Study Protocol

P4-C1-012

DARWIN EU® - Characterisation of systemic treatments for the management of ovarian cancer

26/01/2026

Version 4.0

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Public

CONTENTS

Study title	DARWIN EU® - Characterisation of systemic treatments for the management of ovarian cancer
Protocol version	V4.0
Date	26/01/2026
EUPAS number	EUPAS1000000815
Active Substance	Alkylating agents: Altretamine, Chlorambucil, Cyclophosphamide, Ifosfamide, Lomustine, Melphalan, Thiotepa, Treosulfan Anthracycline: Doxorubicin, Epirubicin, Mitoxantrone Antimetabolites: Fluorouracil, Gemcitabine, Methotrexate DNA agents: Trabectedin Hormonal agents: Dexamethasone, Medroxyprogesterone Monoclonal antibodies: Bevacizumab, mirvetuximab soravtansine PARP inhibitors: Niraparib, Olaparib, Rucaparib Platinum-based: Carboplatin, Cisplatin Taxanes: Docetaxel, Paclitaxel Topoisomerase inhibitors: Etoposide, Topotecan Vinca Alkaloid: Vinblastine
Medicinal Product	None
Research question and objectives	Research question: What systemic treatments are used for the management of ovarian cancer? The specific objectives of this study are: 1. To describe demographic and pre-specified characteristics of patients newly diagnosed with ovarian cancer, overall and by age. 2. To describe the number of patients treated with systemic treatments, by ingredient and treatment class (i.e., alkylating agents, anthracyclines, antimetabolites, DNA agents, platinum-based chemotherapy, taxanes, topoisomerase inhibitors, vinca alkaloid, PARP inhibitors, monoclonal antibodies, hormonal agents), overall and by age, study period and where possible, cancer stage. 3. To describe sequences of treatments and treatment combinations for ovarian cancer, overall and stratified by age, and where possible, cancer stage.
Countries of study	Denmark, France, Netherlands, and Norway.
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LIST OF ABBREVIATIONS

Acronyms/terms	Description
ATC	Anatomical Therapeutic Chemical
BRCA	Breast cancer gene
CC	Coordination centre
CDM	Common Data Model
CDWBordeaux	Clinical Data Warehouse of Bordeaux University Hospital.
CRN	Cancer registry Norway
DARWIN EU®	Data Analysis and Real-World Interrogation Network
DK-DHR	Danish Data Health Registries
DTZ	Data Transfer Zone
ECOG	Eastern Cooperative Oncology Group
EHR	Electronic Health Records
EMA	European Medicines Agency
ENCePP	European Network of Centres for Pharmacoepidemiology and Pharmacovigilance
EOC	Epithelial ovarian cancer
EU	European Union
EUPAS	EU Post-Authorisation Studies Register
FIGO	International Federation of Gynaecology and Obstetrics
GDPR	General Data Protection Regulation
ICD	International Classification of Diseases
ICD-O-3	International Classification of Diseases for Oncology, Third Edition
IP	Inpatient
IRB	Institutional Review Board
IV	Intravenous
NCR	Netherlands Cancer Registry
OHDSI	Observational Health Data Sciences and Informatics
OMOP	Observational Medical Outcomes Partnership
OP	Outpatient
PARP	Poly (ADP-ribose) polymerase
RxNorm	Medical prescription normalised
SNOMED	Systemised Nomenclature of Medicine
TNM	Tumour, Nodes and Metastasis
WHO	World Health Organisation
WHO-PS	WHO Performance Status

1. TITLE

DARWIN EU® - Characterisation of systemic treatments for the management of ovarian cancer

2. DESCRIPTION OF THE STUDY TEAM

Study team role	Names	Organisation
Principal Investigator	Anum Zahra Berta Raventós Talita Duarte-Salles	Erasmus MC
Data Scientist	Cesar Barboza Maarten van Kessel Ross Williams Ioanna Nika Ger Inberg	Erasmus MC
Clinical Domain Expert	Anton Barchuk	Erasmus MC
Study Manager	Natasha Yefimenko	Erasmus MC
Data source	**Names**	**Data Partner Organisation***
DK-DHR	Elvira Bräuner Susanne Bruun	Danish Data Health Registries
CDWBordeaux	Guillaume Verdy	Clinical Data Warehouse of Bordeaux University Hospital.
NCR	Jelle Evers Maaike van Swieten Maaike van der Aa	Netherlands Comprehensive Cancer Organisation
CRN	Espen Enerly Sigrid Leithe Anna Skog	Cancer Registry Norway

*Data partners do not have an investigator role. Data partners execute code at their data source, review, and approve their results.

3. ABSTRACT

Title

DARWIN EU® - Characterisation of systemic treatments for the management of ovarian cancer.

Rationale and background

Ovarian cancer remains a significant health concern in Europe, resulting in more deaths than any other gynaecological cancer. Treatment strategies for ovarian cancer include surgery, chemotherapy, and targeted therapies that are selected based on patient characteristics, as well as type and stage of cancer. Chemotherapy drugs include alkylating agents, anthracyclines, antimetabolites, platinum-based drugs, taxanes, and other targeted therapies, such as poly (ADP-ribose) polymera (PARP) inhibitors, hormonal agents, and anti-angiogenesis drugs (Bevacizumab). The aim of this study is to inform which authorised systemic treatments are actively being used as a treatment for ovarian cancer.

Research question and objectives

Research questions

What systemic treatments are used for the management of ovarian cancer?

Objectives

The aim of this study is to characterise systemic treatments for the management of ovarian cancer.

The specific objectives of this study are:

1. To describe demographic and pre-specified characteristics of patients newly diagnosed with ovarian cancer, overall and by age.
2. To describe the number of patients treated with systemic treatments, by ingredient and treatment class (i.e., alkylating agents, anthracyclines, antimetabolites, DNA agents, platinum-based chemotherapy, taxanes, topoisomerase inhibitors, vinca alkaloid, PARP inhibitors, monoclonal antibodies, hormonal agents), overall and by age, study period and where possible, cancer stage.
3. To describe sequences of treatments and treatment combinations for ovarian cancer, overall and stratified by age, and where possible, cancer stage.

Methods

Study design

Characterisation study to describe systemic treatments and patients with ovarian cancer (objective 1–3).

Population

The study population will include all individuals registered as female sex at birth who are newly diagnosed with epithelial ovarian cancer and are present in the data sources during the study period, from 01/01/2010 (or data sources start, if later) to 2024 or end of available data.

Variables

Exposure:

Systemic treatments for ovarian cancer.

Relevant covariates:

Age, breast cancer (BRCA) gene, stage of ovarian cancer, prespecified list of comorbidities and medications.

Data sources

1. Denmark: Danish Data Health Registries (DK-DHR)
2. France: Clinical Data Warehouse of Bordeaux University Hospital (CDW Bordeaux)
3. Netherlands: Netherlands Cancer Registry (NCR)
4. Norway: Cancer Registry Norway (CRN)

Study size

No sample size has been calculated, as this is an exploratory study which will not test a specific hypothesis. Based on a preliminary feasibility assessment, the expected number of individuals with ovarian cancer is approximately 26,000 in this study. Ranging from 21,700 individuals in DK-DHR to 1,200 individuals in CDW Bordeaux.

Statistical analysis

For objective 1, descriptives for patients with newly diagnosed with ovarian cancer will be conducted at index date (date of cancer diagnosis), using a prespecified list of patient demographics and comorbidities.

For objective 2, a list of systemic treatments will be assessed in terms of number and percentage of patients receiving each treatment, both at level of ingredient and treatment class.

For objective 3, drug utilisation sequences and combinations will be described.

For all analyses, a minimum cell count of 5 will be used when reporting results, with any smaller counts reported as “<5”. All results will be reported by country/data sources, overall and stratified by age groups (18–39; 40–59; >60 years), and, where possible, stage of cancer. Objective 2 will also be stratified by study period (2010–2014, 2015–2019; 2020–2024).

4. AMENDMENTS AND UPDATES

None.

5. MILESTONES

Study milestones and deliverables	Planned dates
Final Study Protocol	To be confirmed by EMA
Creation of Analytical code	December 2025
Execution of Analytical Code on the data	January 2026
Draft Study Report	March 2026
Final Study Report	To be confirmed by EMA

EMA = European Medicines Agency
*Planned dates are dependent on obtaining approvals from the internal review boards of the data sources.

6. RATIONALE AND BACKGROUND

Ovarian cancer is caused when abnormal cells in ovaries, fallopian tubes, or peritoneum begin to grow and multiply in an uncontrolled manner. In Europe, ovarian cancer causes more deaths than any other gynaecological cancer, accounting for 5.2% of all cancer related deaths amongst adult women in 2022.[1, 2] Progressing as a silent disease, most of these cases are diagnosed after it has already spread to distant sites. In the past decades, a non-uniform yet overall decline in ovarian cancer mortality has been observed in most European countries.[3]

Epithelial ovarian cancers (EOC) account for nearly 90% of ovarian cancers, while non-epithelial cancers (germ cell, sex cord stromal, small cell) are rare. EOC are further divided into five major histotypes, high-grade and low-grade serous cancers and (aetiologically and genetically distant) endometrioid, clear-cell and mucinous cancers.[3] Various factors have been found to be associated with increased risk of ovarian cancer, such as certain comorbidities (diabetes mellitus, endometriosis), early mensuration or late menopause, and family history of ovarian cancer.[3] Genetic factors, such as BRCA gene mutations, can increase the risk of ovarian cancer.[4]

Different treatment strategies are available for ovarian cancer, including surgery, chemotherapy, and targeted therapies. The most appropriate line to treatment, often utilised in combination, is based on type, stage, and molecular characteristics of ovarian cancer. Standard first-line treatment often includes surgery followed by chemotherapy regimen. These include alkylating agents, anthracycline, antimetabolites, DNA agents, taxanes, non-platinum, and platinum-based drugs. In recent years, the introduction of targeted therapies, such as Poly (ADP-ribose) polymerase (PARP) inhibitors, has significantly improved survival for patients. Bevacizumab, an anti-angiogenic agent (preventing cancer cells from developing blood vessels), is also commonly used in combination with chemotherapy. Hormonal therapy may be considered, in selected cases, based on cancer cell sensitivity.[5]

An important aspect of improving ovarian cancer treatment is understanding the drug utilisation patterns. Therefore, the objective of this study is to inform which authorised products are actively being used as a treatment for ovarian cancer.

7. RESEARCH QUESTION AND OBJECTIVES

Research questions

What systemic treatments are used for the management of ovarian cancer?

Research objectives

The aim of this study is to characterise systemic treatments for the management of ovarian cancer.

The specific objectives of this study are:

1. To describe demographic and pre-specified characteristics of patients newly diagnosed with ovarian cancer, overall and by age.
2. To describe the number of patients treated with systemic treatments, by ingredient and treatment class (i.e., alkylating agents, anthracyclines, antimetabolites, DNA agents, platinum-based chemotherapy, taxanes, topoisomerase inhibitors, vinca alkaloid, PARP inhibitors, monoclonal antibodies, hormonal agents), overall and by age, study period and where possible, cancer stage.
3. To describe sequences of treatments and treatment combinations for ovarian cancer, overall and stratified by age, and where possible, cancer stage.

8. RESEARCH METHODS

8.1. Study design

A cohort study, describing characteristics of females with newly diagnosed ovarian cancer (objective 1), assessing the number of individuals treated by ingredient and treatment class (objective 2), as well to analyse treatment sequences and combinations (objective 3). A graphical depiction of the study design and definition of index date (i.e., date of ovarian cancer diagnosis) is described in **Figure 1**.

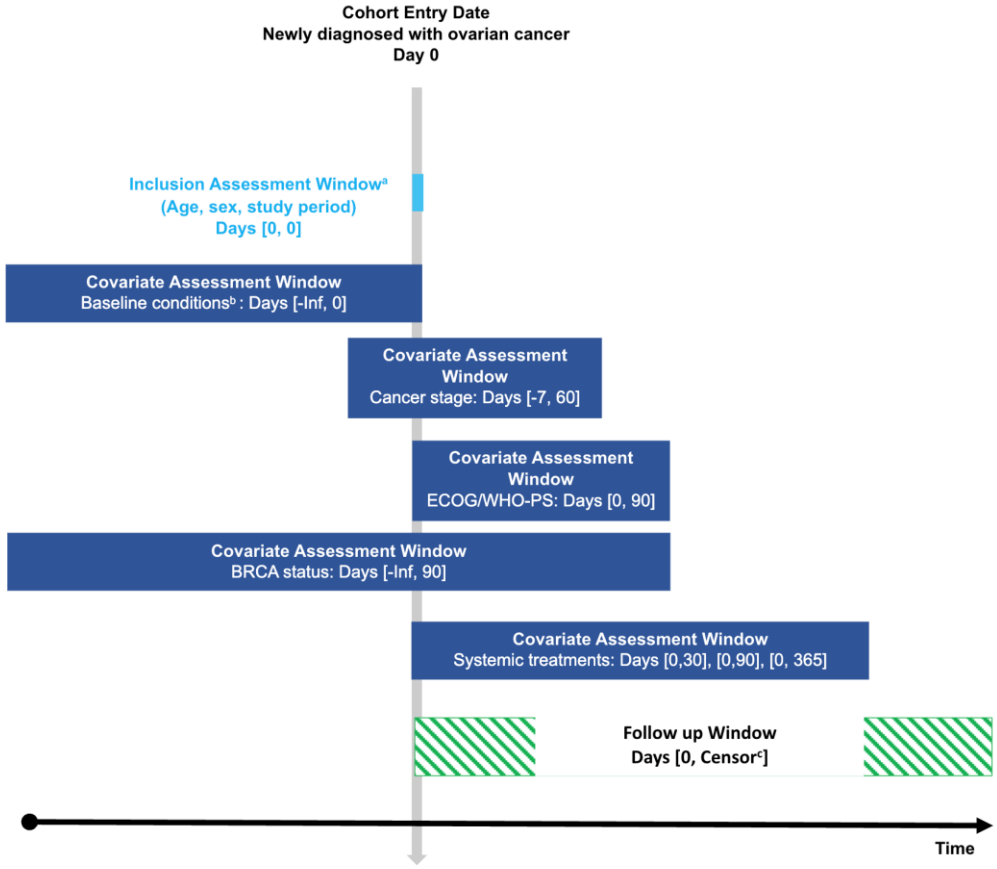

Figure 1. Graphical depiction of the study design.

a. Individuals newly diagnosed with ovarian cancer during the study period, up to one year to the end of data availability, who are females aged ≥18 years at day 0, will be included.
b. Baseline conditions: hyperglycaemia, diabetes mellitus, endometriosis, pelvic inflammatory disease, obesity, personal and family history of breast cancer.
c. Earliest of loss to follow–up, death, or end of observation period. For objective 3, follow-up will be censored at 5 years after diagnosis.

BRCA = Breast cancer gene, ECOG/WHO-PS = Eastern Cooperative Oncology Group/WHO Performance Status, Inf=All prior history

8.2. Follow-up

Follow-up will start on the date of first diagnosis with ovarian cancer. End of follow-up will be defined as the earliest of loss to follow-up, death, or end of observation period (the latest available data), whichever occurs first. For objective 3, females will be followed during 5 years after diagnosis.

8.3. Study population with inclusion and exclusion criteria

For all study objectives, the inclusion criteria include:

- Individuals with a first diagnosis of ovarian cancer during the study period, up to one year prior to end of data availability.
- Females aged ≥18 years at the date of diagnosis.

No prior history requirement has been established for this study, in accordance with how patient's observability is defined in the included data sources (see **Section 8.4**). We will include cases up to one year prior to the end of data availability to ensure some follow-up time for capturing treatments (e.g., if data are available through December 2024, cases will be included up to December 2023).

