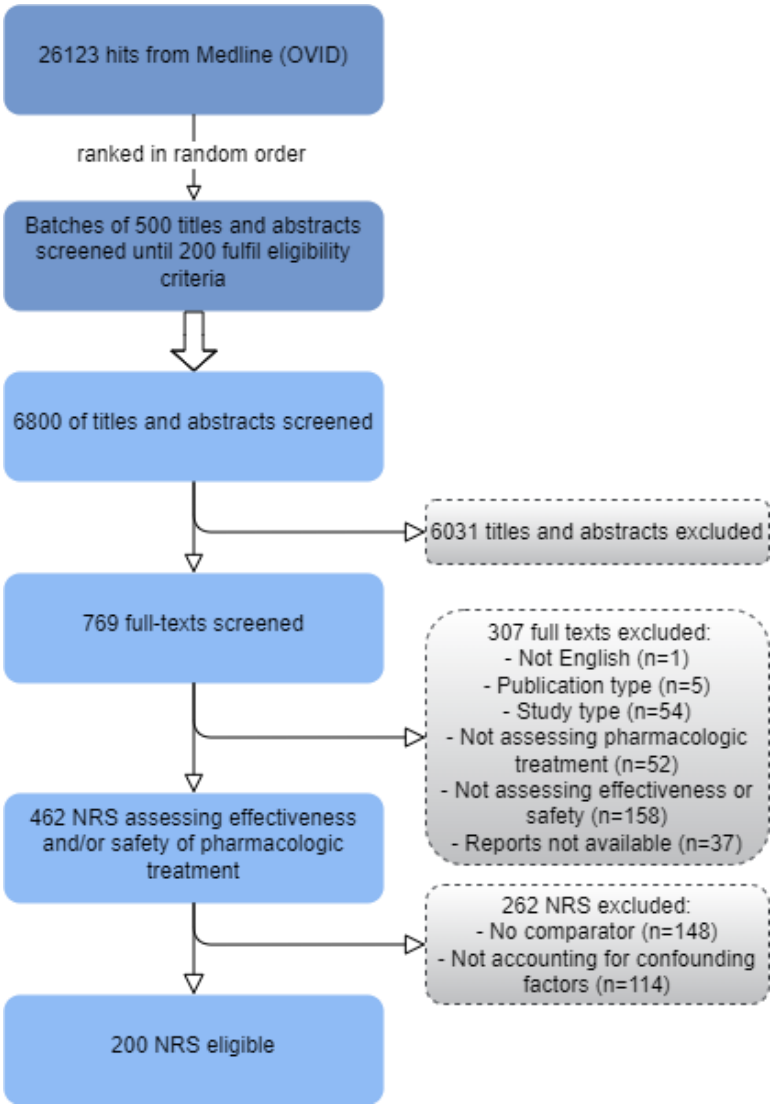
3. Hernán MA, Sauer BC, Hernández-Díaz S, Platt R, Shrier I. Specifying a target trial prevents immortal time bias and other self-inflicted injuries in observational analyses. J Clin Epidemiol. 2016 Nov;79:70-75.

4. Nguyen VT, Engleton M, Davison M, Ravaud P, Porcher R, Boutron I. Risk of bias in observational studies using routinely collected data of comparative effectiveness research: a meta-research study. BMC medicine. 2021;19(1):279.

5. Morgan C. J. (2019). Landmark analysis: A primer. Journal of nuclear cardiology : official publication of the American Society of Nuclear Cardiology, 26(2), 391–393. https://doi.org/10.1007/s12350-019-01624-z

Appendix 6. Flowchart of included reports of non-randomized studies

Abbreviations: NRS: Non-randomized studies



Appendix 7. List of included reports of non-randomized studies

- Arishi H, AlQahtani S, Tamim H, Sadat M, Alenezi FZ, Bin Humaid F, et al. Combination of norepinephrine with phenylephrine versus norepinephrine with vasopressin in critically ill patients with septic shock: A retrospective study. Journal of critical care. 2022;72:154121.
- Frost HM, Bizune D, Gerber JS, Hersh AL, Hicks LA, Tsay SV. Amoxicillin versus other antibiotic agents for the treatment of acute otitis media in children. The Journal of pediatrics. 2022.
- Chang W-C, Wang J-H, Ding D-C. Menopausal hormone therapy with conjugated equine estrogen is associated with a higher risk of hemorrhagic stroke than therapy with estradiol: a retrospective population-based cohort study. Maturitas. 2022;165:72-7.
- Martinez-Ales G, Domingo-Relloso A, Quintana-Diaz M, Fernandez-Capitan C, Hernan MA, Group CH. Thromboprophylaxis with standard-dose vs. flexible-dose heparin for hospitalized COVID-19 patients: a target trial emulation. Journal of clinical epidemiology. 2022;151:96-103.
- Ingason AB, Hreinsson JP, Agustsson AS, Lund SH, Rumba E, Palsson DA, et al. Warfarin Is Associated With Higher Rates of Upper But Not Lower Gastrointestinal Bleeding Compared to Direct Oral Anticoagulants: A Population-Based Propensity-Weighted Cohort Study. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association. 2022.
- Axelrad JE, Li T, Bachour SP, Nakamura TI, Shah R, Sachs MC, et al. Early Initiation of Antitumor Necrosis Factor Therapy Reduces Postoperative Recurrence of Crohn's Disease Following Ileocecal Resection. Inflammatory bowel diseases. 2022.
- Tuckett J, Brierly GI, Tong J, McGowan K, Ramalingam L, Batstone MD. Do Post-injury Prophylactic Antibiotics Reduce Infection for Isolated Midface Fractures: A Cohort Study. Journal of oral and maxillofacial surgery : official journal of the American Association of Oral and Maxillofacial Surgeons. 2022.
- Abbas N, Culver EL, Thorburn D, Halliday N, Crothers H, Dyson JK, et al. UK-wide Multicenter Evaluation of Second-line Therapies in Primary Biliary Cholangitis. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association. 2022.
- Farzaneh CA, Pigazzi A, Duong WQ, Carmichael JC, Stamos MJ, Dekhordi-Vakil F, et al. Analysis of delay in adjuvant chemotherapy in locally advanced rectal cancer. Techniques in coloproctology. 2022.
- Valcarcel S, Gallego J, Jimenez-Fonseca P, Diez M, de Castro EM, Hernandez R, et al. Does HER2 status influence in the benefit of ramucirumab and paclitaxel as second line treatment of advanced gastro-esophageal adenocarcinoma? Data from the AGAMENON-SEOM registry. Journal of cancer research and clinical oncology. 2022.
- de Steenwinkel FDO, Dolhain RJEM, Hazes JMW, Hokken-Koelega ACS. Does prednisone use in pregnant women with rheumatoid arthritis induce insulin resistance in the offspring? Clinical rheumatology. 2022.
- Honda A, Iizuka Y, Michihata N, Uda K, Mieda T, Takasawa E, et al. Effect of Intraoperative Tranexamic Acid on Perioperative Major Hemorrhage Requiring Transfusion in Patients Undergoing Elective Spine Surgery: A Propensity Score-Matched Analysis Using a National Inpatient Database. Global spine journal. 2022:21925682221123317.

- Lahteenvuo M, Luykx JJ, Taipale H, Mittendorfer-Rutz E, Tanskanen A, Batalla A, et al. Associations between antipsychotic use, substance use and relapse risk in patients with schizophrenia: real-world evidence from two national cohorts. The British journal of psychiatry : the journal of mental science. 2022:1-8.
- Yamamoto A, Kawashima A, Uemura T, Yamamichi G, Tomiyama E, Koh Y, et al. Anticancer maintenance chemotherapy prolonged prognosis of metastatic urothelial carcinoma patients: A single institute retrospective study using propensity score matching. International journal of urology : official journal of the Japanese Urological Association. 2022.
- Birkner B, Rech J, Edelmann E, Verheyen F, Schett G, Stargardt T. Patient-individual tapering of DMARDs in rheumatoid arthritis patients in a real-world setting. Rheumatology (Oxford, England). 2022.
- Puaratanaarunkon T, Kerr SJ, Rerknimitr P. Efficacy of antimalarial agents to prevent the progression of discoid lupus erythematosus to systemic lupus erythematosus: A retrospective cross-sectional study. Asian Pacific journal of allergy and immunology. 2022.
- Cogen JD, Hall M, Faino AV, Ambroggio L, Blaschke AJ, Brogan TV, et al. Antibiotics and outcomes of CF pulmonary exacerbations in children infected with MRSA and Pseudomonas aeruginosa. Journal of cystic fibrosis : official journal of the European Cystic Fibrosis Society. 2022.
- Glanz JM, Binswanger IA, Clarke CL, Nguyen AP, Ford MA, Ray GT, et al. The association between buprenorphine treatment duration and mortality: a multi-site cohort study of people who discontinued treatment. Addiction (Abingdon, England). 2022.
- Hedvat J, Lange NW, Salerno DM, DeFilippis EM, Kovac D, Corbo H, et al. COVID-19 therapeutics and outcomes among solid organ transplant recipients during the Omicron BA.1 era. American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons. 2022.
- Brunetti VC, Yu OHY, Platt RW, Filion KB. The association of long-acting insulin analogue use versus neutral protamine Hagedorn insulin use and the risk of major adverse cardiovascular events among individuals with type 2 diabetes: A population-based cohort study. Diabetes, obesity & metabolism. 2022.
- Fang Y-F, Liu J-R, Chang S-H, Kuo C-F, See L-C. Comparative safety of Janus kinase inhibitors and tumor necrosis factor inhibitors in patients undergoing treatment for rheumatoid arthritis. International journal of rheumatic diseases. 2022.
- Chen S, Yuan B, Yu W, Wang X, He C, Chen C. Comparison of Arterial Infusion Chemotherapy and Chemoembolization for Locally Advanced Hepatocellular Carcinoma: a Multicenter Retrospective Study. Journal of gastrointestinal surgery : official journal of the Society for Surgery of the Alimentary Tract. 2022.
- Maeda-Minami A, Takagi M, Mano Y, Ishikawa H, Matsuyama Y, Mutoh M. Association between statins and incidence of cancer in patients with dyslipidemia using large-scale health insurance claims data. Cancer prevention research (Philadelphia, Pa). 2022.
- Gremke N, Kostev K, Kalder M. Association between antihypertensive medication and the risk of urinary tract infection (UTI) of outpatients: a retrospective cohort study. Infection. 2022.
- Altun D, Arnaz A, Dogan A, Yalcinbas Y, Turkoz R, Oktay A, et al. A retrospective analysis of dexmedetomidine and morphine in the fast-track and ultra-fast-track extubation protocol after congenital cardiac surgery. Journal of cardiac surgery. 2022.

- Bajracharya GR, Esa WAS, Mao G, Leung S, Cohen B, Maheshwari K, et al. Regional analgesia and surgical site infections after colorectal surgery: a retrospective cohort analysis. Brazilian journal of anesthesiology (Elsevier). 2022.
- Betrian S, Angeles MA, Gil Moreno A, Cabarrou B, Deslandres M, Ferron G, et al. Survival impact of histological response to neoadjuvant chemotherapy according to number of cycles in patients with advanced ovarian cancer. International journal of gynecological cancer : official journal of the International Gynecological Cancer Society. 2022.
- Jung YS, Kim S, Kim H-Y, Noh SJ, Park JH, Park CH. 7-day versus 14-day tegoprazan-based triple therapy to treat Helicobacter pylori infection: Real-world evidence. Journal of gastroenterology and hepatology. 2022.
- Cranmer LD, Hess LM, Sugihara T, Muntz HG. Cardiac events among patients with sarcoma treated with doxorubicin by method of infusion: A real-world database study. Cancer reports (Hoboken, NJ). 2022:e1681.
- Yu M, Wang Z, Zong L, Xu Q, Li X, Lv Q. A retrospective cohort study of the effectiveness and safety of dabigatran versus rivaroxaban in overweight patients with nonvalvular atrial fibrillation. International journal of clinical pharmacy. 2022.
- Blank M, Katsiampoura A, Wachtendorf LJ, Linhardt FC, Tartler TM, Raub D, et al. Association Between Intraoperative Dexamethasone and Postoperative Mortality in Patients Undergoing Oncologic Surgery: A Multicentric Cohort Study. Annals of surgery. 2022.
- Meyer A, Fumery M, Peyrin-Biroulet L, Filippi J, Altwegg R, Bouhnik Y, et al. Comparative real-world effectiveness of vedolizumab and ustekinumab for patients with ulcerative colitis: a GETAID multicentre cohort study. Scandinavian journal of gastroenterology. 2022:1-9.
- Kaplan S, Bertoia ML, Lass A, Wang FT, Evans A, Dhanda S, et al. Delayed pregnancy detection and return to fertility with extended levonorgestrel-containing oral contraceptives: A real world setting cohort study. Pharmacoepidemiology and drug safety. 2022.
- Rupp T, von Vopelius E, Strahl A, Oheim R, Barvencik F, Amling M, et al. Beneficial effects of denosumab on muscle performance in patients with low BMD: a retrospective, propensity score-matched study. Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA. 2022.
- Imaeda S, Shiraishi Y, Kohsaka S, Niimi N, Goda A, Nagatomo Y, et al. Use of short-acting vs. long-acting loop diuretics after heart failure hospitalization. ESC heart failure. 2022.
- Shahrivar M, Weibull CE, Ekstrom Smedby K, Glimelius B, Syk I, Matthiessen P, et al. Low-dose aspirin use and colorectal cancer survival in 32,195 patients-A national cohort study. Cancer medicine. 2022.
- Li J, He L, Tang H, Peng T, Long Y, Zeng P, et al. Adverse events after different forms of botulinum neurotoxin A injections in children with cerebral palsy: An 8-year retrospective study. Developmental medicine and child neurology. 2022.
- Xu S, Li Z, Yang T, Li L, Song X, Hao Y, et al. Association between Early Oral beta-Blocker Therapy and Risk for In-Hospital Major Bleeding after Percutaneous Coronary Intervention for Acute Coronary Syndrome: Findings from CCC-ACS Project. European heart journal Quality of care & clinical outcomes. 2022.
- Tangkananan A, Thongkhao P, Janmunee N, Hanprasertpong J. Impact of chemotherapy cycles on oncological outcomes in elders with locally advanced cervical cancer treated with concurrent chemoradiotherapy. Journal of medical imaging and radiation oncology. 2022.

- Joyce G, Ferido P, Thunell J, Tysinger B, Zissimopoulos J. Benzodiazepine use and the risk of dementia. Alzheimer's & dementia (New York, N Y). 2022;8(1):e12309.
- Wada A, Narita M, Nagasawa M, Kusaba T, Kubota S, Yoshida T, et al. Androgen receptor axis-targeted agents are not superior to conventional hormonal therapy for treatment of metastatic prostate cancer. Oncology letters. 2022;24(4):333.
- Lee S-J, Choi D-W, Kim C, Suh Y, Hong S-J, Ahn C-M, et al. Prolonged dual antiplatelet therapy after drug-eluting stent implantation in patients with diabetes mellitus: A nationwide retrospective cohort study. Frontiers in cardiovascular medicine. 2022;9:954704.
- Parisi A, Giampieri R, Mammarella A, Felicetti C, Salvatore L, Bensi M, et al. Primary versus secondary antiemetic prophylaxis with NK1 receptor antagonists in patients affected by gastrointestinal malignancies and treated with a doublet or triplet combination regimen including oxaliplatin and/or irinotecan plus fluoropyrimidines: A propensity score matched analysis. Frontiers in oncology. 2022;12:935826.
- Lee CM, Kim SJ, Hah SI, Kwak JY, Choi JW, Cho HC, et al. Comparison of eradication rates of moxifloxacin-rifabutin triple therapy and bismuth quadruple therapy as second-line regimens in patients with peptic ulcers. Health science reports. 2022;5(5):e780.
- Samarkos M, Papanikolaou K, Sourdi A, Paisios N, Mainas E, Paramythiotou E, et al. The Effect of Different Colistin Dosing Regimens on Nephrotoxicity: A Cohort Study. Antibiotics (Basel, Switzerland). 2022;11(8).
- Schupp T, Behnes M, Abumayyaleh M, Weidner K, Rusnak J, Mashayekhi K, et al. Carvedilol versus Metoprolol in Patients with Ventricular Tachyarrhythmias. Journal of cardiovascular development and disease. 2022;9(8).
- Ferretti F, Monico MC, Cannatelli R, Carmagnola S, Lenti MV, Di Sabatino A, et al. The impact of biologic therapies on extra-intestinal manifestations in inflammatory bowel disease: A multicenter study. Frontiers in medicine. 2022;9:933357.
- Dong Y, Xiao S, He J, Shi K, Chen S, Liu D, et al. Angiotensin receptor-neprilysin inhibitor therapy and recurrence of atrial fibrillation after radiofrequency catheter ablation: A propensity-matched cohort study. Frontiers in cardiovascular medicine. 2022;9:932780.
- Mujanovic A, Kurmann CC, Dobrocky T, Olive-Gadea M, Maegerlein C, Pierot L, et al. Bridging intravenous thrombolysis in patients with atrial fibrillation. Frontiers in neurology. 2022;13:945338.
- Komatsu Y, Yokoyama S, Hosomi K, Takada M. Impact of Medication Adherence on the Association Between Oral Anticoagulant Use and Risk of Dementia: A Retrospective Cohort Study using the Japanese Claims Database. Drugs - real world outcomes. 2022;9(3):437-49.
- Cai H-X, Liang C-C, Wang S-J, Guo J-C, Wang Y, Yu B, et al. Renin-angiotensin system antagonists and mortality due to pneumonia, influenza, and chronic lower respiratory disease in patients with hypertension. Journal of geriatric cardiology : JGC. 2022;19(7):511-21.
- Lu X, Yu Y, Wang Y, Lyu Y. Effect of Propofol or Etomidate as General Anaesthesia Induction on Gastric Cancer: A Retrospective Cohort Study with 10 Years' Follow-Up. Cancer management and research. 2022;14:2399-407.
- Beyer J, Jager Y, Balci D, Kolb G, Weschenfelder F, Seeger S, et al. Induction of Labor at Term with Oral Misoprostol or as a Vaginal Insert and Dinoprostone Vaginal Insert - A Multicenter Prospective Cohort Study. Geburtshilfe und Frauenheilkunde. 2022;82(8):868-73.
- Su Y-J, Huang J-Y, Chu C-Q, Wei JC-C. Sulfonylureas or biguanides is associated with a lower risk of rheumatoid arthritis in patients with diabetes: A nationwide cohort study. Frontiers in medicine. 2022;9:934184.