Ovarian cancer will be defined using a range of ovarian cancer types, consisting of several histological subtypes. This also includes cancers that arise in the fallopian tube, as well as the histologically similar primary peritoneal cancers. EOC will be defined using a range of EOC types, consisting of several histological subtypes (such as high-grade and low-grade serous cancers, endometrioid, clear-cell and mucinous cancers) and stages. Systematised Nomenclature of Medicine (SNOMED) and International Classification of Diseases for Oncology, Third Edition (ICD-O-3) codes will be used to identify ovarian cancer cases. A preliminary concept set for the identification of ovarian cancer specific to ovaries is described in **Annex IV**. These codes will be refined during the study execution following the DARWIN EU® phenotyping standard processes, which involve the review of code lists by clinical experts, and the review of phenotypes after their execution in the participating data sources.

8.4. Study setting and data sources

This study will be conducted using routinely collected data from data sources in the DARWIN EU® network of data partners. The study will be informed by 4 data sources from 4 European countries in 3 EU member states. All data were a *priori* mapped to the Observational Medical Outcomes Partnership (OMOP) Common Data Model (CDM).

Information on the data sources is available in **Table 1.**

Table 1. Data sources.

Country	Name of Data source	Health Care setting	Type of Data	Number of active individuals[1]	Calendar period covered by each data source
Denmark	DK-DHR	Hospital care (IP, OP)	EHRs	5.98 M	1995 to 2024
France	CDW Bordeaux	Hospital care (IP, OP)	EHRs, claims	0.26 M	2005 to 2025
Netherlands[2]	NCR	Hospital care (IP), others	Registries	2.43 M	1992 to 2025
Norway	CRN	Hospital care (IP, OP)	Registries	0.35 M	1953 to 2025

IP=inpatient, EHR=Electronic health record, OP=outpatient, DK-DHR=Danish Data Health Registries, CDW Bordeaux=Clinical Data Warehouse of Bordeaux University Hospital, NCR=Netherlands Cancer Registry, CRN=Cancer Registry Norway
[1] Defined as the maximum number of individuals in observation in the last 6 months of data.
[2] NCR has primary treatment registration for first nine months after ovarian cancer diagnosis.

Data sources selection

These data sources fulfil the criteria required in terms of data quality, completeness, timeliness, and representativeness for characterisation study while covering different regions of Europe (**Annex II**).

8.5. Study period

The study will span from January 2010 to December 2024, or end of available data (if earlier) for each contributing data source.

8.6. Variables

8.6.1. Exposure

For this study, the exposure of interest will correspond to pre-defined systemic treatments for ovarian cancer (**Table 2**).

Systemic treatments will be assessed by:

- Treatment class, including 11 pre-specified treatment classes.
- Ingredient (active substance), including 29 pre-specified active substances.

Table 2. Exposure of interest.

Treatment class	Active substance
Alkylating agents	Altretamine, Chlorambucil, Cyclophosphamide, Ifosfamide, Lomustine, Melphalan, Thiotepa, Treosulfan
Anthracyclines	Doxorubicin, Epirubicin, Mitoxantrone
Antimetabolites	Fluorouracil, Gemcitabine, Methotrexate
DNA agents	Trabectedin
Platinum-based	Carboplatin, Cisplatin
Taxanes	Docetaxel, Paclitaxel
Topoisomerase inhibitors	Etoposide, Topotecan
Vinca Alkaloid	Vinblastine
PARP inhibitors	Niraparib, Olaparib, Rucaparib
Monoclonal antibodies	Bevacizumab, mirvetuximab soravtansine
Hormonal agents	Dexamethasone, Medroxyprogesterone

Successive individual drug records (i.e., drug exposures) separated by less than 21 days will be considered the same continuous exposure at ingredient-level (i.e., drug era). The rationale of using 21 days is based on the usual cycle length of chemotherapies. An additional window of 6 days (i.e., surveillance window) will be added to account for the duration of the last administered treatment. This logic will be used to derive continuous treatment episodes, as most data sources record treatments by administration date rather than as continuous treatment (see **Section 12**). The preliminary concept sets active substances will be identified based on ingredient-level codes are described in **Annex IV**, which will be further refined and adjusted following the review of diagnostics (see **Annex III**).

8.6.2. Outcome

None.

8.6.3. Covariates, including confounders, effect modifiers, and other variables

Covariates for stratification:

Covariates for stratification will include age (all objectives), study period (objective 2) and where possible, cancer stage (objective 2 and 3). Age will be assessed at index date (time 0) using three groups (18–44; 45–64; >65 years). Study period will also be assessed at index date and will be categorised into three periods (2010–2014, 2015–2019, 2020–2024). Cancer stage (defined as stage I to IV) will be identified based on Tumour, Nodes, and Metastasis (TNM) staging and will be assessed 1 week prior to 60 days after the index date (i.e., time window in days: [-7, 60]). A preliminary concept set for the identification of TNM staging is described in **Annex IV**. In case of multiple records per patient within this time window, staging will be based on the code more recent to the diagnosis date with preference given to post-diagnosis entries.

Objective 1:

Pre-specified characteristics will include:

- Age (analysed as continuous and categorical variable, with age groups 18–44; 45–64; >65 years)
- Prior and future observation time
- Cancer stage (in DK-DHR, NCR, and CRN)
- BRCA status (in NCR only)
- Eastern Cooperative Oncology Group (ECOG)/WHO Performance Status (WHO-PS) (in NCR and CRN)

Pre-specified baseline comorbidities will include (in DK-DHR and CDW Bordeaux):

- Hyperglycemia
- Diabetes mellitus
- Endometriosis
- Pelvic inflammatory disease
- Obesity
- Breast cancer history
- Family history of breast cancer

Age and observation time will be described at index date (time 0). Definition of cancer stage will be 7 days before to 60 days after index day, while ECOG/WHO-PS will be defined 0 to 90 days after index date. BRCA status will be defined any time prior to index date up to 90 days after (i.e., time window in days: [-Inf, 90]). Pre-specified comorbidities will be described any time prior to index date (i.e., time window in days: [-Inf, 0]).

Importantly, not all information on covariates will be available in data sources included. Cancer stage will not be used for stratification in Objective 1, as this is only available in DK-DHR, NCR, and CRN. Similarly, information on pre-specified baseline comorbidities is not available in the cancer registries. Information about BRCA (from 2015 onwards in NCR only) and ECOG/WHO-PS will only be available in NCR and CRN (see **Section 12**).

The preliminary concept sets used for the identification of covariates are described in **Annex IV**. These codes will be refined during the study execution following the DARWIN EU® phenotyping standard processes, which involves the review of code lists by clinical experts, and the review of phenotypes after their execution in the participating data sources.

Objective 2 and 3:

No additional covariates will be assessed for objectives 2 and 3.

8.7. Study size

No sample size has been calculated, as this is a characterisation study which will not test a specific hypothesis. In addition, we will use already collected available data to estimate treatment pattens and combinations utilised in ovarian cancer. Thus, the sample size is driven by the availability of data for patients with new diagnosis of ovarian cancer. Based on a preliminary feasibility assessment, the expected number of individuals with ovarian cancer in the data sources is approximately 26,000. Ranging from 21,700 (DK-DHR) to 1,200 (CDW Bordeaux) in the selected data sources.

8.8. Analysis

8.8.1. Federated network analyses

All analyses will be conducted separately for each data source, and will be carried out in a federated manner, allowing analyses to be run locally without sharing individuals' data.

Before sharing the study package, test runs of the analytics will be performed on a subset of the data sources, and quality control checks will be performed. After all the tests are passed (**Annex III. Operational and reporting considerations**), the final package will be released in a version-controlled study repository for execution against all the participating data sources.

8.8.2. Data privacy protection

The data partners will locally execute the analytics against the OMOP CDM in R Studio and review and approve the default aggregated results. They will then be made available to the Principal Investigators and study team in secure online repository of the Data Transfer Zone (DTZ). All results will be locked and timestamped for reproducibility and transparency. The study results of all data sources will be checked, after which they are made available to the team, and the Study Dissemination Phase can start. All analyses will be conducted separately for each data source, and will be carried out in a federated manner, allowing analyses to be run locally without sharing patient-level data. Cell counts <5 will be suppressed when reporting results to comply with the data source's privacy protection regulations.

8.8.3. Statistical model specification and assumptions of the analytical approach considered

R-packages

The characterisation study will be calculated based on OMOP CDM mapped data using the following R packages: *PatientProfiles*, *CohortCharacteristics*, *DrugUtilisation*, and *TreatmentPatterns.*[6-9] *PatientProfiles* and *CohortCharacteristics* will be used as part of Objectives 1 and 2 to summarise patient characteristics, including demographics, baseline conditions, and medication use. *DrugUtilisation* will be used to create the drug user cohorts required for Objective 3, which will also involve the use of *TreatmentPatterns* to depict treatment combinations and sequences.

Objective 1

Patients newly diagnosed with ovarian cancer based on pre-defined characteristics and baseline conditions. The list of demographic and pre-specified conditions and time windows for assessment are described in **Section 8.6.3.**, with preliminary concept sets detailed in **Annex IV**. Pre-specified comorbidities will be described in DK-DHR and CDW Bordeaux (see **Section 12**).

Patient characteristics will be summarised using counts and percentages for categorical variables and medians with interquartile ranges for continuous variables. Results will be reported overall and stratified by age groups (18–44; 45–64; >65 years).

Objective 2

We will describe the number and percentage of patients treated with a pre-specified list of systemic treatments. Systemic treatments will be described by treatment class and at ingredient level. Treatment classes are described in **Section 8.6.1.** Systemic treatment will be assessed in three time periods: 1) 0 to 30 days after index date, 2) 0 to 90 days after index date, 3) 0 to 365 days after index date.

Patient characteristics will be summarised using counts and percentages. Results will be reported overall and stratified by age, study period and, where possible, by cancer stage.

Objective 3

Sequences of treatments and treatment combinations will be constructed using the *TreatmentPatterns* R-Package,[6] based on pre-specified ingredients (see **Section 8.6.1.**). The target cohort (i.e., patients in which treatments will be assessed) will include females aged >18 years newly diagnosed with ovarian cancer. Treatments assessed will include those starting from the date of entry into the target cohort (*WindowStart*) and will be followed for up to a maximum of 5 years after diagnosis (*WindowEnd*).

Figure 2 explains how treatment combination will be defined. To align with the time gap used to derive continuous exposures (i.e., drug eras), the maximum allowable gap between two event eras for them to be combined into a single era (*eraCollapseSize*) will also be defined as 21 days. The minimum time an event era should last to be included in the analysis (*minEraDuration*) will be 6 days, to align with the surveillance window, as described in **Section 8.6.1**. The minimum overlap of different treatments to be considered as combination treatment (*combinationWindow*) will be defined as 5 days. This value is shorter than the surveillance window (6 days) to ensure that treatments which were recorded only once, which are not linked to others occurring within 21 days, can still be identified as part of combination treatments. The minimum time that an event era before or after a generated combination treatment (*minPostCombinationDur*ation) should last to be included in the pathway as a separate treatment will be defined as 4 days. This value will be smaller than the *combinationWindow*, in accordance with the R package specifications [6]. The suitability of these preliminary parameters for assessing treatment combinations will be reviewed during diagnostics and adjusted as necessary.

Sequences of treatments and treatment combinations will be described in terms of number and percentages. Treatment pathways will be visualised using sunburst plots depicting treatment patterns and Sankey diagrams depicting treatment sequences. Results will be reported overall and stratified by age and cancer stage (where possible).

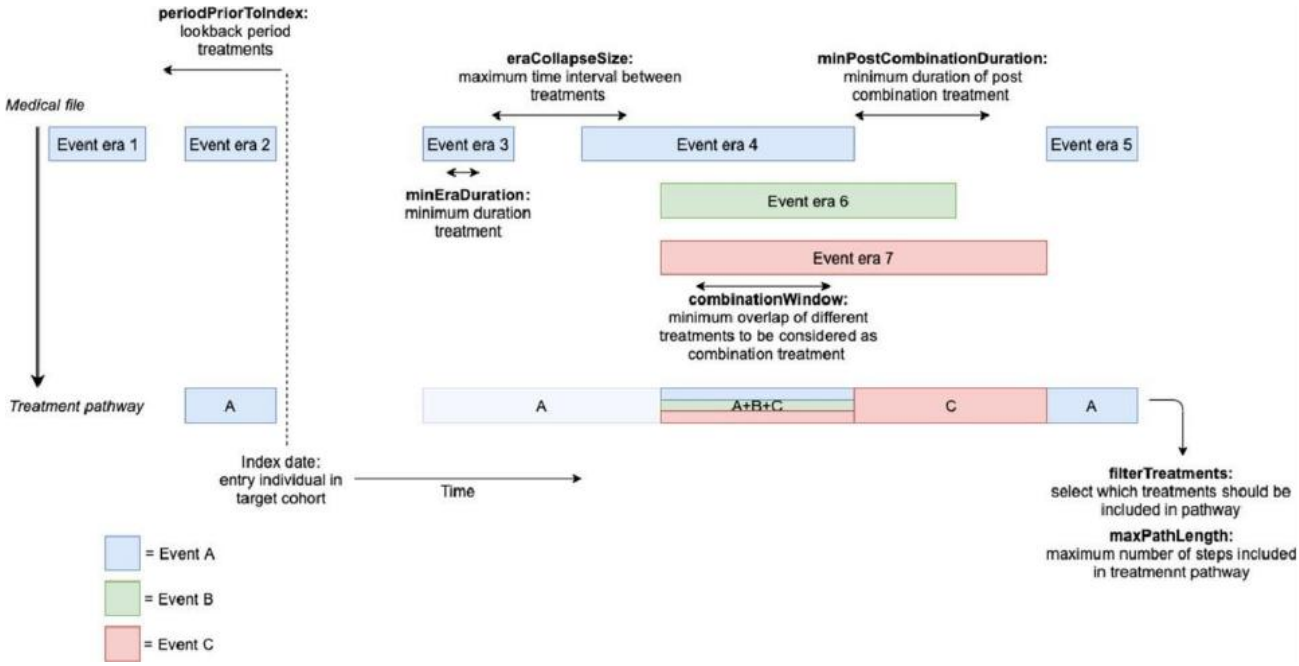

Figure 2. Design choices to construct treatment pathways in *TreatmentPatterns* R package.

Parameters defined in **Table 3** below will be used for objective 3 in this study.

Table 3. Design choices to construct treatment pathways in *TreatmentPatterns* R package.

Individual pathway setting	Description	Value
WindowStart	The start time (number of days) prior to the index date of the target cohort (i.e., cohort of patients newly diagnosed with ovarian cancer) from which treatments should be included	0 days
WindowEnd	The end time (number of days) after the index date of the target cohort (i.e., cohort of patients newly diagnosed with ovarian cancer) from which treatments should be included	1,825 days (i.e., 5 years)
minEraDuration	Minimum time an event era (i.e., span of time an individual is exposed to a specific treatment of interest) should last to be included in the analysis	6 days
eraCollapseSize	Maximum gap within two eras of the same event cohort which would still allow the eras to be collapsed into one era	21 days
combinationWindow	Time that two event eras need to overlap to be considered a combination treatment	5 days
minPostCombinationDuration	Minimum time that an event era before or after a generated combination treatment should last to be included in the pathway as a separate treatment	4 days
filterTreatments	Select which treatments should be included in pathway first time occurrences of treatments ('First'), remove sequential repeated treatments ('Changes'), all treatments ('All')	Changes
maxPathLength	Maximum number of treatments included in pathway	10
Aggregate pathway setting		
groupCombinations	Select to group all non-fixed combinations in one category 'other' in the sunburst plot	FALSE / 10

addNoPaths	Select to include untreated persons without treatment pathway in the sunburst plot	TRUE

All objectives

Analyses for all objectives will be conducted using available data without imputation. As such, no specific methods will be applied to address missingness. For covariates based on conditions or drug exposures, the absence of a recorded entry will be interpreted as the individual not having the condition or medication of interest.

Sensitivity analysis

Description of sensitivity analyses are presented by means of **Table 4**. The number of days selected for the sensitivity analysis in *TreatmentPatterns* is preliminary and will be reviewed in diagnostics, with adjustments made if necessary.

Table 4. Sensitivity analyses – rationale, strengths, and limitations.

	What is being varied? How?	Why? (What do you expect to learn?)	Strengths of the sensitivity analysis compared to the primary	Limitations of the sensitivity analysis compared to the primary
Epithelial ovarian cancer cases only	We will restrict to only epithelial ovarian cancer cases in all data sources. This will be applied to all objectives.	Epithelial ovarian cancer is the most prevalent and important sub-type of ovarian cancer, especially in women >60 years of age, and treatments for this type of cancer might differ from others.	Allows for detailed analysis, specifically in epithelial ovarian cancer cases.	Cancer subtypes are optimally documented within cancer registries. However, cases may be missed in other data sources with less granular data.
Identification of cases DK-DHR	We will restrict ovarian cancer cases to those recorded in the National Cancer Registry from Denmark. This will be applied to all objectives.	Cases identified from the cancer registry are histologically confirmed.	Allow for a more accurate capture of cases, reducing potential misclassification.	We will not provide data after December 2022 (end of data availability for the national cancer registry).
Change in settings for TreatmentPatterns (*combinationWindow*)	We will increase the amount of time drug eras need to overlap to be considered a combination therapy in Objective 3. This will be increased from 5 to 14 days.	Allow more precise classification of sustained combination therapies.	Improve clinical relevance of treatment combinations identified by filtering out short overlaps.	Potentially exclude treatments that overlap for shorter durations than the specified threshold.

8.8.4. Output

Output will include a PDF report including an executive summary, and the following tables and figures:

Objective 1:

- Figure 1. Flowchart depicting study population attrition

- Table 1. Description of demographic and pre-specified characteristics of patients newly diagnosed with ovarian cancer.

Objective 2:

- Table 2. Number and percentage of patients treated with systemic treatments by treatment class.
- Table 3. Number and percentage of patients treated with systemic treatments by treatment class, stratified by age group.
- Table 4. Number and percentage of patients treated with systemic treatments by treatment class, stratified by cancer stage.
- Table 5. Number and percentage of patients treated with systemic treatments by treatment class, stratified by study period.
- Table 6. Number and percentage of patients treated with the top 10 systemic ingredients.
- Table 7. Number and percentage of patients treated with systemic treatments by the top 10 systemic ingredients, stratified by cancer stage.

Objective 3:

- Figure 2. Sunburst plot depicting treatment patterns after newly diagnosed with ovarian cancer.
- Figure 3. Sankey diagram depicting treatment sequences after newly diagnosed with ovarian cancer.
- Figure 4. Sankey diagram depicting treatment sequences after newly diagnosed with ovarian cancer, by age group.
- Figure 5. Sankey diagram depicting treatment sequences after newly diagnosed with ovarian cancer, by cancer stage.

Main results will be presented in the report, while all other outputs will be made available through an interactive dashboard (Shiny App), which will include all study results. Relevant additional results will be presented in the appendix section. These will include results generated using different time windows for assessment or stratifications. For Objective 2, analyses by ingredient will be limited to the top 10 ingredients in the main report. Results of the sensitivity analyses will be available through the Shiny App, with the most relevant figures/tables included in the report.

The current list of tables and figures is preliminary and may be adapted during the report writing to include additional elements that support the interpretation of findings. **Annex V** includes examples of the tables and figures that will be included in the report.

8.9. Evidence synthesis

Results from analyses described in **Section 8.8.** will be presented separately for each data source. No meta-analysis of results will be conducted.

9. STRENGTHS AND LIMITATIONS

The study will be informed by routinely collected health care data and so, data quality issues inherent to the secondary use of data must be considered. The included data sources have unavailability of certain relevant ovarian cancer information, such as BRCA gene (which is only available in NCR from 2015 onwards) or platinum sensitivity status. In addition, information on high-grade cases is not possible across selected data sources. Since these factors are important determinants of treatment choices in clinical settings, lack of information on these factors will limit the description and understanding of systemic treatment patterns

in these sub-groups of ovarian cancer patients. Additionally, cancer staging is not captured in the data sources using the International Federation of Gynaecology and Obstetrics (FIGO) staging for ovarian cancer and will be computed using TNM staging as a proxy. This information will be available in cancer registries (NCR and CRN) and DK-DHR. In contrast, these registries will not have information on pre-specified baseline comorbidities other than those related to cancer. Consequently, non-cancer-related comorbidities will not be assessed in individuals included from these registries.

Importantly, information on systemic treatments is mostly recorded at ingredient-level in most included data sources (except DK-DHR). Treatments assessed in Objective 2 will reflect the use of individual systemic therapies within pre-specified time windows (e.g., 0 to 30 days after the index date). These treatments will be analysed at the ingredient or treatment class level, and not as combinations, which will only be assessed as part of objective 3.

Regarding the selected data sources, it should be noted that NCR only has registration for primary treatment i.e., within first nine months of ovarian cancer diagnosis, and therefore, treatments sequences in this data source will not capture information beyond this period. CRN has limitations in capturing data on hospital administered drugs from the Northern Region (representing around 10% of the population) and will not include information on hormonal therapy as treatment for ovarian cancer. Most of included data sources record intravenous (IV) treatments on the date of administration, rather than as a continuous exposure lasting from the first to the last cycle. In contrast, treatments administered orally (e.g., olaparib, niraparib) are typically recorded as exposures lasting from first to last prescription/dispensation. In NCR, both intravenous (IV) and oral treatments are recorded with a start and end date that reflect the entire treatment series. However, in CRN, the exact duration of oral treatments is not available, and a fixed duration of 30 days is assigned to all oral treatment records. This limitation may impair the accurate assessment of treatment duration and will be further explored during the execution of diagnostics. These limitations in systemic treatment registration will result in constrains in comprehensively characterising treatment pathways and sequences for ovarian cancer.

Lastly, the findings of this study will reflect only the populations and healthcare settings captured in the included data sources and will only capture exposures occurring within the healthcare settings covered by each data source. As such, results may not be generalisable to other DARWIN EU® Data Network data sources.

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11. ANNEXES

ANNEX I. Description of data sources

Danish Data Health Registries (DK-DHR)

#	Section	Description
1	Database Identification and country	DK-DHR (Danish Data Health Registries) Denmark
2	Data partner information section	Danish Medicines Agency (DKMA) Data Analytics Centre (DAC)
3	Coverage and timespan	Data collection since: 1995 Extent: Nation-wide. The data is representative of the entire Danish population.
4	Healthcare setting / type of data	Community pharmacists, and secondary care – specialists (ambulatory or hospital outpatient care), and hospital inpatient care. The following data elements are collected: diagnosis (including rare diseases and pregnancy data), hospital admissions, discharge and ICU data, Cause of death, Drug prescriptions, dispensing, vaccination and contraception, Procedures, Devices, and Sociodemographic information.
5	Data collection process	Outpatient electronic health records, and Inpatient hospital electronic health records, and Registries, and Other. All causes of deaths, all retrieved drug prescriptions, all records of vaccinations, all hospital inpatient and outpatients contacts including disease diagnoses and hospital surgical and non-surgical procedures, cancers, laboratory test results for the entire Danish population from 1/1/1995 onwards.
6	General representativeness	The data is representative of the entire Danish population. Healthcare is free in Denmark, so we do not expect any bias in data collection based on socio-economic status.
7	Data content /source coding	Diagnoses and causes of death are collected using the ICD-10 vocabulary. ATC and RxNorm are used for Drugs. SNOMED codes are used for Procedures.
8	Data Harmonization	The data has been mapped to the OMOP CDM v5.4 and the OMOP standard vocabularies (SNOMED, RxNorm, LOINC). The format, structural and semantic conformance has been verified upon onboarding into the DARWIN EU® data network. No.
9	Quality control (database specific)	The data we have received relating to nationwide Danish Health Data registries offer an opportunity for large-scale, population-based studies with several advantages 1) Their large size improves the precision of estimates and enables the study of rare exposures and outcomes with long-term latency, 2) Inclusion of nearly all individuals in the target population ensures that the data reflect routine clinical care and all clinical segments of the source population, 3) Data are collected independently of each research study, thus minimising certain types of bias, e.g., non-response, and the influence from attention to the research question on the diagnostic process. Before the source data is sent to us, the Danish Health Data Authority runs and does comprehensive checks of the registry table data validity of the variables, breaks in data, changes in variable coding, missingness, etc. We perform checks of missingness/completeness in relation to requested variables. In essence, we are receiving a dump of a mirror of the data that is controlled by the SDS. The documentation performed by SDS is available online, in Danish primarily https://www.esundhed.dk/Dokumentation (all variables), but also in English https://sundhedsdatastyrelsen.dk/da/english/health_data_and_registers/national_health_registers
10	Linkage	There is no linkage in this data source.
11	Vital status	The Cause of Death registry (DAR) is used, the cause of death is collected using ICD-10 codes.
12	Limitations	No database-specific limitations documented. General limitations for the data type applicable.
13	Main references	Schmidt M, Schmidt SAJ,Adelborg K,Sundbøll J,Laugesen K,Ehrenstein V,Sørensen HT "The Danish health care system and epidemiological research: from health care contacts to database records." Clinical epidemiology (2019): 31372058

#	Section	Description
14	Link to HMA-EMA catalogue and database webpage	HMA-EMA Catalogue entry: https://catalogues.ema.europa.eu/data-source/1111217 Website: https://sundhedsdatastyrelsen.dk/da/english/health_data_and_registers/healthdatadenmark

Clinical Data Warehouse of Bordeaux University Hospital (CDW Bordeaux)

#	Section	Description
1	Database Identification and country	CDW Bordeaux (Clinical Data Warehouse of Bordeaux University Hospital) Nouvelle-Aquitaine, France
2	Data partner information section	CHU DE BORDEAUX - DIRECTION GENERALE Gironde / Nouvelle-Aquitaine
3	Coverage and timespan	Data collection since: 2005 Extent: Regional. It covers the population of Bordeaux metropolitan area, and possibly beyond, as the health care centre for referrals and expertise for the Nouvelle Aquitaine region. The database contains data from 2005 onwards.
4	Healthcare setting / type of data	Secondary care – specialists (ambulatory or hospital outpatient care), and hospital inpatient care, and claims data. The database currently captures information about patient demographics, visit details, conditions, procedures, drugs, measurements, and mortality.
5	Data collection process	Outpatient electronic health records, and Inpatient hospital electronic health records, and Inpatient hospital billing systems, and Biobank. The integrated data is extracted from the hospital production information system via a real-time research database. The data is then processed and quality controlled by a team dedicated to maintaining the database. Internal evaluations were carried out to ensure consistency between the research database and the patient bedside software.
6	General representativeness	This is the 6th largest metropolitan area in France, and CHUBX is the largest hospital in the region. More than 75% of the patients administered to Bordeaux university hospital reside in the Gironde departments, with almost 50% coming directly from the Bordeaux metropolitan area. The hospital also captures additional cases from Nouvelle-Aquitaine region.
7	Data content /source coding	Diagnosis source data is coded in ICD-10 terminology. Procedures are coded in CCAM (French terminology). Laboratory measurements are coded in local terminology and partially mapped to LOINC. Drugs are coded through a local terminology and then mapped to UCD (French terminology), as well as ATC codes.
8	Data Harmonization	The data has been mapped to the OMOP CDM v5.4 and the OMOP standard vocabularies (SNOMED, RxNorm, LOINC). The format, structural and semantic conformance has been verified upon onboarding into the DARWIN EU® data network. We use the hospital's unique identifier to generate the patient identifier in OMOP. If two identities are merged at the hospital, the merge is taken into account in the CDW. An automatic (hourly) detection of suspected duplicated identities has been implemented at the hospital since 2020, with merging of duplicated identities by a specialized team. Identities since 2015 were processed retrospectively. Thus, the rate of identity duplication in the database is low, especially since 2015.
9	Quality control (database specific)	- The integrated data comes from the hospital production information system through a real-time replicated database. Consistency evaluations between the replicated database and the production system are performed by the technical team in charge of maintaining the replicated database. - In the same way, consistency checks are performed between the replicated database and the data integrated into the i2b2 CDW. In addition, dashboards enable monitoring the data integrated into the i2B2 CDW, in particular by controlling the amount of data available over time, and its evolution, according to the various data sources. - An internal evaluation was carried out to ensure the consistency between the data integrated into i2b2 and the data available in the software used at the patient's bedside. In addition, many

#	Section	Description
		use cases were performed on the i2b2 CDW, with return to the patient chart and comparison of the data integrated into i2b2 and the data available in the care file.
10	Linkage	Death certificates (without the cause of death).
11	Vital status	The database is linked to the French death registry.
12	Limitations	CDW Bordeaux is limited to events captured in the hospital setting, and thus does not include patient events not treated by the hospital (e.g. rare cancers). Patient events that are not included in CDW Bordeaux are rare disease treatments or specialist events that occur outside of CHUBX.
13	Main references	Cossin S, Diouf S,Griffier R,Le Barrois d'Orgeval P,Diallo G,Jouhet V "Linkage of Hospital Records and Death Certificates by a Search Engine and Machine Learning." JAMIA open (2021): 33709061
14	Link to HMA-EMA catalogue and database webpage	HMA-EMA Catalogue entry: https://catalogues.ema.europa.eu/data-source/1111112 Website: https://www.chu-bordeaux.fr/

Netherlands Cancer Registry (NCR)

#	Section	Description
1	Database Identification and country	NCR (Netherlands Cancer Registry) Netherlands
2	Data partner information section	IKNL Clinical Data Science
3	Coverage and timespan	Data collection since: 1992 Extent: Nation-wide. The NCR compiles clinical data of all individuals newly diagnosed with cancer in the Netherlands. Cancer registration clerks register newly diagnosed cancer patients, starting in 1989, on a national basis, with 3 million patients included.
4	Healthcare setting / type of data	Hospital inpatient care, and other (specify). The NCR is a registry that contains details about the cancer diagnosis of the patient, the primary treatment, and the vital status.
5	Data collection process	Registries. Cancer registration clerks enter and process the data.
6	General representativeness	The data has nationwide coverage in The Netherlands of people having a cancer diagnosis since 1993.
7	Data content /source coding	ATC codes, ICD-O-3. The diagnosis contains the type of cancer (ICD-O-3) and the stage (TNM).
8	Data Harmonization	The data has been mapped to the OMOP CDM v5.4 and the OMOP standard vocabularies (SNOMED, RxNorm, LOINC). The format, structural and semantic conformance has been verified upon onboarding into the DARWIN EU® data network. No, we use identifiable data for linkage and identification across hospitals.
9	Quality control (database specific)	All data is collected and checked by data managers. These are some of the quality control procedures: - All data managers receive a training when they start, and they get yearly refresher courses. - The registration application limits what can be registered,

#	Section	Description
		depending on certain disease characteristics. This prevents a lot of errors. - A team of data managers is responsible for quality (werkgroep kwaliteit). - Random samples of registered data are checked. - Automatic checks are done. - Researchers, who use the data, can request quality checks if they suspect issues.
10	Linkage	Established linkages: National statistics from CBS PROMS from PROFILES Pathology data from PALGA Other info from other Dutch sources
11	Vital status	Source for vital status unknown.
12	Limitations	The database only has patients with a cancer diagnosis. The primary treatment is mainly registered. There are some lab results, mainly around the diagnosis. There is no sociodemographic information. Only ATC codes are available for some drugs, and this can only be mapped to ingredient level in OMOP.
13	Main references	Gijs Geleijnse, RuRu Chun-Ju Chiang, Melle Sieswerda, Melinda Schuurman, K. C. Lee, Johan van Soest, Andre Dekker, Wen-Chung Lee & Xander A. A. M. Verbeek "Prognostic factors analysis for oral cavity cancer survival in the Netherlands and Taiwan using a privacy-preserving federated infrastructure" Scientific Reports (2020):
14	Link to HMA-EMA catalogue and database webpage	HMA-EMA Catalogue entry: https://catalogues.ema.europa.eu/data-source/1111117 Website: https://iknl.nl/en

Cancer Registry Norway (CRN)

#	Section	Description
1	Database Identification and country	CRN (Cancer Registry Norway) Norway
2	Data partner information section	Norwegian Institute of Public Health Cancer Registry of Norway
3	Coverage and timespan	Data collection since: 1953 Extent: Nation-wide. The catchment area is all of Norway. The approximate population is around 5.6 Million.
4	Healthcare setting / type of data	Secondary care – specialists (ambulatory or hospital outpatient care), and hospital inpatient care. The following data elements are collected: diagnoses, pathology, lab reports, clinical notifications, deaths, procedures, measurements, drug prescription and dispensing.
5	Data collection process	Registries. Data is entered and processed by the data controllers, where a standard SOP of data quality checks are completed. As well, strict quality assessment procedures are done to manually assess the quality of the information in regards to general statistics and cancer-specific domain information.