- Lee YJ, Seon KE, Jung DC, Lee J-Y, Nam EJ, Kim SW, et al. Interval debulking surgery with or without hyperthermic intraperitoneal chemotherapy in advanced-stage ovarian cancer: Single-institution cohort study. Frontiers in oncology. 2022;12:936099.
- Wang J, Fu H, Zhong Z, Jiang Y, Pan H, Sun X, et al. Local and systemic therapy may be safely de-escalated in elderly breast cancer patients in China: A retrospective cohort study. Frontiers in oncology. 2022;12:958116.
- Marconi L, Tedeschi S, Zamparini E, Terzi S, Rossi N, Boriani L, et al. Oral Versus Standard Antimicrobial Treatment for Pyogenic Native Vertebral Osteomyelitis: A Single-Center, Retrospective, Propensity Score-Balanced Analysis. Open forum infectious diseases. 2022;9(8):ofac366.
- Liu Q, Qiu J, Lu Q, Ma Y, Fang S, Bu B, et al. Comparison of endocrine therapy and chemotherapy as different systemic treatment modes for metastatic luminal HER2-negative breast cancer patients -A retrospective study. Frontiers in oncology. 2022;12:873570.
- Matikas A, Kotsakis A, Perraki M, Hatzidaki D, Kalbakis K, Kontopodis E, et al. Objective Response to First-Line Treatment as a Predictor of Overall Survival in Metastatic Breast Cancer: A Retrospective Analysis from Two Centers over a 25-Year Period. Breast care (Basel, Switzerland). 2022;17(3):264-71.
- Cho H-Y, Lee H-J, Kim WH, Lee H-C, Jung C-W, Hong SK, et al. Influence of anesthesia type on post-reperfusion syndrome during liver transplantation: a single-center retrospective study. Anesthesia and pain medicine. 2022;17(3):304-11.
- Yang L, Wang C, Liu M, Wang S. Evaluation of Adjuvant Treatments for Adenoid Cystic Carcinoma of the Breast: A Population-Based, Propensity Score Matched Cohort Study from the SEER Database. Diagnostics (Basel, Switzerland). 2022;12(7).
- Hu J, Chen Z, Lv J, Zheng Z, Bei Y, Chen X, et al. The Application of Nimotuzumab Combined With Definitive Chemoradiotherapy Toward the Treatment of Locally Advanced Cervical Esophageal Carcinoma: A Retrospective Study. Frontiers in oncology. 2022;12:905422.
- Lu Y-Y, Wang C-L, Chang S-H, Hsiao F-C, Huang Y-C, Huang Y-T, et al. Dual versus Single Antiplatelet Therapy in Medically Treated Acute Myocardial Infarction Patients with Baseline Thrombocytopenia - Insights from a Multi-Institute Cohort Study. Acta Cardiologica Sinica. 2022;38(4):443-54.
- Liu M, Bian X, Wang L, Li G. The Effect of Hydroxychloroquine on Residual Proteinuria in Patients With Immunoglobulin A Nephropathy: A Retrospective Study Based on Propensity Score Matching. Frontiers in medicine. 2022;9:922365.
- Scott LC, Li J, Cafuir LA, Gaddh M, Kempton CL. Comparing direct oral anticoagulants and vitamin K antagonist use in morbidly obese patients with venous thromboembolism: A single center retrospective cohort study. EJHaem. 2022;3(2):457-62.
- Yu M-X, Jia Y-N, Yang D-D, Zhang R-H, Jiang Y, Zhang G-T, et al. Association between antiplatelet medication and cerebral microbleeds in stroke-free population. Journal of geriatric cardiology : JGC. 2022;19(6):409-17.
- Zhou L, Li Y, Gao Q, Lin Y, Su L, Chen R, et al. Loop Diuretics Are Associated with Increased Risk of Hospital-Acquired Acute Kidney Injury in Adult Patients: A Retrospective Study. Journal of clinical medicine. 2022;11(13).
- Hua R, Ding N, Guo H, Wu Y, Yuan Z, Li T. Contrast-Induced Acute Kidney Injury in Patients on SGLT2 Inhibitors Undergoing Percutaneous Coronary Interventions: A Propensity-Matched Analysis. Frontiers in cardiovascular medicine. 2022;9:918167.

- Kawachi H, Tamiya M, Taniguchi Y, Yokoyama T, Yokoe S, Oya Y, et al. Efficacy of Immune Checkpoint Inhibitor With or Without Chemotherapy for Nonsquamous NSCLC With Malignant Pleural Effusion: A Retrospective Multicenter Cohort Study. JTO clinical and research reports. 2022;3(7):100355.
- Huang Y, Chen L, Huang R, Zhu C, Shang J, Qian Y, et al. Tenofovir is superior to entecavir in reducing HCC for patients with HBV-related compensated cirrhosis at high HCC risk scores. Therapeutic advances in chronic disease. 2022;13:20406223221102791.
- Chen Y, Wang Q, Xu Y, Wu D, Xu L, Zhu G, et al. Comparison of Lamotrigine and Oxcarbazepine Monotherapy Among Chinese Adult Patients With Newly-Diagnosed Focal-Onset Epilepsy: A Prospective Observational Study. Frontiers in neurology. 2022;13:855498.
- Hung K-H, Tsao S-L, Yang S-F, Wang B-Y, Huang J-Y, Li W-T, et al. Association of General Anesthesia and Neuraxial Anesthesia in Caesarean Section with Maternal Postpartum Depression: A Retrospective Nationwide Population-Based Cohort Study. Journal of personalized medicine. 2022;12(6).
- Pinte L, Ceasovschih A, Niculae C-M, Stoichitoiu LE, Ionescu RA, Balea MI, et al. Antibiotic Prescription and In-Hospital Mortality in COVID-19: A Prospective Multicentre Cohort Study. Journal of personalized medicine. 2022;12(6).
- Jahn N, Volker MT, Laudi S, Stehr S, Schneeberger S, Brandacher G, et al. Analysis of Volatile Anesthetic-Induced Organ Protection in Simultaneous Pancreas-Kidney Transplantation. Journal of clinical medicine. 2022;11(12).
- Lee HH, Kwon HM, Lee W-S, Yang IH, Choi YS, Park KK. Effectiveness of ERAS (Enhanced Recovery after Surgery) Protocol via Peripheral Nerve Block for Total Knee Arthroplasty. Journal of clinical medicine. 2022;11(12).
- Wong CKH, Lau KTK, Au ICH, Xiong X, Chung MSH, Leung BYC, et al. Initiation of Tocilizumab or Baricitinib Were Associated With Comparable Clinical Outcomes Among Patients Hospitalized With COVID-19 and Treated With Dexamethasone. Frontiers in pharmacology. 2022;13:866441.
- Rey JR, Merino Llorens JL, Iniesta Manjavacas AM, Rosillo Rodriguez SO, Castrejon-Castrejon S, Arbas-Redondo E, et al. Influence of statin treatment in a cohort of patients admitted for COVID-19. Medicina clinica (English ed). 2022;158(12):586-95.
- Meng Y, Yang Y, Fang Y, Lin X, Xie X, Deng H, et al. The Treatment Status of Patients in NSCLC With RET Fusion Under the Prelude of Selective RET-TKI Application in China: A Multicenter Retrospective Research. Frontiers in oncology. 2022;12:864367.
- Mavrakanas TA, Soomro QH, Charytan DM. Hydralazine-Isosorbide Dinitrate Use in Patients With End-Stage Kidney Disease on Dialysis. Kidney international reports. 2022;7(6):1332-40.
- Goh LGH, Sun J, Ong BSK, Khoo D, Sum CF, Ng K. Real-world evaluation of sodium-glucose co-transporter-2 inhibitors and dipeptidyl peptidase-4 inhibitors for managing type 2 diabetes mellitus: a retrospective multi-ethnic cohort study. Journal of diabetes and metabolic disorders. 2022;21(1):521-55.
- Lagier J-C, Million M, Cortaredona S, Delorme L, Colson P, Fournier P-E, et al. Outcomes of 2111 COVID-19 Hospitalized Patients Treated with Hydroxychloroquine/Azithromycin and Other Regimens in Marseille, France, 2020: A Monocentric Retrospective Analysis. Therapeutics and clinical risk management. 2022;18:603-17.
- Trujillo-Santos J, Farge-Bancel D, Pedrajas JM, Gomez-Cuervo C, Ballaz A, Braester A, et al. Enoxaparin versus dalteparin or tinzaparin in patients with cancer and venous thromboembolism: The RIETECAT study. Research and practice in thrombosis and haemostasis. 2022;6(4):e12736.