#	Section	Description
6	General representativeness	All cancer patients in Norway must be registered in the CRN, independent of age or sociodemographic factors. Therefore the database should mirror the source population well.
7	Data content /source coding	ICD03 and ICD10 are used for topography/morphology/disease of the cancer diagnosis. Other used systems are ISUP, ECOG and SNOMED. Drugs prescriptions and dispensing is recorded with ATC codes, indications for the prescriptions are recorded with ICD10 codes.
8	Data Harmonization	The data has been mapped to the OMOP CDM v5.4 and the OMOP standard vocabularies (SNOMED, RxNorm, LOINC). The format, structural and semantic conformance has been verified upon onboarding into the DARWIN EU® data network. No. All patients have 11-digit unique identifiers used. Persons who have changed their unique identifier have a link between the old and new number.
9	Quality control (database specific)	The CRN has a strict QA-regime, with validation of all received information and a rule-engine ensuring that international, national, and in-house rules are being implemented the same way for all cases. In addition, we have manual quality assurance checks for different cancer sites, to uncover unlikely information, for instance checking all cases of melanoma where the diameter of the tumour exceeds 2 cm etc. The quality of the CRN-data is described in articles and by different quality measures in our annual statistics (for instance: percentage of cases morphologically verified, estimated completeness of cases, percentage cases only documented by a death certificate, male to female ratio, etc.).
10	Linkage	Every citizen has a unique personal identifier, and via this identifier, patients can be linked to other national data sources. But none are specifically mentioned.
11	Vital status	Information about death is collected when the patient's information from the cause of death registry has cancer as the primary or secondary cause of death.
12	Limitations	No database-specific limitations documented. General limitations for the data type applicable.
13	Main references	Larsen IK, Småstuen M,Johannesen TB,Langmark F,Parkin DM,Bray F,Møller B "Data quality at the Cancer Registry of Norway: an overview of comparability, completeness, validity and timeliness." European journal of cancer (Oxford, England : 1990) (2009): 19091545
14	Link to HMA-EMA catalogue and database webpage	HMA-EMA Catalogue entry: https://catalogues.ema.europa.eu/data-source/1111128 Website: https://www.kreftregisteret.no/en/

ANNEX II. Fitness for use assessment

Data source justification for inclusion and key characteristics

In this section we provide a justification for including the selected data sources. We also provide the expected number of person counts based on a preliminary feasibility assessment. Please note that these numbers are approximate, rounded to the nearest multiple of 100, and correspond to the entire data source, with no restriction on age, sex, or study period. Therefore, the number of individuals who will be included in the study might differ to those reported in this section.

Danish Data Health Registries (DK-DHR):

DK-DHR will be included in this study due to its nationwide coverage and its comprehensive record of cancer diagnoses. DK-DHR is a registry-based data source that includes secondary inpatient, outpatient, and emergency health data from the entire population of Denmark (approximately 4.3 million female patients). Data on cancer is obtained from the National Patient Registry (with data up to end of data availability) and the National Cancer Registry (with data up to December 2022). The National Cancer Registry contains information on all primary cancer cases histologically confirmed in the country.

Based on a preliminary feasibility assessment, the expected number of person counts for ovarian cancer is approximately 20,000. Person counts of treatments of interest (assessed at ingredient-level) range from 100 to 1,895,200. Data availability in DK-DHR starts in 1995. The date of the most recent data extraction is November 2024. Observability is defined as the time from the earliest of date of birth or registry start through to death. The median follow-up of the first observation period in DK-DHR is 7,920 days (2,610–1,090).

DK-DHR has blanket Institutional Review Board (IRB) approval.

Clinical Data Warehouse of Bordeaux University Hospital (CDW Bordeaux):

CDW Bordeaux will be included in this study because it is a hospital registry that includes secondary inpatient, outpatient, and emergency room health data (approximately 1.22 million women). Based on a preliminary feasibility assessment, the expected number of person counts is approximately 1,200. Data availability in CDW Bordeaux starts in 2005, and the date of the most recent data extraction is September 2025. Observability is defined as the period between a patient's first hospital admission and their most recent hospital discharge. The median follow-up of the first observation period in CDW Bordeaux is 2,470 days (1370–5,550).

IRB approval for CDW Bordeaux is estimated to take 1 to 2 weeks.

Netherlands Cancer Registry (NCR):

NCR will be included in this study because it is a cancer registry, compiling clinical data for all newly diagnosed cancer patients in the Netherlands. The number of female patients included is approximately 1.32 million. Based on a preliminary feasibility assessment, the expected number of person counts is 6,400. Person counts of treatments of interest (assessed at ingredient-level) range from 100 to 70,900. In the current onboarded data source, data availability extends up to January 2025 and includes data on individuals aged 18 or older. Due to lack of completeness of most recent data, the study will be restricted up to December 2023. Observability is defined as the time from the earliest of date of birth or registry start through to death, last vital status update (collected annually, latest in 2023), or emigration. The median follow-up of the first observation period in NCR is 1,020 days (6,220–1,170).

IRB approval for NCR is estimated to take 1 to 3 months.

Cancer Registry Norway (CRN):

CRN will be included in this study because it is the national cancer registry in Norway (approximately 585,000 women). Based on a preliminary feasibility assessment, the expected number of person count is

6200. Person counts of treatments of interest (assessed at ingredient-level) range from 100 to 12,500. Moreover, data availability and follow-up in CRN starts in 1951 and extends up to September 2025. However, due to lack of completeness of most recent data, the study will be restricted up to December 2024. Observability is defined as the time from the earliest of date of birth or registry start through to death, last vital status update (collected annually, latest in 2024), or emigration. The median follow-up of the first observation period in CRN is 1,890 days (1,200–2,400).

IRB approval for CRN is estimated to take 2 to 4 weeks.

ANNEX III. Operational and reporting considerations

DATA MANAGEMENT

Data management

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

The analytic code for this study will be written in R and will use standardized analytics wherever possible. Each data partner will execute the study code against their data source containing patient-level data and then return the results (csv files), which will only contain aggregated data. The results from each of the contributing data sites will then be combined in tables and figures for the study report.

Data storage and protection

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

All data sources used in this study are already used for pharmaco-epidemiological research and have a well-developed mechanism to ensure that European and local regulations dealing with ethical use of the data and adequate privacy control are adhered to. In agreement with these regulations, rather than combining person level data and performing only a central analysis, local analyses will be run, which generate non-identifiable aggregate summary results.

The output files are stored in the DARWIN EU® Remote Research Environment (RRE). These output files do not contain any data that allow identification of subjects included in the study. The RRE implements further security measures to ensure a high level of stored data protection to comply with the local implementation of the General Data Protection Regulation (GDPR) (EU) 679/20161 in the various member states.

QUALITY CONTROL

Data source quality control

When defining drug cohorts, non-systemic products will be excluded from the list of included codes summarised on the ingredient level.

When defining cohorts, a systematic search of possible codes for inclusion will be identified using the *CodelistGenerator* R package (https://github.com/darwin-eu/CodelistGenerator). This package allows the user to define a search strategy and will use this to query the vocabulary tables of the OMOP common data model so as to find potentially relevant codes. In addition, the *CohortDiagnostics* (https://github.com/OHDSI/CohortDiagnostics) and *DrugExposureDiagnostics* (https://cran.r-project.org/web/packages/DrugExposureDiagnostics/index.html) R packages will be run, if needed, to assess the use of different codes across the data sources contributing to the study and identify any codes potentially omitted in error. The *DrugExposureDiagnostics* package evaluates ingredient-specific attributes and patterns in drug exposure records.

The study code will be based on DARWIN EU® R packages: *DrugUtilisation* to characterise the drug use, and *CohortCharacteristics* to characterise the cohort of interest. These packages will include numerous automated unit tests to ensure the validity of the codes, alongside software peer review and user testing. The R package will be made publicly available via GitHub.

PLANS FOR DISSEMINATING AND COMMUNICATING STUDY RESULTS

A PDF report including an executive summary, and the specified tables and/or figures will be submitted to the European Medicines Agency (EMA) by the DARWIN EU® Coordination Centre (CC) upon completion of the study.

An interactive dashboard incorporating all the results (tables and figures) will be provided alongside the PDF report. The full set of underlying aggregated data used in the dashboard will also be made available, if requested.

ANNEX IV. Preliminary concept sets

Table S1. Preliminary list of conditions definitions.

Phenotype	Concept name	Concept id (including descendants)	Vocabulary
Ovarian cancer	Adenocarcinoma in villous adenoma of ovary	44501799	ICDO3
	Adenocarcinoid tumor of ovary	36557481	ICDO3
	Adenocarcinoma in tubulovillous adenoma of ovary	36517442	ICDO3
	Adenocarcinoma in villous adenoma of ovary	44501799	ICDO3
	Adenocarcinoma with apocrine metaplasia of ovary	36533493	ICDO3
	Adenocarcinoma with cartilaginous and osseous metaplasia of ovary	36555833	ICDO3
	Adenocarcinoma with mixed subtypes of ovary	44501497	ICDO3
	Adenocarcinoma with neuroendocrine differentiation of ovary	36549048	ICDO3
	Adenocarcinoma with spindle cell metaplasia of ovary	36555562	ICDO3
	Adenocarcinoma with squamous metaplasia of ovary	44502635	ICDO3
	Adenocarcinoma, intestinal type of ovary	42512706	ICDO3
	Adenocarcinoma, NOS, of ovary	44500057	ICDO3
	Adenoid cystic carcinoma of ovary	36522016	ICDO3
	Adenosarcoma of ovary	44501979	ICDO3
	Adenosquamous carcinoma of ovary	44502118	ICDO3
	Androblastoma, malignant of ovary	36561709	ICDO3
	Angiomyosarcoma of ovary	36547231	ICDO3
	Astrocytoma, NOS, of ovary	44500697	ICDO3
	Basal cell adenocarcinoma of ovary	36564919	ICDO3
	Brenner tumor, malignant of ovary	44501034	ICDO3
	Carcinoma of ovary, stage 1	4311576	SNOMED
	Carcinoma of ovary, stage 2	4311462	SNOMED
	Carcinoma of ovary, stage 3	4313202	SNOMED
	Carcinoma of ovary, stage 4	4310444	SNOMED
	Carcinoma simplex of ovary	36518615	ICDO3
	Carcinoma with osteoclast-like giant cells of ovary	36555513	ICDO3
	Carcinoma, anaplastic, NOS, of ovary	44500115	ICDO3
	Carcinosarcoma of bilateral ovaries	36687125	SNOMED
	Carcinosarcoma of left ovary	36687123	SNOMED
	Carcinosarcoma of ovary	45765433	SNOMED
	Carcinosarcoma of right ovary	36687124	SNOMED

Phenotype	Concept name	Concept id (including descendants)	Vocabulary
	Carcinosarcoma, embryonal of ovary	36565621	ICDO3
	Chondrosarcoma, NOS, of ovary	42512428	ICDO3
	Choriocarcinoma combined with other germ cell elements of ovary	44499580	ICDO3
	Choriocarcinoma of ovary	4112865	SNOMED
	Clear cell adenocarcinofibroma of ovary	44503153	ICDO3
	Clear cell adenocarcinoma of Mullerian origin of ovary	1246658	SNOMED
	Clear cell adenocarcinoma of ovary	35621826	SNOMED
	CNS embryonal tumor, NOS, of ovary	44500698	ICDO3
	Combined small cell carcinoma of ovary	42512649	ICDO3
	Cystadenocarcinoma of ovary	4198275	SNOMED
	Dedifferentiated liposarcoma of ovary	42511808	ICDO3
	Desmoplastic small round cell tumor of ovary	36541965	ICDO3
	Embryonal carcinoma of ovary	4116076	SNOMED
	Embryonal rhabdomyosarcoma, NOS, of ovary	42512212	ICDO3
	Endodermal sinus tumor of ovary	4110870	SNOMED
	Endometrial stromal sarcoma, low grade of ovary	36551251	ICDO3
	Endometrioid adenocarcinoma, ciliated cell variant of ovary	36549177	ICDO3
	Endometrioid adenocarcinoma, secretory variant of ovary	36546706	ICDO3
	Endometrioid adenofibroma, malignant of ovary	44501646	ICDO3
	Endometrioid carcinoma ovary	4112857	SNOMED
	Enterochromaffin cell carcinoid of ovary	36526539	ICDO3
	Enterochromaffin-like cell tumor of ovary	36522186	ICDO3
	Ependymoma, NOS, of ovary	36554315	ICDO3
	Epithelial-myoepithelial carcinoma of ovary	36560084	ICDO3
	Epithelioid leiomyosarcoma of ovary	36523542	ICDO3
	Epithelioid sarcoma, NOS, of ovary	36563283	ICDO3
	Epithelioma, malignant of ovary	36541361	ICDO3
	Extra-adrenal paraganglioma, NOS, of ovary	1553496	ICDO3
	Familial ovarian cancer	37162600	SNOMED
	Fascial fibrosarcoma of ovary	36557412	ICDO3
	Fibrosarcoma, NOS, of ovary	44501972	ICDO3
	Germ cell tumor, nonseminomatous of ovary	44499578	ICDO3
	Giant cell and spindle cell carcinoma of ovary	36540048	ICDO3
	Giant cell carcinoma of ovary	44500481	ICDO3

Phenotype	Concept name	Concept id (including descendants)	Vocabulary
	Giant cell sarcoma of ovary	36558110	ICDO3
	Glassy cell carcinoma of ovary	36551702	ICDO3
	Goblet cell carcinoid of ovary	36530159	ICDO3
	Granular cell carcinoma of ovary	44499811	ICDO3
	Hemangiosarcoma of ovary	42512346	ICDO3
	Hepatoid adenocarcinoma of ovary	36567568	ICDO3
	Hereditary breast and ovarian cancer syndrome	37397555	SNOMED
	Infantile fibrosarcoma of ovary	36537077	ICDO3
	Large cell carcinoma with rhabdoid phenotype of ovary	36526802	ICDO3
	Large cell carcinoma, NOS, of ovary	44499710	ICDO3
	Large cell neuroendocrine carcinoma of ovary	36566846	ICDO3
	Left ovarian primary endometrioid carcinoma	602311	SNOMED
	Left ovarian primary mucinous cystadenocarcinoma	602307	SNOMED
	Left ovarian primary sarcoma	608867	SNOMED
	Leiomyosarcoma, NOS, of ovary	44502971	ICDO3
	Leydig cell tumor, malignant of ovary	44501960	ICDO3
	Malignant Brenner tumor of ovary	1245142	SNOMED
	Malignant dysgerminoma of ovary	4116077	SNOMED
	Malignant epithelial tumor of ovary	4116073	SNOMED
	Malignant germ cell neoplasm of left ovary	36686094	SNOMED
	Malignant germ cell neoplasm of right ovary	36686093	SNOMED
	Malignant germ cell tumor of ovary	4112864	SNOMED
	Malignant granulosa cell tumor of ovary	4112862	SNOMED
	Malignant immature teratoma of ovary	37311080	SNOMED
	Malignant melanoma, NOS, of ovary	44501734	ICDO3
	Malignant neoplasm of ovary	4181351	SNOMED
	Malignant non-dysgerminomatous germ cell tumor of ovary	37166979	SNOMED
	Malignant sex cord tumor of left ovary	37159982	SNOMED
	Malignant sex cord tumor of ovary	4116074	SNOMED
	Malignant sex cord tumor of right ovary	37159981	SNOMED
	Malignant teratoma, intermediate of ovary	36554907	ICDO3
	Malignant teratoma, undifferentiated of ovary	36549316	ICDO3
	Malignant tumor involving left ovary by direct extension from endometrium	4289391	SNOMED
	Malignant tumor involving left ovary by direct extension from fallopian tube	4281028	SNOMED

Phenotype	Concept name	Concept id (including descendants)	Vocabulary
	Malignant tumor involving left ovary by direct extension from right ovary	4289682	SNOMED
	Malignant tumor involving left ovary by direct extension from uterine cervix	4289683	SNOMED
	Malignant tumor involving left ovary by direct extension from uterus	4281029	SNOMED
	Malignant tumor involving left ovary by direct extension from vagina	4289691	SNOMED
	Malignant tumor involving right ovary by direct extension from endometrium	4281032	SNOMED
	Malignant tumor involving right ovary by direct extension from fallopian tube	4281033	SNOMED
	Malignant tumor involving right ovary by direct extension from left ovary	4283749	SNOMED
	Malignant tumor involving right ovary by direct extension from uterine cervix	4283750	SNOMED
	Malignant tumor involving right ovary by direct extension from uterus	4281159	SNOMED
	Malignant tumor involving right ovary by direct extension from vagina	4289522	SNOMED
	Malignant tumor, clear cell type of ovary	36521466	ICDO3
	Malignant tumor, giant cell type of ovary	36559221	ICDO3
	Malignant tumor, small cell type of ovary	36524459	ICDO3
	Malignant tumor, spindle cell type of ovary	36564832	ICDO3
	Medullary carcinoma, NOS, of ovary	36521027	ICDO3
	Medulloepithelioma, NOS, of ovary	36555512	ICDO3
	Mesodermal mixed tumor of ovary	44499765	ICDO3
	Mesonephroma, malignant of ovary	36539989	ICDO3
	Mesothelioma, malignant of ovary	44500093	ICDO3
	Metaplastic carcinoma, NOS, of ovary	44500675	ICDO3
	Mixed adenoneuroendocrine carcinoma of ovary	36519660	ICDO3
	Mixed cell adenocarcinoma of ovary	44502626	ICDO3
	Mixed germ cell tumor of ovary	44503047	ICDO3
	Mixed tumor, malignant, NOS, of ovary	42512021	ICDO3
	Mucin-producing adenocarcinoma of ovary	44501089	ICDO3
	Mucinous adenocarcinofibroma of ovary	44503112	ICDO3
	Mucinous carcinoma, gastric type of ovary	36546343	ICDO3
	Mucinous cystadenocarcinoma of ovary	4112856	SNOMED
	Mullerian mixed tumor of ovary	44502729	ICDO3
	Myoepithelial carcinoma of ovary	36533456	ICDO3
	Myofibroblastic sarcoma of ovary	42512745	ICDO3

Phenotype	Concept name	Concept id (including descendants)	Vocabulary
	Myosarcoma of ovary	36533215	ICDO3
	Myxofibrosarcoma of ovary	36548200	ICDO3
	Myxoid leiomyosarcoma of ovary	36518902	ICDO3
	Myxosarcoma of ovary	36549503	ICDO3
	Nephroblastoma, NOS, of ovary	36551146	ICDO3
	Neuroblastoma, NOS, of ovary	42512400	ICDO3
	Neuroendocrine carcinoma, NOS, of ovary	44500500	ICDO3
	Neuroendocrine tumor, grade 2 of ovary	36537956	ICDO3
	Neuroendocrine tumor, NOS, of ovary	44500023	ICDO3
	Non-small cell carcinoma of ovary	44501472	ICDO3
	Oxyphilic adenocarcinoma of ovary	44502948	ICDO3
	Papillary adenocarcinoma, NOS, of ovary	44501638	ICDO3
	Papillary carcinoma, follicular variant of ovary	42512613	ICDO3
	Papillary carcinoma, NOS, of ovary	44502916	ICDO3
	Papillary cystadenocarcinoma, NOS, of ovary	44502628	ICDO3
	Papillary pseudomucinous cystadenocarcinoma of ovary	36403096	ICDO3
	Papillary serous cystadenocarcinoma of ovary	36403161	ICDO3
	Papillary squamous cell carcinoma of ovary	44502604	ICDO3
	Pleomorphic carcinoma of ovary	36548557	ICDO3
	Polyembryoma of ovary	36529012	ICDO3
	Polygonal cell carcinoma of ovary	36528200	ICDO3
	Primary carcinosarcoma of ovary	37167583	SNOMED
	Primary clear cell adenocarcinoma of ovary	37167592	SNOMED
	Primary cystadenocarcinoma of ovary	37166281	SNOMED
	Primary endometrioid carcinoma of ovary	37167518	SNOMED
	Primary high grade serous adenocarcinoma of ovary	36716618	SNOMED
	Primary low grade serous adenocarcinoma of ovary	36717228	SNOMED
	Primary malignant dysgerminoma of ovary	37167659	SNOMED
	Primary malignant granulosa cell tumor of ovary	37167658	SNOMED
	Primary malignant neoplasm of both ovaries	36712933	SNOMED
	Primary malignant neoplasm of left ovary	4289681	SNOMED
	Primary malignant neoplasm of ovary	200051	SNOMED
	Primary malignant neoplasm of right ovary	4289392	SNOMED
	Primary malignant Sertoli-Leydig cell tumor of ovary	37168510	SNOMED
	Primary malignant sex cord tumor of ovary	37167657	SNOMED

Phenotype	Concept name	Concept id (including descendants)	Vocabulary
	Primary mucinous adenocarcinoma of ovary	37116598	SNOMED
	Primary mucinous cystadenocarcinoma of ovary	37166252	SNOMED
	Primary non-gestational choriocarcinoma of ovary	37396690	SNOMED
	Primary serous papillary cystadenocarcinoma of left ovary	602309	SNOMED
	Primary serous papillary cystadenocarcinoma of right ovary	602308	SNOMED
	Primary serous papillary cystadenocarcinoma ovary	37166251	SNOMED
	Primary small cell neuroendocrine carcinoma of ovary	37167594	SNOMED
	Primary theca steroid producing cell malignant neoplasm of ovary	37167733	SNOMED
	Primary undifferentiated carcinoma of ovary	37166253	SNOMED
	Pseudosarcomatous carcinoma of ovary	36529849	ICDO3
	Rhabdoid tumor, NOS, of ovary	44500161	ICDO3
	Rhabdomyosarcoma, NOS, of ovary	44502642	ICDO3
	Right ovarian primary endometrioid carcinoma	602310	SNOMED
	Right ovarian primary mucinous cystadenocarcinoma	602306	SNOMED
	Right ovarian primary sarcoma	608868	SNOMED
	Sarcoma of ovary	4307986	SNOMED
	Scirrhous adenocarcinoma of ovary	44501486	ICDO3
	Sebaceous carcinoma of ovary	36527913	ICDO3
	Seminoma, NOS, of ovary	44502582	ICDO3
	Seromucinous carcinoma of ovary	42512888	ICDO3
	Serous adenocarcinofibroma of ovary	44501671	ICDO3
	Serous carcinoma, NOS, of ovary	44499443	ICDO3
	Serous papillary cystadenocarcinoma ovary	4112855	SNOMED
	Sertoli cell carcinoma of ovary	44502962	ICDO3
	Sertoli-Leydig cell tumor, poorly differentiated, with heterologous elements of ovary	36533533	ICDO3
	Signet ring cell carcinoma of ovary	44499561	ICDO3
	Small cell carcinoma of ovary	36674767	SNOMED
	Small cell carcinoma, intermediate cell of ovary	42511825	ICDO3
	Small cell neuroendocrine carcinoma of ovary	1244622	SNOMED
	Small cell sarcoma of ovary	36546973	ICDO3
	Solid carcinoma, NOS, of ovary	36549054	ICDO3

Phenotype	Concept name	Concept id (including descendants)	Vocabulary
	Solitary fibrous tumor, malignant of ovary	36519688	ICDO3
	Spindle cell carcinoma, NOS, of ovary	36550763	ICDO3
	Spindle cell sarcoma of ovary	44499569	ICDO3
	Squamous cell carcinoma with horn formation of ovary	36567017	ICDO3
	Squamous cell carcinoma, adenoid of ovary	36562826	ICDO3
	Squamous cell carcinoma, keratinizing, NOS, of ovary	36550805	ICDO3
	Squamous cell carcinoma, large cell, nonkeratinizing, NOS, of ovary	36563636	ICDO3
	Squamous cell carcinoma, microinvasive of ovary	36550888	ICDO3
	Squamous cell carcinoma, NOS, of ovary	44500986	ICDO3
	Squamous cell carcinoma, small cell, nonkeratinizing of ovary	36518848	ICDO3
	Squamous cell carcinoma, spindle cell of ovary	36562083	ICDO3
	Steroid cell tumor, malignant of ovary	44505882	ICDO3
	Stromal sarcoma, NOS, of ovary	44501102	ICDO3
	Struma ovarii, malignant of ovary	44502732	ICDO3
	Superficial spreading adenocarcinoma of ovary	36527293	ICDO3
	Teratocarcinoma of ovary	36517655	ICDO3
	Teratoma with malignant transformation of ovary	44502731	ICDO3
	Teratoma, malignant, NOS, of ovary	44500162	ICDO3
	Theca steroid producing cell malignant neoplasm of ovary	37396882	SNOMED
	Thecoma, malignant of ovary	36519879	ICDO3
	Transitional cell carcinoma, NOS, of ovary	44500991	ICDO3
	Trophoblastic tumor, epithelioid of ovary	36522229	ICDO3
	Tumor cells, malignant of ovary	36568387	ICDO3
	Undifferentiated carcinoma of left ovary	37159984	SNOMED
	Undifferentiated carcinoma of ovary	4110863	SNOMED
	Undifferentiated carcinoma of right ovary	37159983	SNOMED
	Undifferentiated sarcoma of ovary	36557833	ICDO3
	Verrucous carcinoma, NOS, of ovary	36565806	ICDO3
	Villous adenocarcinoma of ovary	36524110	ICDO3

Table S2. Preliminary list of covariates definitions.

Covariates	Concept name	Concept id	Vocabulary
ECOG/WHO-PS	WHO performance status grade 0	4190931	SNOMED
	WHO performance status grade 1	4161577	SNOMED
	WHO performance status grade 2	4161578	SNOMED
	WHO performance status grade 3	4162590	SNOMED
	WHO performance status grade 4	4161579	SNOMED
	WHO performance status scale	4162588	SNOMED
BRCA gene	BRCA1 gene mutations tested for in Blood or Tissue by Molecular genetics method Nominal	3002832	LOINC
	BRCA2 gene mutation not detected	4133516	SNOMED
	BRCA1 gene mutation detected	4135410	SNOMED
	BRCA2 gene mutation detected	4135411	SNOMED
	BRCA1 gene mutation not detected	4136450	OMOP Genomic
	BRCA2 on GRCh38 chr13: Substitution in position 32316435 of G replaced by A measurement	36734714	SNOMED
	BRCA1 on GRCh38 chr17: Substitution in position 43125170 of G replaced by C measurement	36737496	OMOP Genomic
Hyperglycaemia	Hyperglycaemia	4214376	SNOMED
Diabetes mellitus	Diabetes mellitus	201820	SNOMED
Endometriosis	Endometriosis (clinical)	433527	SNOMED
Pelvic inflammatory disease	Female pelvic inflammatory disease	199067	SNOMED
Obesity	Obesity	433736	SNOMED
History of breast cancer	Primary malignant neoplasm of breast	4162253	SNOMED
Family history of breast cancer	Family history of neoplasm of breast	4179963	SNOMED

Table S3. Preliminary list of ingredient definitions.

Substance Name	Ingredient Concept ID
Altretamine	1368823
Chlorambucil	1390051
Cyclophosphamide	1310317
Ifosfamide	19078187
Lomustine	1391846
Melphalan	1301267
Thiotepa	19137385
Treosulfan	19042545
Doxorubicin	1338512

Substance Name	Ingredient Concept ID
Epirubicin	1344354
Mitoxantrone	1309188
Fluorouracil	955632
Gemcitabine	1314924
Methotrexate	1305058
Trabectedin	35603017
Carboplatin	1344905
Cisplatin	1397599
Docetaxel	1315942
Paclitaxel	1378382
Etoposide	1350504
Topotecan	1378509
Vinblastine	19008264
Niraparib	1593861
Olaparib	45892579
Rucaparib	1718850
Bevacizumab	1397141
Mirvetuximab soravtansine	741947
Dexamethasone	1518254
Medroxyprogesterone	1500211

Table S4. Preliminary list of TNM staging definitions.

Concept ID	TNM staging names
1633268	AJCC/UICC 7th pathological T1a Category
1633270	AJCC/UICC 6th clinical Stage 4C
1633271	AJCC/UICC 8th clinical N2c Category
1633273	AJCC/UICC 6th pathological N2a Category
1633275	AJCC/UICC 7th clinical N1a Category
1633276	AJCC/UICC 7th clinical M1 Category
1633279	AJCC/UICC 6th pathological T0 Category
1633281	AJCC/UICC clinical Ta Category
1633282	AJCC/UICC 8th pathological T1b Category
1633288	AJCC/UICC pathological T3a Category
1633290	AJCC/UICC 6th pathological Stage 1B
1633300	AJCC/UICC pathological T4a Category
1633301	AJCC/UICC pathological N2c Category
1633307	AJCC/UICC 8th pathological T2 Category

Concept ID	TNM staging names
1633315	AJCC/UICC 6th clinical N0 Category
1633323	AJCC/UICC 8th clinical N2b Category
1633324	AJCC/UICC 7th clinical T3 Category
1633326	AJCC/UICC 6th pathological T4c Category
1633334	AJCC/UICC 6th clinical N3c Category
1633336	AJCC/UICC 8th pathological N2 Category
1633341	AJCC/UICC 7th pathological T2a Category
1633345	AJCC/UICC 7th clinical Stage 2A
1633355	AJCC/UICC 6th pathological Stage 0a
1633366	AJCC/UICC 7th clinical Stage 1C
1633374	AJCC/UICC 8th pathological T1a Category
1633375	AJCC/UICC 8th clinical M1b Category
1633384	AJCC/UICC pathological N3b Category
1633386	AJCC/UICC 7th pathological Stage 2C
1633401	AJCC/UICC pathological N3a Category
1633404	AJCC/UICC 8th pathological N1b Category
1633406	AJCC/UICC pathological T3b Category
1633413	AJCC/UICC post therapy clinical M1 Category
1633417	AJCC/UICC 7th clinical T1a2 Category
1633429	AJCC/UICC clinical N2a Category
1633430	AJCC/UICC 8th pathological Stage 2B
1633432	AJCC/UICC 8th clinical T1c1 Category
1633433	AJCC/UICC 6th clinical N2b Category
1633434	AJCC/UICC 6th clinical N3a Category
1633436	AJCC/UICC post therapy pathological T3 Category
1633445	AJCC/UICC 6th pathological T1 Category
1633452	AJCC/UICC 8th pathological Stage 1A
1633453	AJCC/UICC 8th pathological T2a Category
1633454	AJCC/UICC 7th clinical T1b1 Category
1633458	AJCC/UICC 8th clinical Stage 0a
1633460	AJCC/UICC pathological N2b Category
1633468	AJCC/UICC 7th clinical M0 Category
1633469	AJCC/UICC 6th pathological M1 Category
1633492	AJCC/UICC 6th clinical T1b Category
1633499	AJCC/UICC 6th pathological Stage 3
1633500	AJCC/UICC 6th pathological N3b Category
1633513	AJCC/UICC 6th pathological N1b Category
1633519	AJCC/UICC pathological Stage 3A