- Amjad W, Kamal F, Malik A, Singh R, Mahmood S. Histamine 2 receptor antagonists do not improve the outcomes of hospitalized COVID-19 patients. Przeglad gastroenterologiczny. 2022;17(2):146-51.
- Moon JY, Bae GH, Jung J, Shin DH. Restarting anticoagulant therapy after intracranial hemorrhage in patients with atrial fibrillation: A nationwide retrospective cohort study. International journal of cardiology Heart & vasculature. 2022;40:101037.
- Ding F, Chen R-Y, Hou J, Guo J, Dong T-Y. Efficacy and prognostic factors of neoadjuvant chemotherapy for triple-negative breast cancer. World journal of clinical cases. 2022;10(12):3698-708.
- Lo C-H, Ni P, Yan Y, Ma W, Joshi AD, Nguyen LH, et al. Association of Proton Pump Inhibitor Use With All-Cause and Cause-Specific Mortality. Gastroenterology. 2022;163(4):852-61.e2.
- Assimon MM, Pun PH, Wang L, Al-Khatib SM, Brookhart MA, Weber DJ, et al. Azithromycin use increases the risk of sudden cardiac death in patients with hemodialysis-dependent kidney failure. Kidney international. 2022;102(4):894-903.
- Johansson T, Fowler P, Ek WE, Skalkidou A, Karlsson T, Johansson A. Oral Contraceptives, Hormone Replacement Therapy, and Stroke Risk. Stroke. 2022;53(10):3107-15.
- Rifkin RM, Crawford J, Mahtani RL, Dale DC, Narang M, MacLaughlin WW, et al. A prospective study to evaluate febrile neutropenia incidence in patients receiving pegfilgrastim on-body injector vs other choices. Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer. 2022;30(10):7913-22.
- Kim Y, DeCarlo CS, Patel SS, McElroy IE, Majumdar M, Jessula S, et al. Impact of anticoagulation/antiplatelet therapy on femoropopliteal bypass graft outcomes. Journal of vascular surgery. 2022;76(4):1045-52.e1.
- Khan SZ, O'Brien-Irr MS, Fakhoury E, Montross B, Rivero M, Dosluoglu HH, et al. P2Y12 inhibitor monotherapy is associated with superior outcomes as compared with aspirin monotherapy in chronic limb-threatening ischemia. Journal of vascular surgery. 2022;76(4):1053-9.
- Li C, Zhang W, Chang Q, Li Y. Combination effect of intraoperative and postoperative intravenous tranexamic acid in hip hemiarthroplasty. A propensity score matched analysis. Injury. 2022;53(10):3401-6.
- Lopez PD, Bhatia K, Bohra C, Mahmood K, Baruch L, Eng C. Benefits of Adding Glucagon-Like Peptide 1 Receptor Agonists to Sodium-Glucose Co-Transporter 2 Inhibitors in Diabetic Patients With Atherosclerotic Disease and Heart Failure. The American journal of cardiology. 2022;181:87-93.
- Park JY, Hong S, Jo JH, Shin IH, Kim GY, Ko HS, et al. The effect of tocolytics in women with preterm labor after 34 weeks of gestation: A propensity score-matched study. European journal of obstetrics, gynecology, and reproductive biology. 2022;277:1-6.
- Gupta N, Settle L, Brown BR, Armaignac DL, Baram M, Perkins NE, et al. Association of Renin Angiotensin Aldosterone System Inhibitors and Outcomes of Hospitalized Patients With COVID-19. Critical care medicine. 2022;50(10):e744-e58.
- Lauper K, Iudici M, Mongin D, Bergstra SA, Choquette D, Codreanu C, et al. Effectiveness of TNF-inhibitors, abatacept, IL6-inhibitors and JAK-inhibitors in 31 846 patients with rheumatoid arthritis in 19 registers from the 'JAK-pot' collaboration. Annals of the rheumatic diseases. 2022;81(10):1358-66.

- Chiang C-H, Chiang C-H, Peng C-Y, Hsia YP, See XY, Horng C-S, et al. Efficacy of cationic amphiphilic antihistamines on outcomes of patients treated with immune checkpoint inhibitors. European journal of cancer (Oxford, England : 1990). 2022;174:1-9.
- McElwee ER, Wilkinson K, Crowe R, Hardy KT, Newman JC, Chapman A, et al. Latency of late preterm steroid administration to delivery and risk of neonatal hypoglycemia. American journal of obstetrics & gynecology MFM. 2022;4(5):100687.
- O'Kelly J, Bartsch R, Kossack N, Borchert J, Pignot M, Hadji P. Real-world effectiveness of osteoporosis treatments in Germany. Archives of osteoporosis. 2022;17(1):119.
- Nasioudis D, Mastroyannis SA, Ko EM, Haggerty AF, Cory L, Giuntoli RL, 2nd, et al. Delay in adjuvant chemotherapy administration for patients with FIGO stage I epithelial ovarian carcinoma is associated with worse survival; an analysis of the National Cancer Database. Gynecologic oncology. 2022;166(2):263-8.
- Piekarski BL, Rogers J, Zurakowski D, Thiagarajan R, Emani SM. Exploratory Use of Glycoprotein IIb/IIIa Inhibition in Prevention of Blalock-Taussig Shunt Thrombosis. Pediatric critical care medicine : a journal of the Society of Critical Care Medicine and the World Federation of Pediatric Intensive and Critical Care Societies. 2022;23(9):727-35.
- Mu X, Liu H, Wu J, Chen S, Peng X, Wang J, et al. Induction versus adjuvant chemotherapy combined with concurrent chemoradiotherapy in locoregionally advanced nasopharyngeal carcinoma: a retrospective cohort study. Aging. 2022;14(16):6727-39.
- Kim D-S, Kim HJ, Ahn HS. Statins and the risk of gastric, colorectal, and esophageal cancer incidence and mortality: a cohort study based on data from the Korean national health insurance claims database. Journal of cancer research and clinical oncology. 2022;148(10):2855-65.
- Kim SI, Kim JH, Noh JJ, Kim S-H, Kim TE, Kim K, et al. Impact of bevacizumab and secondary cytoreductive surgery on survival outcomes in platinum-sensitive relapsed ovarian clear cell carcinoma: A multicenter study in Korea. Gynecologic oncology. 2022;166(3):444-52.
- Guan Q, Men S, Juurlink DN, Bronskill SE, Wunsch H, Gomes T. Opioid Initiation and the Hazard of Falls or Fractures Among Older Adults with Varying Levels of Central Nervous System Depressant Burden. Drugs & aging. 2022;39(9):729-38.
- Smith EE, Zerna C, Solomon N, Matsouaka R, Mac Grory B, Saver JL, et al. Outcomes After Endovascular Thrombectomy With or Without Alteplase in Routine Clinical Practice. JAMA neurology. 2022;79(8):768-76.
- Becchetti C, Dirchwolf M, Schropp J, Magini G, Mullhaupt B, Immer F, et al. Use of statins after liver transplantation is associated with improved survival: results of a nationwide study. Alimentary pharmacology & therapeutics. 2022;56(7):1194-204.
- Khalil L, Gao X, Switchenko JM, Alese OB, Akce M, Wu C, et al. Survival Outcomes of Adjuvant Chemotherapy in Elderly Patients with Stage III Colon Cancer. The oncologist. 2022;27(9):740-50.
- Kim SY, Yoo DM, Kwon MJ, Kim JH, Kim J-H, Lee JS, et al. Association between Benign Paroxysmal Positional Vertigo and Previous Proton Pump Inhibitor Use: A Nested Case-Control Study Using a National Health Screening Cohort. International journal of environmental research and public health. 2022;19(16).
- Min J, Kim HW, Kang JY, Kim SK, Kim JW, Kim YH, et al. Comparison of different regimens with or without fluoroquinolone in isoniazid-resistant tuberculosis: A multicenter cohort study. PloS one. 2022;17(8):e0273263.