Concept ID	TNM staging names
1633520	AJCC/UICC 6th clinical T1a Category
1633525	AJCC/UICC 8th clinical T3c Category
1633527	AJCC/UICC post therapy pathological N0 Category
1633529	AJCC/UICC T1c Category
1633531	AJCC/UICC 8th clinical T1b Category
1633537	AJCC/UICC 7th pathological Stage 1C
1633540	AJCC/UICC 6th clinical T3c Category
1633542	AJCC/UICC pathological Stage 0
1633545	AJCC/UICC 6th clinical T2c Category
1633558	AJCC/UICC pathological N1b3 Category
1633561	AJCC/UICC 7th clinical Stage 3A
1633563	AJCC/UICC 6th clinical T3a Category
1633569	AJCC/UICC 7th pathological N2 Category
1633577	AJCC/UICC pathological Stage 4B
1633581	AJCC/UICC 8th pathological T3c Category
1633594	AJCC/UICC 7th pathological Stage 1A
1633595	AJCC/UICC 7th pathological T1b2 Category
1633607	AJCC/UICC 7th pathological N2b Category
1633613	AJCC/UICC 8th pathological Ta Category
1633618	AJCC/UICC clinical Stage 1B
1633623	AJCC/UICC post therapy pathological T4a Category
1633624	AJCC/UICC 8th pathological Stage 1A1
1633636	AJCC/UICC 8th pathological Stage 3A
1633640	AJCC/UICC 7th pathological N1a Category
1633651	AJCC/UICC 8th clinical N1 Category
1633658	AJCC/UICC 8th pathological T4b Category
1633659	AJCC/UICC 8th pathological N1 Category
1633663	AJCC/UICC 7th clinical Ta Category
1633668	AJCC/UICC 7th pathological N3 Category
1633680	AJCC/UICC 7th pathological T1a1 Category
1633693	AJCC/UICC pathological T1b Category
1633697	AJCC/UICC 8th pathological Stage 4
1633699	AJCC/UICC 7th pathological T4b Category
1633702	AJCC/UICC pathological Stage 2
1633707	AJCC/UICC clinical Stage 0is
1633709	AJCC/UICC 6th clinical M1a Category
1633712	AJCC/UICC 7th clinical Stage 0is
1633721	AJCC/UICC post therapy pathological T3b Category

Concept ID	TNM staging names
1633722	AJCC/UICC pathological T1a Category
1633723	AJCC/UICC 7th pathological T4a Category
1633726	AJCC/UICC 7th pathological N0 Category
1633730	AJCC/UICC 7th pathological N1b Category
1633736	AJCC/UICC 8th pathological Stage 3C
1633737	AJCC/UICC 8th clinical Tis Category
1633739	AJCC/UICC 7th clinical T3d Category
1633742	AJCC/UICC clinical T1a Category
1633747	AJCC/UICC 6th clinical T2 Category
1633751	AJCC/UICC 6th pathological Stage 2
1633757	AJCC/UICC 8th pathological MX Category
1633758	AJCC/UICC clinical T3a Category
1633759	AJCC/UICC 6th pathological Stage 3B
1633763	AJCC/UICC 8th clinical N2 Category
1633765	AJCC/UICC clinical T3b Category
1633767	AJCC/UICC 8th clinical T4c Category
1633777	AJCC/UICC clinical M1a Category
1633781	AJCC/UICC clinical T2b Category
1633784	AJCC/UICC 8th clinical M1c Category
1633785	AJCC/UICC 8th clinical N1c Category
1633788	AJCC/UICC 8th clinical N2a Category
1633813	AJCC/UICC pathological Stage 2B
1633815	AJCC/UICC 7th clinical T0 Category
1633819	AJCC/UICC 8th pathological N1c Category
1633824	AJCC/UICC 8th pathological T4e Category
1633828	AJCC/UICC 7th clinical Stage 0
1633830	AJCC/UICC pathological N1b Category
1633835	AJCC/UICC 6th clinical Stage 2C
1633839	AJCC/UICC 8th clinical N1a Category
1633841	AJCC/UICC clinical Stage 2
1633848	AJCC/UICC 6th pathological T1a2 Category
1633852	AJCC/UICC 6th clinical Stage 0a
1633854	AJCC/UICC 8th clinical N3 Category
1633859	AJCC/UICC pathological Stage 2C
1633864	AJCC/UICC pathological N2 Category
1633869	AJCC/UICC pathological Stage 1B
1633873	AJCC/UICC 6th pathological Stage 2C
1633877	AJCC/UICC 6th clinical T3 Category

Concept ID	TNM staging names
1633883	AJCC/UICC 8th clinical T1 Category
1633890	AJCC/UICC pathological N2a Category
1633891	AJCC/UICC pathological Stage 1A
1633892	AJCC/UICC 8th pathological T4d Category
1633895	AJCC/UICC 8th pathological N3c Category
1633896	AJCC/UICC 8th clinical T2a2 Category
1633897	AJCC/UICC 6th clinical Stage 1B
1633900	AJCC/UICC 6th pathological T4b Category
1633905	AJCC/UICC 6th clinical Stage 1
1633914	AJCC/UICC clinical N3 Category
1633915	AJCC/UICC 7th pathological Stage 2B
1633920	AJCC/UICC 8th pathological Tis Category
1633922	AJCC/UICC 6th clinical Stage 4B
1633934	AJCC/UICC 7th clinical N3c Category
1633935	AJCC/UICC post therapy pathological T1c Category
1633937	AJCC/UICC 8th pathological Stage 1A3
1633942	AJCC/UICC 7th clinical N0 Category
1633943	AJCC/UICC pathological T4 Category
1633946	AJCC/UICC 7th clinical T3b Category
1633947	AJCC/UICC 6th clinical T2a Category
1633958	AJCC/UICC 7th clinical T2b Category
1633962	AJCC/UICC 6th pathological T1c Category
1633970	AJCC/UICC 8th clinical Stage 1A1
1633974	AJCC/UICC 8th clinical M1 Category
1633978	AJCC/UICC pathological T2 Category
1633980	AJCC/UICC 8th clinical T1b2 Category
1633999	AJCC/UICC 6th pathological T2c Category
1634002	AJCC/UICC 6th clinical N1b Category
1634004	AJCC/UICC pathological T1 Category
1634005	AJCC/UICC 8th pathological Stage 4A
1634006	AJCC/UICC 8th clinical Stage 3B
1634008	AJCC/UICC 6th clinical Stage 2B
1634012	AJCC/UICC 6th pathological T1b2 Category
1634021	AJCC/UICC 8th clinical Stage 1A2
1634029	AJCC/UICC 7th clinical T2 Category
1634037	AJCC/UICC 7th clinical N3 Category
1634045	AJCC/UICC 8th pathological T1b1 Category
1634046	AJCC/UICC 7th clinical T4c Category

Concept ID	TNM staging names
1634047	AJCC/UICC 6th pathological T1a1 Category
1634056	AJCC/UICC 8th clinical Stage 2B
1634059	AJCC/UICC 8th pathological T1b3 Category
1634060	AJCC/UICC 8th pathological Stage 1B
1634066	AJCC/UICC 8th clinical Stage 1A
1634070	AJCC/UICC 8th clinical N0 Category
1634071	AJCC/UICC 8th Ta Category
1634088	AJCC/UICC clinical T3c Category
1634089	AJCC/UICC 8th pathological T1a2 Category
1634093	AJCC/UICC pathological M1b Category
1634101	AJCC/UICC 6th pathological T4a Category
1634116	AJCC/UICC 7th pathological Tis Category
1634117	AJCC/UICC 8th pathological NX Category
1634118	AJCC/UICC clinical N2c Category
1634120	AJCC/UICC 7th clinical T4b Category
1634125	AJCC/UICC pathological N1b2 Category
1634126	AJCC/UICC 7th clinical T1b2 Category
1634139	AJCC/UICC 7th clinical N1 Category
1634143	AJCC/UICC 6th clinical N2a Category
1634145	AJCC/UICC clinical N0 Category
1634160	AJCC/UICC 8th clinical Stage 1B
1634172	AJCC/UICC 6th clinical Stage 0is
1634188	AJCC/UICC 7th pathological M1c Category
1634190	AJCC/UICC 7th clinical T1a1 Category
1634192	AJCC/UICC clinical T4a Category
1634194	AJCC/UICC 6th clinical M0 Category
1634205	AJCC/UICC 6th clinical Stage 1A
1634206	AJCC/UICC pathological N1a Category
1634208	AJCC/UICC 6th pathological Stage 4
1634212	AJCC/UICC 6th pathological N0 Category
1634221	AJCC/UICC 6th pathological T2a Category
1634236	AJCC/UICC 7th pathological T1b Category
1634237	AJCC/UICC 7th pathological T1b1 Category
1634245	AJCC/UICC 7th pathological N1 Category
1634246	AJCC/UICC post therapy pathological T2a Category
1634247	AJCC/UICC 6th clinical T4a Category
1634251	AJCC/UICC 6th pathological T3c Category
1634252	AJCC/UICC pathological Stage 1

Concept ID	TNM staging names
1634264	AJCC/UICC post therapy pathological T1b Category
1634268	AJCC/UICC 7th pathological M1a Category
1634271	AJCC/UICC 6th pathological N3a Category
1634291	AJCC/UICC clinical T4b Category
1634299	AJCC/UICC 7th pathological Stage 3C
1634307	AJCC/UICC 6th clinical Stage 4
1634312	AJCC/UICC pathological M1a Category
1634320	AJCC/UICC clinical T1c Category
1634332	AJCC/UICC clinical Stage 2B
1634348	AJCC/UICC 7th clinical Stage 3B
1634359	AJCC/UICC 7th clinical Stage 0a
1634363	AJCC/UICC 6th pathological T3b Category
1634373	AJCC/UICC 8th pathological Tis(Paget) Category
1634381	AJCC/UICC 6th clinical T1 Category
1634383	AJCC/UICC 8th pathological N2c Category
1634386	AJCC/UICC 8th pathological T3 Category
1634390	AJCC/UICC 8th pathological Stage 2C
1634397	AJCC/UICC 7th pathological N3a Category
1634406	AJCC/UICC pathological T3 Category
1634418	AJCC/UICC post therapy pathological Tis Category
1634424	AJCC/UICC 6th pathological M1c Category
1634432	AJCC/UICC 6th clinical T1a2 Category
1634437	AJCC/UICC 8th clinical T1a1 Category
1634442	AJCC/UICC 6th clinical M1b Category
1634445	AJCC/UICC 7th clinical N1c Category
1634447	AJCC/UICC clinical Stage 4
1634450	AJCC/UICC clinical Tis Category
1634451	AJCC/UICC 7th clinical Stage 4A
1634455	AJCC/UICC 7th pathological T3c Category
1634457	AJCC/UICC 7th clinical Stage 1
1634460	AJCC/UICC clinical TX Category
1634465	AJCC/UICC 7th clinical Stage 2C
1634472	AJCC/UICC 7th pathological Stage 4B
1634477	AJCC/UICC 6th clinical T4d Category
1634487	AJCC/UICC 8th pathological Stage 4B
1634491	AJCC/UICC 7th pathological T2 Category
1634492	AJCC/UICC 7th pathological Stage 4C
1634501	AJCC/UICC 6th clinical T1c Category

Concept ID	TNM staging names
1634502	AJCC/UICC clinical Stage 0
1634503	AJCC/UICC pathological T2c Category
1634510	AJCC/UICC 8th pathological Stage 1A2
1634514	AJCC/UICC clinical T2c Category
1634522	AJCC/UICC 7th clinical T4a Category
1634523	AJCC/UICC clinical N2 Category
1634525	AJCC/UICC clinical Stage 4B
1634541	AJCC/UICC 6th pathological N2 Category
1634547	AJCC/UICC 6th clinical T1b2 Category
1634551	AJCC/UICC 8th pathological Stage 4C
1634562	AJCC/UICC 6th pathological N1 Category
1634571	AJCC/UICC clinical Stage 3C
1634578	AJCC/UICC 6th pathological T1b Category
1634581	AJCC/UICC pathological Tis Category
1634587	AJCC/UICC 6th clinical T1b1 Category
1634591	AJCC/UICC pathological N1b4 Category
1634596	AJCC/UICC 8th clinical Stage 3
1634597	AJCC/UICC pathological T2a Category
1634601	AJCC/UICC 7th pathological N2c Category
1634605	AJCC/UICC 8th pathological Stage 0is
1634606	AJCC/UICC 8th pathological M0 Category
1634612	AJCC/UICC 8th pathological Stage 3B
1634614	AJCC/UICC 7th clinical Stage 4C
1634615	AJCC/UICC 6th pathological Stage 2A
1634618	AJCC/UICC pathological M0 Category
1634619	AJCC/UICC 7th pathological Stage 2
1634624	AJCC/UICC 6th clinical T4b Category
1634635	AJCC/UICC 8th pathological T0 Category
1634637	AJCC/UICC 6th pathological M1a Category
1634645	AJCC/UICC 8th pathological N2b Category
1634649	AJCC/UICC clinical N3a Category
1634651	AJCC/UICC 8th clinical T2 Category
1634654	AJCC/UICC T4 Category
1634657	AJCC/UICC 8th pathological M1c Category
1634658	AJCC/UICC 7th pathological T3 Category
1634659	AJCC/UICC clinical T1b2 Category
1634660	AJCC/UICC post therapy pathological T2 Category
1634662	AJCC/UICC 7th clinical T1b Category

Concept ID	TNM staging names
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1634677	AJCC/UICC 6th pathological Stage 2B
1634678	AJCC/UICC 6th clinical N2c Category
1634683	AJCC/UICC 8th pathological T1a1 Category
1634686	AJCC/UICC 6th pathological Stage 0is
1634688	AJCC/UICC pathological Stage 4
1634689	AJCC/UICC clinical T2a Category
1634705	AJCC/UICC 8th pathological Stage 3
1634709	AJCC/UICC 8th pathological T2c Category
1634711	AJCC/UICC 8th pathological T1b2 Category
1634712	AJCC/UICC 8th pathological M1b Category
1634714	AJCC/UICC 7th pathological T3a Category
1634718	AJCC/UICC 6th clinical Stage 2
1634722	AJCC/UICC clinical NX Category
1634723	AJCC/UICC 7th pathological N3c Category
1634727	AJCC/UICC 7th clinical N2c Category
1634728	AJCC/UICC 7th clinical T1a Category
1634731	AJCC/UICC 6th pathological Stage 4A
1634734	AJCC/UICC pathological N1b1 Category
1634736	AJCC/UICC 7th pathological T1a2 Category
1634741	AJCC/UICC 6th pathological Stage 0
1634749	AJCC/UICC 8th clinical T1c2 Category
1634755	AJCC/UICC clinical MX Category
1634757	AJCC/UICC 8th clinical M0 Category
1634765	AJCC/UICC 7th pathological T2a1 Category
1634766	AJCC/UICC 7th clinical Stage 4
1634770	AJCC/UICC 8th pathological N3b Category
1634773	AJCC/UICC 6th pathological N2b Category
1634781	AJCC/UICC 8th pathological T2b Category
1634786	AJCC/UICC 8th pathological T2a1 Category
1634787	AJCC/UICC 8th pathological Stage 0
1634788	AJCC/UICC post therapy pathological N1 Category
1634789	AJCC/UICC pathological Stage 3B
1634791	AJCC/UICC 7th pathological Ta Category
1634792	AJCC/UICC 6th pathological T2 Category
1634793	AJCC/UICC post therapy pathological T1a Category
1634797	AJCC/UICC 8th clinical NX Category