- Zo S, Kim H, Kwon OJ, Jhun BW. Antibiotic Maintenance and Redevelopment of Nontuberculous Mycobacteria Pulmonary Disease after Treatment of Mycobacterium avium Complex Pulmonary Disease. Microbiology spectrum. 2022;10(4):e0108822.
- Xiong L, Xu L, Lv X, Zheng X. Effects of corticosteroid treatment in patients with severe fever with thrombocytopenia syndrome: A single-center retrospective cohort study. International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases. 2022;122:1026-33.
- Hasan MM, Noor-E-Alam M, Shi J, Young LD, Young GJ. Long-term patient outcomes following buprenorphine/naloxone treatment for opioid use disorder: a retrospective analysis in a commercially insured population. The American journal of drug and alcohol abuse. 2022;48(4):481-91.
- Pham TT, Chen X, Barron J, Hart R, Abarca J, DeVries A. Effectiveness, safety and treatment adherence of biosimilar follow-on insulin in diabetes management. Diabetes, obesity & metabolism. 2022;24(10):1989-97.
- Kim NK, Suh DH, Kim K, No JH, Kim YB. Maximum daily dose of G-CSF is critical for preventing recurrence of febrile neutropenia in patients with gynecologic cancer: A case-control study. Medicine. 2022;101(34):e30155.
- Guberina M, Guberina N, Pottgen C, Gauler T, Richlitzki C, Metzenmacher M, et al. Effectiveness of durvalumab consolidation in stage III non-small-cell lung cancer: focus on treatment selection and prognostic factors. Immunotherapy. 2022;14(12):927-44.
- Yoon CH, Bartlett S, Stoesser N, Pouwels KB, Jones N, Crook DW, et al. Mortality risks associated with empirical antibiotic activity in Escherichia coli bacteraemia: an analysis of electronic health records. The Journal of antimicrobial chemotherapy. 2022;77(9):2536-45.
- Ludwick L, Shohat N, Van Nest D, Paladino J, Ledesma J, Parvizi J. Aspirin May Be a Suitable Prophylaxis for Patients with a History of Venous Thromboembolism Undergoing Total Joint Arthroplasty. The Journal of bone and joint surgery American volume. 2022;104(16):1438-46.
- Zhang S-J, Yang Y, Sun W-W, Zhang Z-S, Xiao H-P, Li Y-P, et al. Effectiveness and safety of bedaquiline-containing regimens for treatment on patients with refractory RR/MDR/XDR-tuberculosis: a retrospective cohort study in East China. BMC infectious diseases. 2022;22(1):715.
- Yun B, Ahn SH, Yoon J-H, Kim BK. Statin use and risk of progression to liver cirrhosis in chronic hepatitis B independent of conventional risk factors: A nationwide study. Hepatology communications. 2022;6(9):2455-64.
- Olson J, Franz-O'Neal E, Cipriano FA, Ou Z, Presson AP, Thorell EA. Impact of Early Oral Antibiotic Therapy in Infants With Bacteremic Urinary Tract Infections. Hospital pediatrics. 2022;12(7):632-8.
- Al Sulaiman K, Aljuhani O, Korayem GB, Altebainawi AF, Al Harbi S, Al Shaya A, et al. The impact of HMG-CoA reductase inhibitors use on the clinical outcomes in critically ill patients with COVID-19: A multicenter, cohort study. Frontiers in public health. 2022;10:877944.
- Guin S, Liaw BK, Jun T, Ayers K, Patel B, O'Connell T, et al. Management of de novo metastatic hormone-sensitive prostate cancer: A comprehensive report of a single-center experience. PloS one. 2022;17(8):e0264800.
- Cheung EYH, Chan DYC, Lee MWY, Hung CY, Pang KY. Urokinase Is Safe and Effective in Reducing Recurrence in Chronic Subdural Hematoma After Burr-Hole Drainage. World neurosurgery. 2022;164:e1209-e13.

- Luo H-D, Xia F-J, Wu J-H, Yi B. Efficacy of chemoradiotherapy in survival of stage IV nasopharyngeal carcinoma and establishment of a prognostic model. Oral oncology. 2022;131:105927.
- Nakai M, Iwanaga Y, Kanaoka K, Sumita Y, Nishioka Y, Myojin T, et al. Contemporary use of SGLT2 inhibitors in heart failure patients with diabetes mellitus: a comparison of DPP4 inhibitors in a nationwide electric health database of the superaged society. Cardiovascular diabetology. 2022;21(1):157.
- Lee J, Kim JM, Lee YH, Chong GO, Hong DG. Survival Outcomes With Reduced Doses of Adjuvant Chemotherapy in Advanced Epithelial Ovarian Cancer. In vivo (Athens, Greece). 2022;36(4):1868-74.
- Beydoun HA, Saquib N, Wallace RB, Chen J-C, Coday M, Naughton MJ, et al. Psychotropic medication use and Parkinson's disease risk amongst older women. Annals of clinical and translational neurology. 2022;9(8):1163-76.
- Burchard PR, Melucci AD, Lynch O, Loria A, Dave YA, Strawderman M, et al. Intrathecal Morphine and Effect on Opioid Consumption and Functional Recovery after Pancreaticoduodenectomy. Journal of the American College of Surgeons. 2022;235(3):392-400.
- Bartoletti R, Claps F, Tulone G, Perotti A, Zucchi A, Riccardi N, et al. Antibiotic prophylaxis in patients who had undergone to prostate biopsy in between the EMA warning era: effects of fluoroquinolones in diabetic and non-diabetic patients. Results of an observational cohort study. World journal of urology. 2022;40(8):2025-31.
- Hsiao F-C, Yen K-C, Chao T-F, Chen S-W, Chan Y-H, Chu P-H. New-Onset Atrial Fibrillation in Patients With Type 2 Diabetes Treated With Novel Glucose-Lowering Therapies. The Journal of clinical endocrinology and metabolism. 2022;107(9):2493-9.
- Chen Y, Ye X, Wu H, Yuan X, Yu X, Wu H, et al. Delivery, maternal and neonatal outcomes in nulliparous women with gestational diabetes undergoing epidural labour analgesia: a propensity score-matched analysis. BMJ open. 2022;12(7):e060245.
- Dilaghi E, Bellisario M, Esposito G, Carabotti M, Annibale B, Lahner E. The Impact of Proton Pump Inhibitors on the Development of Gastric Neoplastic Lesions in Patients With Autoimmune Atrophic Gastritis. Frontiers in immunology. 2022;13:910077.
- Udumyan R, Botteri E, Jerlstrom T, Montgomery S, Smedby KE, Fall K. Beta-blocker use and urothelial bladder cancer survival: a Swedish register-based cohort study. Acta oncologica (Stockholm, Sweden). 2022;61(8):922-30.
- Grant RRC, Khan TM, Gregory SN, Coakley BA, Hernandez JM, Davis JL, et al. Adjuvant chemotherapy is associated with improved overall survival in select patients with Stage II colon cancer: A National Cancer Database analysis. Journal of surgical oncology. 2022;126(4):748-56.
- Amitay EL, Niedermaier T, Alwers E, Chang-Claude J, Hoffmeister M, Brenner H. Reproductive Factors and Colorectal Cancer Risk: A Population-Based Case-Control Study. JNCI cancer spectrum. 2022;6(4).
- Kwon CH, Kim Y-J, Kim M-J, Cha M-J, Cho MS, Nam G-B, et al. Effect of Sodium-Glucose Cotransporter Inhibitors on Major Adverse Cardiovascular Events and Hospitalization for Heart Failure in Patients With Type 2 Diabetes Mellitus and Atrial Fibrillation. The American journal of cardiology. 2022;178:35-42.
- Shimony S, Canaani J, Kugler E, Nachmias B, Ram R, Henig I, et al. Gilteritinib monotherapy for relapsed/refractory FLT3 mutated acute myeloid leukemia: a real-world, multi-center, matched analysis. Annals of hematology. 2022;101(9):2001-10.