Concept ID	TNM staging names
1634799	AJCC/UICC 8th pathological Stage 1
1634801	AJCC/UICC 6th clinical Stage 2A
1634810	AJCC/UICC 8th clinical Stage 4A
1634811	AJCC/UICC 8th clinical Stage 3C
1634828	AJCC/UICC 6th clinical T1a1 Category
1634829	AJCC/UICC 6th clinical M1 Category
1634840	AJCC/UICC 8th clinical T2a1 Category
1634842	AJCC/UICC 7th pathological Stage 3A
1634846	AJCC/UICC 8th pathological T1c3 Category
1634847	AJCC/UICC 7th pathological N3b Category
1634854	AJCC/UICC 8th clinical T4b Category
1634860	AJCC/UICC 7th clinical Stage 1A
1634867	AJCC/UICC pathological T1a1 Category
1634876	AJCC/UICC clinical Stage 3
1634877	AJCC/UICC clinical T4c Category
1634882	AJCC/UICC 7th pathological N1c Category
1634890	AJCC/UICC 8th pathological Stage 2A
1634891	AJCC/UICC 8th pathological M1 Category
1634894	AJCC/UICC 8th pathological T4a Category
1634903	AJCC/UICC Stage 2C
1634922	AJCC/UICC clinical Stage 3A
1634932	AJCC/UICC 8th clinical Stage 2C
1634933	AJCC/UICC 8th pathological T1c2 Category
1634936	AJCC/UICC 7th clinical T2c Category
1634938	AJCC/UICC 8th pathological T2a2 Category
1634941	AJCC/UICC 7th pathological T4d Category
1634945	AJCC/UICC 8th clinical T1a2 Category
1634947	AJCC/UICC 7th pathological Stage 3
1634955	AJCC/UICC pathological Stage 0is
1634957	AJCC/UICC pathological T4b Category
1634958	AJCC/UICC 7th clinical Stage 1B
1634960	AJCC/UICC pathological Stage 2A
1634961	AJCC/UICC 6th pathological T1b1 Category
1634963	AJCC/UICC 8th clinical T4a Category
1634973	AJCC/UICC 8th clinical T4 Category
1634977	AJCC/UICC clinical N2b Category
1634991	AJCC/UICC 8th clinical Stage 0is
1634993	AJCC/UICC 7th clinical T2a2 Category

Concept ID	TNM staging names
1634996	AJCC/UICC 6th clinical Stage 3A
1635003	AJCC/UICC pathological T4d Category
1635004	AJCC/UICC 7th clinical N3a Category
1635006	AJCC/UICC 8th clinical Stage 4C
1635008	AJCC/UICC 7th pathological M1b Category
1635010	AJCC/UICC 7th pathological T1c Category
1635017	AJCC/UICC pathological T1c Category
1635022	AJCC/UICC 8th clinical T4d Category
1635026	AJCC/UICC 7th clinical T2a1 Category
1635027	AJCC/UICC pathological T3c Category
1635029	AJCC/UICC 8th clinical Stage 4
1635033	AJCC/UICC clinical T2 Category
1635035	AJCC/UICC post therapy pathological T3a Category
1635037	AJCC/UICC 8th pathological T3b Category
1635038	AJCC/UICC 7th pathological T2b Category
1635039	AJCC/UICC clinical T1b Category
1635056	AJCC/UICC clinical Stage 2C
1635059	AJCC/UICC 6th pathological T1a Category
1635061	AJCC/UICC post therapy pathological N2 Category
1635064	AJCC/UICC 6th pathological N1c Category
1635067	AJCC/UICC 6th clinical M1c Category
1635070	AJCC/UICC 8th pathological T1 Category
1635081	AJCC/UICC clinical T1a2 Category
1635082	AJCC/UICC post therapy pathological T4 Category
1635084	AJCC/UICC 7th clinical N3b Category
1635085	AJCC/UICC clinical M1 Category
1635090	AJCC/UICC clinical M1b Category
1635094	AJCC/UICC post therapy pathological N3 Category
1635097	AJCC/UICC 8th pathological M1a Category
1635104	AJCC/UICC 6th clinical NX Category
1635113	AJCC/UICC 6th pathological N2c Category
1635116	AJCC/UICC 8th clinical T3a Category
1635120	AJCC/UICC pathological T1b2 Category
1635125	AJCC/UICC 7th clinical Stage 3
1635133	AJCC/UICC 8th clinical N3c Category
1635142	AJCC/UICC M1 Category
1635145	AJCC/UICC 7th clinical T3c Category
1635149	AJCC/UICC 8th clinical M1a Category

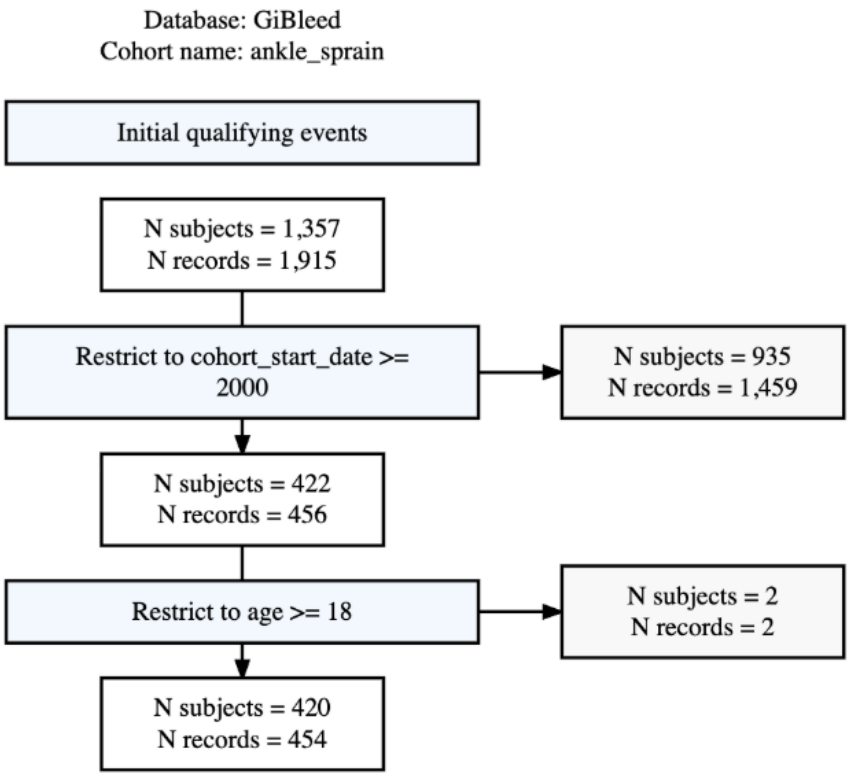
Concept ID	TNM staging names
1635155	AJCC/UICC clinical T0 Category
1635160	AJCC/UICC 6th pathological M1b Category
1635164	AJCC/UICC clinical N1a Category
1635168	AJCC/UICC pathological T1b1 Category
1635171	AJCC/UICC 8th pathological T3a Category
1635182	AJCC/UICC 7th clinical Stage 2
1635196	AJCC/UICC 6th pathological N1a Category
1635199	AJCC/UICC clinical Stage 1
1635214	AJCC/UICC 6th clinical Stage 3C
1635217	AJCC/UICC 8th clinical Stage 2
1635227	AJCC/UICC 7th clinical Tis Category
1635229	AJCC/UICC 8th clinical T1a Category
1635230	AJCC/UICC 7th pathological Stage 4
1635232	AJCC/UICC pathological Stage 4A
1635241	AJCC/UICC 7th pathological T4c Category
1635254	AJCC/UICC 7th pathological T2c Category
1635255	AJCC/UICC clinical M1c Category
1635262	AJCC/UICC 6th pathological Tis Category
1635265	AJCC/UICC 8th clinical Stage 3A
1635283	AJCC/UICC 6th clinical N3b Category
1635287	AJCC/UICC 8th clinical T2c Category
1635291	AJCC/UICC clinical M0 Category
1635302	AJCC/UICC 7th clinical M1b Category
1635307	AJCC/UICC 8th pathological N3 Category
1635311	AJCC/UICC 6th pathological T4 Category
1635318	AJCC/UICC 6th pathological T3a Category
1635322	AJCC/UICC 8th clinical T1c3 Category
1635331	AJCC/UICC post therapy pathological T3c Category
1635333	AJCC/UICC 7th pathological T3b Category
1635336	AJCC/UICC 7th pathological M1 Category
1635341	AJCC/UICC 7th pathological T4 Category
1635342	AJCC/UICC 7th pathological T2d Category
1635345	AJCC/UICC 6th pathological M0 Category
1635349	AJCC/UICC 6th clinical Ta Category
1635354	AJCC/UICC 6th pathological N3c Category
1635368	AJCC/UICC clinical T4d Category
1635370	AJCC/UICC 6th pathological Stage 4B
1635372	AJCC/UICC pathological Stage 3C

Concept ID	TNM staging names
1635375	AJCC/UICC 7th clinical T3a Category
1635381	AJCC/UICC 7th pathological Stage 2A
1635386	AJCC/UICC 8th pathological Stage 2
1635392	AJCC/UICC 6th clinical N1a Category
1635396	AJCC/UICC 8th pathological T4 Category
1635404	AJCC/UICC clinical Stage 4C
1635422	AJCC/UICC 7th pathological T1 Category
1635434	AJCC/UICC clinical Stage 0a
1635439	AJCC/UICC 7th pathological Stage 0is
1635440	AJCC/UICC 6th pathological Stage 3C
1635442	AJCC/UICC 7th pathological T2a2 Category
1635446	AJCC/UICC pathological T4c Category
1635450	AJCC/UICC clinical Stage 4A
1635451	AJCC/UICC 8th clinical T2b Category
1635461	AJCC/UICC 7th clinical M1c Category
1635468	AJCC/UICC 8th clinical Ta Category
1635470	AJCC/UICC 6th clinical N2 Category
1635480	AJCC/UICC 7th clinical N1b Category
1635486	AJCC/UICC clinical Stage 2A
1635487	AJCC/UICC 8th pathological T1c1 Category
1635490	AJCC/UICC 7th pathological T3d Category
1635496	AJCC/UICC 8th clinical N3a Category
1635497	AJCC/UICC 8th pathological Tis(DCIS) Category
1635505	AJCC/UICC pathological M1 Category
1635509	AJCC/UICC 6th clinical T2b Category
1635511	AJCC/UICC 7th pathological Stage 0
1635512	AJCC/UICC 8th clinical T1b3 Category
1635522	AJCC/UICC 6th clinical T4 Category
1635530	AJCC/UICC 7th clinical T4 Category
1635535	AJCC/UICC 6th clinical Stage 4A
1635536	AJCC/UICC 7th pathological M0 Category
1635545	AJCC/UICC 8th pathological N3a Category
1635556	AJCC/UICC 8th clinical T3 Category
1635558	AJCC/UICC clinical T4 Category
1635560	AJCC/UICC 8th pathological N0 Category
1635566	AJCC/UICC pathological Stage 3
1635567	AJCC/UICC pathological Stage 4C
1635568	AJCC/UICC 8th clinical T1b1 Category

Concept ID	TNM staging names
1635575	AJCC/UICC pathological T2b Category
1635592	AJCC/UICC 8th pathological T4c Category
1635597	AJCC/UICC pathological N0 Category
1635599	AJCC/UICC clinical N1b Category
1635602	AJCC/UICC 7th pathological Stage 3B
1635605	AJCC/UICC 6th clinical N3 Category
1635613	AJCC/UICC pathological N1 Category
1635615	AJCC/UICC 6th pathological T4d Category
1635623	AJCC/UICC post therapy pathological T4b Category
1635624	AJCC/UICC M0 Category
1635634	AJCC/UICC 7th clinical N2 Category
1635635	AJCC/UICC 8th clinical T2a Category
1635643	AJCC/UICC 6th clinical T4c Category
1635647	AJCC/UICC 8th clinical T1c Category
1635651	AJCC/UICC 8th pathological T3d Category
1635653	AJCC/UICC 7th pathological Stage 1B
1635656	AJCC/UICC 6th clinical T0 Category
1635661	AJCC/UICC clinical T1 Category
1635664	AJCC/UICC 7th clinical T1 Category
1635670	AJCC/UICC 6th pathological T3 Category
1635676	AJCC/UICC clinical T1a1 Category
1635677	AJCC/UICC 7th clinical N2b Category
1635679	AJCC/UICC 8th clinical N1b Category
1635697	AJCC/UICC 6th clinical N1 Category
1635700	AJCC/UICC 7th clinical T2a Category
1635701	AJCC/UICC clinical T1b1 Category
1635706	AJCC/UICC pathological N3 Category
1635708	AJCC/UICC 8th clinical Stage 4B
1635717	AJCC/UICC 7th pathological N2a Category
1635723	AJCC/UICC 6th pathological Ta Category
1635728	AJCC/UICC 6th clinical Stage 3B
1635729	AJCC/UICC clinical N1 Category
1635739	AJCC/UICC 7th clinical N2a Category
1635740	AJCC/UICC pathological T0 Category
1635745	AJCC/UICC 7th pathological Stage 4A
1635749	AJCC/UICC 8th pathological Stage 0a
1635754	AJCC/UICC 7th pathological Stage 0a
1635757	AJCC/UICC 7th clinical Stage 4B

Concept ID	TNM staging names
1635758	AJCC/UICC 8th clinical Stage 1
1635761	AJCC/UICC 7th clinical Stage 3C
1635764	AJCC/UICC clinical Stage 3B
1635768	AJCC/UICC 7th clinical T4d Category
1635781	AJCC/UICC post therapy pathological T1 Category
1635786	AJCC/UICC 8th clinical Stage 2A
1635794	AJCC/UICC 8th clinical T0 Category
1635797	AJCC/UICC 6th pathological Stage 1
1635800	AJCC/UICC 7th pathological Stage 1
1635802	AJCC/UICC 8th clinical Stage 1A3
1635810	AJCC/UICC 8th pathological T1c Category
1635813	AJCC/UICC 8th clinical T3b Category
1635823	AJCC/UICC 6th pathological NX Category
1635824	AJCC/UICC 8th clinical Stage 0
1635828	AJCC/UICC 8th clinical N3b Category
1635837	AJCC/UICC 6th clinical T3b Category
1635842	AJCC/UICC 6th clinical Stage 0
1635848	AJCC/UICC 6th clinical Stage 3
1635857	AJCC/UICC 6th clinical Tis Category
1635860	AJCC/UICC 8th pathological N1a Category
1635861	AJCC/UICC 7th clinical T1c Category
1635862	AJCC/UICC 6th pathological Stage 3A
1635865	AJCC/UICC pathological Stage 0a
1635871	AJCC/UICC 8th pathological N2a Category
1635876	AJCC/UICC 6th pathological T2b Category
1635878	AJCC/UICC 7th clinical M1a Category
1635881	AJCC/UICC pathological T1a2 Category
1635884	AJCC/UICC 6th pathological Stage 1A
1635888	AJCC/UICC pathological Ta Category
1635893	AJCC/UICC 6th pathological Stage 4C
1635895	AJCC/UICC clinical T3 Category
1635896	AJCC/UICC 7th clinical Stage 2B

ANNEX V. Mock Tables



Mock Figure 1. Flowchart depicting study population attrition.

Example figure obtained from: Catala M, Guo Y, Lopez-Guell K, Burn E, Mercade-Besora N, Alcalde M (2025). CohortCharacteristics: Summarise and Visualise Characteristics of Patients in the OMOP CDM. R package version 1.0.1, https://darwin-eu.github.io/CohortCharacteristics/.

Mock Table 1. Description of demographic and pre-specified characteristics of patients newly diagnosed with ovarian cancer.

Characteristics		DK-DHR	CDW Bordeaux	NCR	CRN
Number of individuals, N (%)					
Age group (years)	18–44				
	45–64				
	>65				
Prior observation time (in days), median (IQR)					
Future observation time (in days), median (IQR)					
BRCA status[1]					
ECOG[2]					
Stage[3]	1				
	2				
	3				
	4				
Pre-specified comorbidities[4]					
Hyperglycaemia					
Diabetes mellitus					
Endometriosis					
Obesity					
Pelvic inflammatory disease					
History of breast cancer					
Family history of breast cancer					

[1] Assessed any time prior to index date. Not assessed in NCR and CRN.
[2] Cancer stage not available in CDW Bordeaux
[3] BRCA status available in NCR only
[4] ECOG status not available in DK-DHR and CDW Bordeaux

Mock Table 2. Number and percentage of patients treated with systemic treatments by treatment class.