- Heath DM, Boyer BJ, Ghali AN, Momtaz DA, Nagel SC, Brady CI. Use of Clindamycin for Necrotizing Soft Tissue Infection Decreases Amputation Rate. Journal of orthopaedic trauma. 2022;36(7):327-31.
- Kitchin A, Huerta C, Llorente-Garcia A, Martinez D, Ortega P, Cea-Soriano L. The role of prenatal exposure to antidepressants, anxiolytic, and hypnotics and its underlying illness on the risk of miscarriage using BIFAP database. Pharmacoepidemiology and drug safety. 2022;31(8):901-12.
- Pires da Silva I, Zakria D, Ahmed T, Trojanello C, Dimitriou F, Allayous C, et al. Efficacy and safety of anti-PD1 monotherapy or in combination with ipilimumab after BRAF/MEK inhibitors in patients with BRAF mutant metastatic melanoma. Journal for immunotherapy of cancer. 2022;10(7).
- Mohamed A, Shemanski SM, Saad MO, Ploetz J, Haines MM, Schlachter AB, et al. Anti-Xa Directed Thromboprophylaxis in Critically Ill Patients with Coronavirus Disease 2019. Clinical and applied thrombosis/hemostasis : official journal of the International Academy of Clinical and Applied Thrombosis/Hemostasis. 2022;28:10760296221116350.
- Lamouche-Wilquin P, Souchard J, Pere M, Raymond M, Asfar P, Darreau C, et al. Early steroids and ventilator-associated pneumonia in COVID-19-related ARDS. Critical care (London, England). 2022;26(1):233.
- Al Sulaiman K, Korayem GB, Eljaaly K, Altebainawi AF, Al Harbi O, Badreldin HA, et al. Early dexamethasone use as a protective measure in non-mechanically ventilated critically ill patients with COVID-19: a multicenter, cohort study. Scientific reports. 2022;12(1):9766.
- Huang H-Y, Lin S-Y, Katz AJ, Sheu J-J, Lin F-J, Wang C-C, et al. Effectiveness and Safety of Clopidogrel vs Aspirin in Elderly Patients With Ischemic Stroke. Mayo Clinic proceedings. 2022;97(8):1483-92.
- Epstein E, Schale S, Brambatti M, You H, Hansen P, McCain J, et al. Impact of transitioning patients to oral diuretics 24 hours before discharge from heart failure hospitalization on 30 day outcomes. International journal of cardiology. 2022;364:72-6.
- Cantarutti A, Amidei CB, Bonaugurio AS, Rescigno P, Canova C. Early-life exposure to antibiotics and subsequent development of atopic dermatitis. Expert review of clinical pharmacology. 2022;15(6):779-85.
- Tsai M-H, Wu S-Y, Lu H-H, Yu T, Tsai S-T, Wu Y-H. Improved overall survival is associated with adjuvant chemotherapy after definitive concurrent chemoradiotherapy for N3 nasopharyngeal cancer. Scientific reports. 2022;12(1):13390.
- Ng HS, Zhu F, Kingwell E, Yao S, Ekuma O, Evans C, et al. Disease-Modifying Drugs for Multiple Sclerosis and Association With Survival. Neurology(R) neuroimmunology & neuroinflammation. 2022;9(5).
- Kim H, Yoo J, Han K, Lee D-Y, Fava M, Mischoulon D, et al. Hormone therapy and the decreased risk of dementia in women with depression: a population-based cohort study. Alzheimer's research & therapy. 2022;14(1):83.
- Lee K-C, Cheng J-S, Chang M-L, Chien R-N, Liaw Y-F. Comparable outcomes of decompensated chronic hepatitis B patients treated with entecavir or tenofovir: an 8-year cohort study. Hepatology international. 2022;16(4):799-806.
- Rakers F, Schleusner E, Muth I, Hoyer D, Rupprecht S, Schiecke K, et al. Association between antenatal glucocorticoid exposure and the activity of the stress system, cognition, and behavior in 8- to 9-year-old children: A prospective observational study. Acta obstetricia et gynecologica Scandinavica. 2022;101(9):996-1006.

- Zhang Y, Wang F, Zhang H, Wei Y, Deng Y, Wang D. Volatile anesthesia versus propofol-based total intravenous anesthesia: A retrospective analysis of charts of patients who underwent elective digestive tract cancer curative surgeries. Medicine. 2022;101(29):e29169.
- Winter Y, Uphaus T, Sandner K, Klimpe S, Stuckrad-Barre Sv, Groppa S. Efficacy and safety of antiseizure medication in post-stroke epilepsy. Seizure. 2022;100:109-14.
- Torres A, Motos A, Cilloniz C, Ceccato A, Fernandez-Barat L, Gabarrus A, et al. Major candidate variables to guide personalised treatment with steroids in critically ill patients with COVID-19: CIBERESUCICOVID study. Intensive care medicine. 2022;48(7):850-64.
- Di Dalmazi G, Coluzzi S, Baldassarre MPA, Ghit A, Graziano G, Rossi MC, et al. Effectiveness and Tolerability of Once-Weekly GLP-1 Receptor Agonists in Clinical Practice: A Focus on Switching Between Once-Weekly Molecules in Type 2 Diabetes. Frontiers in endocrinology. 2022;13:892702.
- He Y, Zhou Y, Wang H, Peng X, Chang Y, Hu P, et al. The efficacy of pegylated interferon alpha-2a and entecavir in HBeAg-positive children and adolescents with chronic hepatitis B. BMC pediatrics. 2022;22(1):426.
- Morhart P, Gartner J, Weiss C, Stumpfe FM, Dammer U, Faschingbauer F, et al. Influence of Timing of Antenatal Corticosteroid Administration on Morbidity of Preterm Neonates. In vivo (Athens, Greece). 2022;36(4):1777-84.
- Yang S-F, Su Y-C, Lim C-C, Huang J-Y, Hsu S-M, Wu L-W, et al. Risk of dialysis in patients receiving intravitreal anti-vascular endothelial growth factor treatment: a population-based cohort study. Aging. 2022;14(12):5116-30.
- Jonusas J, Drevinskaite M, Patasius A, Kincius M, Janulionis E, Smailyte G. Androgen-deprivation therapy and risk of death from cardio-vascular disease in prostate cancer patients: a nationwide lithuanian population-based cohort study. The aging male : the official journal of the International Society for the Study of the Aging Male. 2022;25(1):173-9.
- Conforti F, Gronchi A, Penel N, Jones RL, Broto JM, Sala I, et al. Chemotherapy in patients with localized angiosarcoma of any site: A retrospective european study. European journal of cancer (Oxford, England : 1990). 2022;171:183-92.
- Voss EA, Ali SR, Singh A, Rijnbeek PR, Schuemie MJ, Fife D. Hip Fracture Risk After Treatment with Tramadol or Codeine: An Observational Study. Drug safety. 2022;45(7):791-807.
- Yang L, Wang W, Mao B, Qiu J, Guo H, Yi B, et al. Maternal Folic Acid Supplementation, Dietary Folate Intake, and Low Birth Weight: A Birth Cohort Study. Frontiers in public health. 2022;10:844150.
- Li A, Huang T, Zheng R, Chi P, Li Z, Wang X, et al. Preoperative chemoradiotherapy with capecitabine and triweekly oxaliplatin versus capecitabine monotherapy for locally advanced rectal cancer: a propensity-score matched study. BMC cancer. 2022;22(1):789.
- Broman J, Aarnio K, But A, Marinkovic I, Rodriguez-Pardo J, Kaste M, et al. Association of post-stroke-initiated antidepressants with long-term outcomes in young adults with ischaemic stroke. Annals of medicine. 2022;54(1):1757-66.
- Li J-R, Wang S-S, Chen C-S, Cheng C-L, Hung S-C, Lin C-H, et al. Conventional androgen deprivation therapy is associated with an increased risk of cardiovascular disease in advanced prostate cancer, a nationwide population-based study. PloS one. 2022;17(6):e0270292.
- Zhong P, Lu Z, Li Z, Li T, Lan Q, Liu J, et al. Effect of Renin-Angiotensin-Aldosterone System Inhibitors on the Rupture Risk Among Hypertensive Patients With Intracranial Aneurysms. Hypertension (Dallas, Tex : 1979). 2022;79(7):1475-86.

- Luo C, Chen K, Doshi R, Rickles N, Chen Y, Schwartz H, et al. The association of prescription opioid use with suicide attempts: An analysis of statewide medical claims data. PloS one. 2022;17(6):e0269809.
- Wang T-F, Clarke AE, Awan AA, Tanuseputro P, Carrier M, Sood MM. Hemorrhage Risk Among Patients With Breast Cancer Receiving Concurrent Direct Oral Anticoagulants With Tamoxifen vs Aromatase Inhibitors. JAMA network open. 2022;5(6):e2219128.
- Desai AV, Applebaum MA, Karrison TG, Oppong A, Yuan C, Berg KR, et al. Efficacy of post-induction therapy for high-risk neuroblastoma patients with end-induction residual disease. Cancer. 2022;128(15):2967-77.
- Harris GM, Wood M, Ystrom E, Nordeng H. Association of Maternal Use of Triptans During Pregnancy With Risk of Attention-Deficit/Hyperactivity Disorder in Offspring. JAMA network open. 2022;5(6):e2215333.
- Blomquist A, Inghammar M, Al Shakirchi M, Ericson P, Krantz C, Svedberg M, et al. Persistent Aspergillus fumigatus infection in cystic fibrosis: impact on lung function and role of treatment of asymptomatic colonization-a registry-based case-control study. BMC pulmonary medicine. 2022;22(1):263.
- Naser N, Kulic M, Jatic Z. Our Experience With Sacubitril/Valsartan in Chronic Heart Failure Management - HFrEF in the Ambulatory Setting. Medical archives (Sarajevo, Bosnia and Herzegovina). 2022;76(2):101-7.
- Heinonen E, Forsberg L, Norby U, Wide K, Kallen K. Neonatal morbidity after fetal exposure to antipsychotics: a national register-based study. BMJ open. 2022;12(6):e061328.
- La YJ, Kim HR, Oh DH, Ahn JY, Kim YC. Comparison of Clinical Outcomes for Glycopeptides and Beta-Lactams in Methicillin-Susceptible Staphylococcus Aureus Bloodstream Infections. Yonsei medical journal. 2022;63(7):611-8.
- Savoldi A, Morra M, De Nardo P, Cattelan AM, Mirandola M, Manfrin V, et al. Clinical efficacy of different monoclonal antibody regimens among non-hospitalised patients with mild to moderate COVID-19 at high risk for disease progression: a prospective cohort study. European journal of clinical microbiology & infectious diseases : official publication of the European Society of Clinical Microbiology. 2022;41(7):1065-76.
- Zhang L, Zhang J, Wang Y, Li W, Yu S, Li Q, et al. Efficacy of AS versus SOX regimen as first-line chemotherapy for gastric cancer patients with peritoneal metastasis: a real-world study. BMC gastroenterology. 2022;22(1):296.
- Moon I, Go T-H, Kim JY, Kang DR, Sohn SH, Lee H-J, et al. Effectiveness and safety of non-vitamin K direct oral anticoagulants in atrial fibrillation patients with bioprosthetic valve. PloS one. 2022;17(6):e0268113.
- Wang H, Fan L, Wu X, Han Y. Efficacy evaluation of albumin-bound paclitaxel combined with carboplatin as neoadjuvant chemotherapy for primary epithelial ovarian cancer. BMC women's health. 2022;22(1):224.
- Cacioppo F, Schwameis M, Schuetz N, Oppenauer J, Schnaubelt S, Simon A, et al. Cardioversion of Post-Ablation Atrial Tachyarrhythmia with Ibutilide and Amiodarone: A Registry-Based Cohort Study. International journal of environmental research and public health. 2022;19(11).
- Eroglu TE, Blom MT, Souverein PC, Yasmina A, de Boer A, Tan HL, et al. Acetylsalicylic acid use is associated with reduced risk of out-of-hospital cardiac arrest in the general population: Real-world data from a population-based study. PloS one. 2022;17(6):e0267016.
- Bertsias A, Avgoustidis N, Papalopoulos I, Repa A, Kougkas N, Kalogiannaki E, et al. Rheumatoid arthritis patients initiating rituximab with low number of previous bDMARDs

failures may effectively reduce rituximab dose and experience fewer serious adverse events than patients on full dose: a 5-year cohort study. Arthritis research & therapy. 2022;24(1):132.
- Phillips EC, Warren CA, Ma JZ, Madden GR. Impact of Tigecycline on C. difficile Outcomes: Case Series and Propensity-Matched Retrospective Study. Antimicrobial agents and chemotherapy. 2022;66(6):e0000122.
- Lu Y, Gehr AW, Meadows RJ, Ghabach B, Neerukonda L, Narra K, et al. Timing of adjuvant chemotherapy initiation and mortality among colon cancer patients at a safety-net health system. BMC cancer. 2022;22(1):593.
- Nicholas JA, Gudesblatt M, Garabedian M, Belviso N, Shen C, Geremakis C, et al. Dimethyl fumarate is associated with lower rates of infection and lower infection-related healthcare costs when compared with ocrelizumab. Multiple sclerosis and related disorders. 2022;63:103921.
- Luo Y, Li J, Huang L, Liu X, Zhang B, Lin J, et al. Safety and efficacy of a new modified intravenous recombinant tissue plasminogen activator (rt-PA) regimen in Chinese patients with acute ischemic stroke: A descriptive retrospective cohort study with subgroup-analysis of different rt-PA dose. Journal of clinical neuroscience : official journal of the Neurosurgical Society of Australasia. 2022;101:244-51.
- Coyer L, Prins M, Davidovich U, van Bilsen WPH, Schim van der Loeff MF, Hoornenborg E, et al. Trends in Sexual Behavior and Sexually Transmitted Infections After Initiating Human Immunodeficiency Virus Pre-Exposure Prophylaxis in Men Who Have Sex with Men from Amsterdam, the Netherlands: A Longitudinal Exposure-Matched Study. AIDS patient care and STDs. 2022;36(6):208-18.
- Huang W, Zhang Q, Da L, Shen Y, Xiong F, Zhang C. Effectiveness and safety of camrelizumab combined with chemotherapy in nonsquamous nonsmall cell lung cancer as the second-line therapy: A retrospective analysis. Journal of cancer research and therapeutics. 2022;18(2):576-80.
- Barkhordar M, Kasaeian A, Janbabai G, Kamranzadeh Fumani H, Tavakoli S, Rashidi AA, et al. Modified combination of anti-thymocyte globulin (ATG) and post-transplant cyclophosphamide (PTCy) as compared with standard ATG protocol in haploidentical peripheral blood stem cell transplantation for acute leukemia. Frontiers in immunology. 2022;13:921293.
- Stogios N, Maksyutynska K, Navagnanavel J, Sanches M, Powell V, Gerretsen P, et al. Metformin for the prevention of clozapine-induced weight gain: A retrospective naturalistic cohort study. Acta psychiatrica Scandinavica. 2022;146(3):190-200.
- Tarhini Z, Manceur K, Magne J, Mathonnet M, Jost J, Christou N. The effect of metformin on the survival of colorectal cancer patients with type 2 diabetes mellitus. Scientific reports. 2022;12(1):12374.
- Yuan S, Chen C, Xu F, Han D, Yang R, Zheng S, et al. Antithrombotic Therapy Improves ICU Mortality of Septic Patients with Peripheral Vascular Disease. International journal of clinical practice. 2022;2022:1288535.
- Quenzer FC, Lafree AT, Grey L, Singh S, Smyers C, Balog B, et al. Bamlanivimab Reduces ED Returns and Hospitalizations and May Reduce COVID-19 Burden on Low-resource Border Hospitals. The western journal of emergency medicine. 2022;23(3):302-11.
- Jourdain H, de Gage SB, Desplas D, Dray-Spira R. Real-world effectiveness of pre-exposure prophylaxis in men at high risk of HIV infection in France: a nested case-control study. The Lancet Public health. 2022;7(6):e529-e36.
- Chalandon Y, Mamez A-C, Giannotti F, Beauverd Y, Dantin C, Mahne E, et al. Defibrotide Shows Efficacy in the Prevention of Sinusoidal Obstruction Syndrome After Allogeneic

Hematopoietic Stem Cell Transplantation: A Retrospective Study. Transplantation and cellular therapy. 2022.

- Guclu OA, Onal U, Akalin H, Ozturk NAA, Belik HO, Demirdogen E, et al. Tocilizumab treatment in COVID-19: A prognostic study using propensity score matching. Advances in clinical and experimental medicine : official organ Wroclaw Medical University. 2022.
- Ohwada S, Todaka A, Nakase H, Shirasu H, Kawakami T, Hamauchi S, et al. Effectiveness and safety of gemcitabine plus nab-paclitaxel in elderly patients with advanced pancreatic cancer: a single-center retrospective cohort study. Investigational new drugs. 2022;40(5):1106-16.
- AlLehaibi LH, Alomar M, Almulhim A, Al-Makki S, Alrwaili NR, Al-Bassam S, et al. Effectiveness and Safety of Enoxaparin Versus Unfractionated Heparin as Thromboprophylaxis in Hospitalized COVID-19 Patients: Real-World Evidence. The Annals of pharmacotherapy. 2022:10600280221115299.
- Zhao B, Liao S, Zhong X, Luo Y, Hong S, Cheng M, et al. Effectiveness and Safety of Oxcarbazepine vs. Levetiracetam as Monotherapy for Infantile Focal Epilepsy: A Longitudinal Cohort Study. Frontiers in neurology. 2022;13:909191.
- Fadini GP, Buzzetti R, Nicolucci A, Larosa M, Rossi MC, Cucinotta D, et al. Comparative effectiveness and safety of glargine 300 U/mL versus degludec 100 U/mL in insulin-naive patients with type 2 diabetes. A multicenter retrospective real-world study (RESTORE-2 NAIVE STUDY). Acta diabetologica. 2022;59(10):1317-30.

Appendix 8. General characteristics of the included reports of non-randomized studies (N=200)

Characteristics*		Frequency (%)
Study characteristics		
Medical area†		
	Oncology	54 (27.0)
	Infectious Disease	41 (20.5)
	Cardiology	24 (12.0)
	Obstetrics and Gynecology	14 (7.0)
	Neurology	14 (7.0)
Region		
	Central and East Asia and Pacific	82 (41.0)
	Europe	59 (29.5)
	North America	50 (25.0)
	Middle East and North Africa	5 (2.5)
	More than one	4 (2.0)
Journal		
	Specialized medical journal	151 (75.5)
	General medical journal	45 (22.5)
	Non-medical journal	4 (2.0)
Statistician/Methodologist in authors or acknowledgements		94 (47.0)
	Author affiliation	83 (88.3)
	Explicitly reported	11 (11.7)
Research question		
Explicit statement		166 (83.0)
No effect of active comparator (N=112) reported		1 (0.9)
Study design and data		
Setting		189 (94.5)
	Primary	31 (16.4)
	Secondary	12 (6.3)
	Tertiary	102 (54.0)
	More than one	44 (23.3)
Centers (N=135)		
	Monocentric	72 (53.3)
	Number of centers	1.0 (1.0; 6.0)
Participants		
	Number of participants included	949 (288; 9 881)
	Number of participants analyzed	633 (216; 7 708)
Follow-up time (months) (N=175)		17.6 (3.0; 43.0)
Funding		168 (84.0)
	Internal funding	8 (4.8)
	Governmental	52 (31.0)
	Private-for-profit (companies/entities)	17 (10.1)

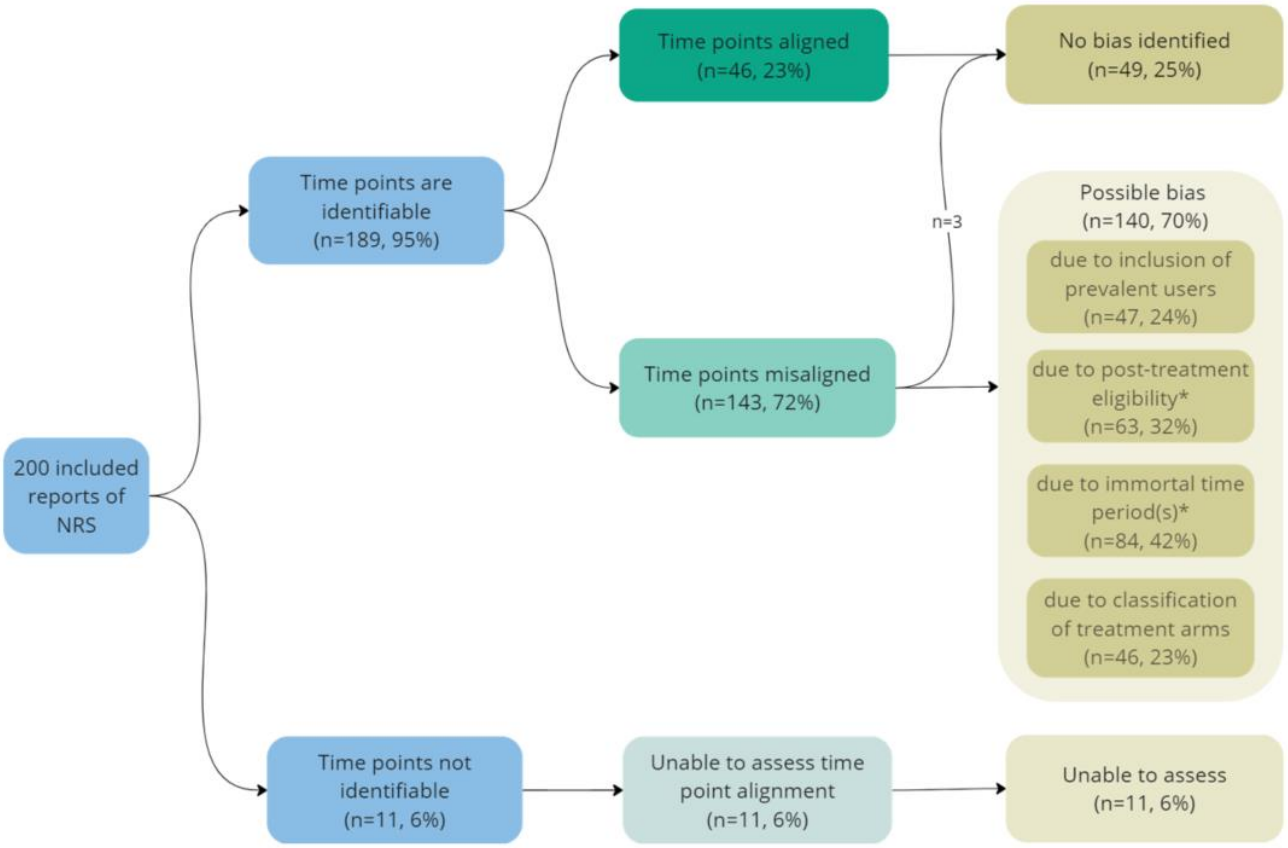
	Private not-for-profit (organizations/philanthropies)	17 (10.1)
	More than one	31 (18.4)
	Unclear	2 (1.2)
	No funding	41 (24.4)
Conflict of interest statement		196 (98.0)
	None declared	141 (72.0)
	Financial COI	24 (12.2)
	Non-financial COI	2 (1.0)
	Both types of COIs	29 (14.8)
Registration		14 (7.0)
Protocol		5 (2.5)
	Yes (open-access)	2 (40.0)
	Yes (not open-access)	3 (60.0)
Changes reported from protocol		0 (0.0)
Data sharing statement		123 (61.5)
	Data available in a public open-access repository	4 (3.3)
	Data are available upon reasonable request	61 (49.6)
	Data may be obtained from a third party	27 (21.9)
	All data relevant to the study are included	21 (17.1)
	Data sharing not available	10 (8.1)
Access to the codes and algorithms		9 (4.5)
	Available upon request	7 (77.8)
	Codes and algorithms provided	2 (22.2)
Ethical approval		190 (95.0)
	Approved	167 (87.9)
	Waived	13 (6.8)
	Not reviewed	10 (5.3)
Use of causal language in the abstract		
	Yes	69 (34.5)

COI: conflict of interest

*The median (25^{th} percentile; 75^{th} percentile) are reported for continuous outcomes.

†We only include the five most reported medical areas. Other areas include: Surgery (n=11), Endocrinology (n=10), Gastroenterology (n=7), Rheumatology (n=7), Psychiatry/Psychology (n=), Respiratory (n=4), Nephrology (n=4) and other (n=4).

Appendix 9. Time points for eligibility, treatment assignment and start of follow-up and possible related biases (N=200).

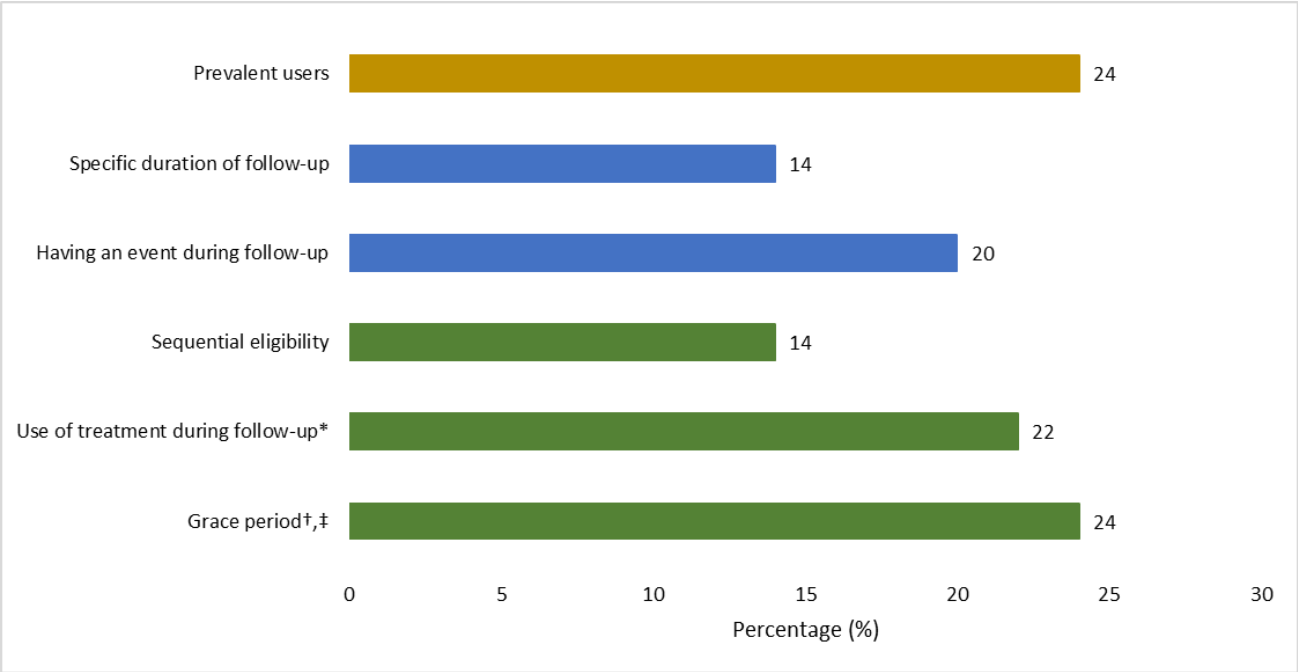


Abbreviations: NRS: non-randomized study

Note: Percentages might add up to more than a 100 due to rounding.

*Might have been underestimated due to the inadequate reporting of information (e.g., no reporting of eligibility criteria)

Appendix 10. Methodological characteristics that can lead to bias related to time point misalignment (N=200).



Brown: relevant to bias due to prevalent users; Blue: relevant to bias due to post-treatment eligibility; Green: relevant to bias due to immortal time periods.
*the requirement to use the treatment during follow-up was addressed in 5 reports
†relevant to bias due to classification of treatment arms
‡the grace period was addressed in 11 reports