Treatment class	DK-DHR	CDW Bordeaux	NCR	CRN
Alkylating agents				
Anthracyclines				
Antimetabolites				
DNA agents				
Platinum-based chemotherapy				
Taxanes				
Topoisomerase inhibitors				
Vinca Alkaloid				
PARP inhibitors				
Monoclonal antibodies				
Hormonal agents				
Alkylating agents				

Mock Table 3. Number and percentage of patients treated with systemic treatments by treatment class, stratified by age group.

Treatment class	Age group	DK-DHR	CDW Bordeaux	NCR	CRN
Alkylating agents	18–44				
	45–64				
	>65 years				
Anthracyclines	18–44				
	45–64				
	>65 years				
Antimetabolites	18–44				
	45–64				
	>65 years				
DNA agents	18–44				
	45–64				
	>65 years				
Platinum-based chemotherapy	18–44				
	45–64				
	>65 years				
Taxanes	18–44				
	45–64				
	>65 years				
Topoisomerase inhibitors	18–44				
	45–64				
	>65 years				
Vinca Alkaloid	18–44				
	45–64				
	>65 years				
PARP inhibitors	18–44				
	45–64				
	>65 years				
Monoclonal antibodies	18–44				
	45–64				
	>65 years				
Hormonal agents	18–44				
	45–64				
	>65 years				
Alkylating agents	18–44				
	45–64				
	>65 years				

Mock Table 4. Number and percentage of patients treated with systemic treatments by treatment class, stratified by cancer stage.

Treatment Class	Ingredient	DK-DHR				NCR				CRN			
		Stage 1	Stage 2	Stage 3	Stage 4	Stage 1	Stage 2	Stage 3	Stage 4	Stage 1	Stage 2	Stage 3	Stage 4
Alkylating agents	Altretamine												
	Chlorambucil												
	Cyclophosphamide												
	Ifosfamide												
	Lomustine												
	Melphalan												
	Thiotepa												
	Treosulfan												
Anthracyclines	Doxorubicin												
	Epirubicin												
	Mitoxantrone												
Antimetabolites	Fluorouracil												
	Gemcitabine												
	Methotrexate												
DNA agents	Trabectedin												
Platinum-based chemotherapy	Carboplatin												
	Cisplatin												

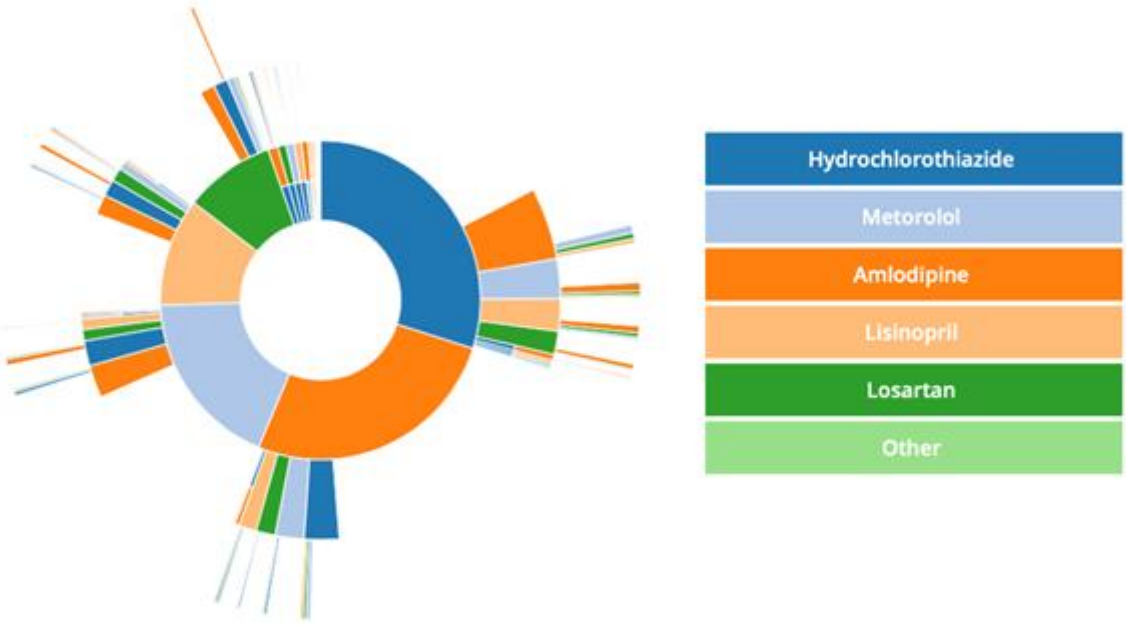
Treatment Class	Ingredient	DK-DHR				NCR				CRN			
		Stage 1	Stage 2	Stage 3	Stage 4	Stage 1	Stage 2	Stage 3	Stage 4	Stage 1	Stage 2	Stage 3	Stage 4
Taxanes	Docetaxel												
	Paclitaxel												
Topoisomerase inhibitors	Etoposide												
	Topotecan												
Vinca Alkaloid	Vinblastine												
PARP inhibitors	Niraparib												
	Olaparib												
	Rucaparib												
Monoclonal antibodies	Bevacizumab												
	mirvetuximab soravtansine												
Hormonal agents	Dexamethasone												
	Medroxyprogesterone												

Mock Table 5. Number and percentage of patients treated with systemic treatments by treatment class, stratified by study period.

Treatment class	Study period	DK-DHR	CDW Bordeaux	NCR	CRN
Alkylating agents	2010-2014				
	2015-2019				
	2020-2024				
Anthracyclines	2010-2014				
	2015-2019				
	2020-2024				
Antimetabolites	2010-2014				
	2015-2019				
	2020-2024				
DNA agents	2010-2014				
	2015-2019				
	2020-2024				
Platinum-based chemotherapy	2010-2014				
	2015-2019				
	2020-2024				
Taxanes	2010-2014				
	2015-2019				
	2020-2024				
Topoisomerase inhibitors	2010-2014				
	2015-2019				
	2020-2024				
Vinca Alkaloid	2010-2014				
	2015-2019				
	2020-2024				
PARP inhibitors	2010-2014				
	2015-2019				
	2020-2024				
Monoclonal antibodies	2010-2014				
	2015-2019				
	2020-2024				
Hormonal agents	2010-2014				
	2015-2019				
	2020-2024				
Alkylating agents	2010-2014				
	2015-2019				
	2020-2024				

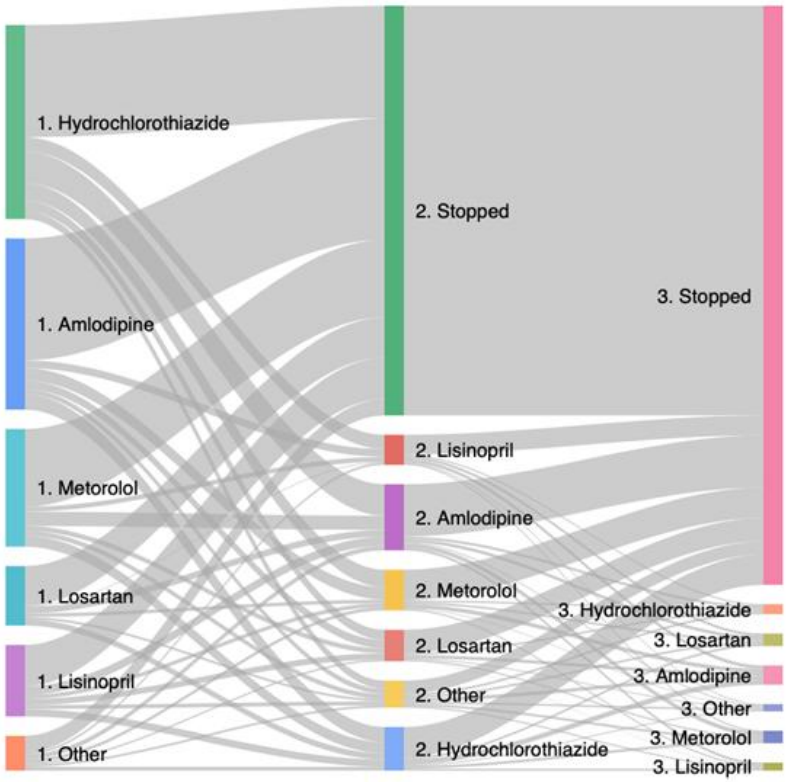
Mock Table 6. Number and percentage of patients treated with the top 10 systemic ingredients.

DK-DHR	CDW Bordeaux	NCR	CRN
Top 1 ingredient in DK-DHR	Top 1 ingredient in CDW Bordeaux	Top 1 ingredient in NCR	Top 1 ingredient in CRN
Top 2 ingredient in DK-DHR	Top 2 ingredient in CDW Bordeaux	Top 2 ingredient in NCR	Top 2 ingredient in CRN
Top 3 ingredient in DK-DHR	Top 3 ingredient in CDW Bordeaux	Top 3 ingredient in NCR	Top 3 ingredient in CRN



Mock Figure 2. Sunburst plot depicting treatment patterns.

Example figure obtained from: Markus, Aniek & Verhamme, Katia & Kors, Jan & Rijnbeek, Peter. (2022). TreatmentPatterns: An R package to analyse treatment patterns of a study population of interest. 10.1101/2022.01.24.22269588.



Mock Figure 3. Sankey diagram depicting treatment sequences.

Example figure obtained from: Markus, Aniek & Verhamme, Katia & Kors, Jan & Rijnbeek, Peter. (2022). TreatmentPatterns: An R package to analyse treatment patterns of a study population of interest. 10.1101/2022.01.24.22269588.

ANNEX VI. ENCePP checklist for study protocols

ENCePP Checklist for Study Protocols (Revision 4)

Study title: DARWIN EU® - Characterisation of systemic treatments for the management of ovarian cancer

EU PAS Register® number: EUPAS1000000815
Study reference number: P4-C1-012

Section 1: Milestones	**Yes**	**No**	**N/A**	**Section Number**
1.1 Does the protocol specify timelines for				
1.1.1 Start of data collection[1]	☐	☐	☒	
1.1.2 End of data collection[2]	☐	☐	☒	
1.1.3 Progress report(s)	☒	☐	☐	5
1.1.4 Interim report(s)	☐	☐	☒	
1.1.5 Registration in the EU PAS Register®	☐	☒	☐	
1.1.6 Final report of study results.	☒	☐	☐	5

Comments:

Registration in the EU PAS Register® : Study not registered yet

Section 2: Research question	**Yes**	**No**	**N/A**	**Section Number**
2.1 Does the formulation of the research question and objectives clearly explain:	☒	☐	☐	3
2.1.1 Why the study is conducted? (e.g. to address an important public health concern, a risk identified in the risk management plan, an emerging safety issue)	☒	☐	☐	4
2.1.2 The objective(s) of the study?	☒	☐	☐	5
2.1.3 The target population? (i.e. population or subgroup to whom the study results are intended to be generalised)	☒	☐	☐	8.3
2.1.4 Which hypothesis(-es) is (are) to be tested?	☐	☐	☒	
2.1.5 If applicable, that there is no *a priori* hypothesis?	☐	☐	☒	

Comments:

[1] Date from which information on the first study is first recorded in the study dataset or, in the case of secondary use of data, the date from which data extraction starts.
[2] Date from which the analytical dataset is completely available.

Section 3: Study design		**Yes**	**No**	**N/A**	**Section Number**
3.1	Is the study design described? (e.g. cohort, case-control, cross-sectional, other design)	☒	☐	☐	8.1
3.2	Does the protocol specify whether the study is based on primary, secondary or combined data collection?	☐	☐	☒	
3.3	Does the protocol specify measures of occurrence? (e.g., rate, risk, prevalence)	☐	☐	☒	
3.4	Does the protocol specify measure(s) of association? (e.g. risk, odds ratio, excess risk, rate ratio, hazard ratio, risk/rate difference, number needed to harm (NNH))	☐	☐	☒	
3.5	Does the protocol describe the approach for the collection and reporting of adverse events/adverse reactions? (e.g. adverse events that will not be collected in case of primary data collection)	☐	☐	☒	

Comments:

Section 4: Source and study populations		**Yes**	**No**	**N/A**	**Section Number**
4.1	Is the source population described?	☒	☐	☐	8.4
4.2	Is the planned study population defined in terms of:				
	4.2.1 Study time period	☒	☐	☐	8.2
	4.2.2 Age and sex	☒	☐	☐	8.6.3
	4.2.3 Country of origin	☒	☐	☐	8.4
	4.2.4 Disease/indication	☒	☐	☐	8.3
	4.2.5 Duration of follow-up	☒	☐	☐	8.2
4.3	Does the protocol define how the study population will be sampled from the source population? (e.g. event or inclusion/exclusion criteria)	☒	☐	☐	8.3

Comments:

Section 5: Exposure definition and measurement		**Yes**	**No**	**N/A**	**Section Number**
5.1	Does the protocol describe how the study exposure is defined and measured? (e.g. operational details for defining and categorising exposure, measurement of dose and duration of drug exposure)	☒	☐	☐	8.6.1
5.2	Does the protocol address the validity of the exposure measurement? (e.g. precision, accuracy, use of validation sub-study)	☒	☐	☐	8.6.1/8.8.3
5.3	Is exposure categorised according to time windows?	☒	☐	☐	8.6.1

Section 5: Exposure definition and measurement	**Yes**	**No**	**N/A**	**Section Number**
5.4 Is intensity of exposure addressed? (e.g. dose, duration)	☒	☐	☐	8.6.1/8.8.3
5.5 Is exposure categorised based on biological mechanism of action and taking into account the pharmacokinetics and pharmacodynamics of the drug?	☐	☐	☒	
5.6 Is (are) (an) appropriate comparator(s) identified?	☐	☐	☒	

Comments:

Section 6: Outcome definition and measurement	**Yes**	**No**	**N/A**	**Section Number**
6.1 Does the protocol specify the primary and secondary (if applicable) outcome(s) to be investigated?	☐	☐	☒	
6.2 Does the protocol describe how the outcomes are defined and measured?	☐	☐	☒	
6.3 Does the protocol address the validity of outcome measurement? (e.g. precision, accuracy, sensitivity, specificity, positive predictive value, use of validation sub-study)	☐	☐	☒	
6.4 Does the protocol describe specific outcomes relevant for Health Technology Assessment? (e.g. HRQoL, QALYs, DALYS, health care services utilisation, burden of disease or treatment, compliance, disease management)	☐	☐	☒	

Comments:

Section 7: Bias	**Yes**	**No**	**N/A**	**Section Number**
7.1 Does the protocol address ways to measure confounding? (e.g. confounding by indication)	☒	☐	☐	8.8
7.2 Does the protocol address selection bias? (e.g. healthy user/adherer bias)	☒	☐	☐	9
7.3 Does the protocol address information bias? (e.g. misclassification of exposure and outcomes, time-related bias)	☒	☐	☐	9

Comments:

Section 8: Effect measure modification	Yes	No	N/A	Section Number
8.1 Does the protocol address effect modifiers? (e.g. collection of data on known effect modifiers, sub-group analyses, anticipated direction of effect)	☒	☐	☐	8.6.3

Comments:

Section 9: Data sources	Yes	No	N/A	Section Number
9.1 Does the protocol describe the data source(s) used in the study for the ascertainment of:				
9.1.1 Exposure? (e.g. pharmacy dispensing, general practice prescribing, claims data, self-report, face-to-face interview)	☒	☐	☐	8.6.1
9.1.2 Outcomes? (e.g. clinical records, laboratory markers or values, claims data, self-report, patient interview including scales and questionnaires, vital statistics)	☐	☐	☒	
9.1.3 Covariates and other characteristics?	☒	☐	☐	8.6.3
9.2 Does the protocol describe the information available from the data source(s) on:				
9.2.1 Exposure? (e.g. date of dispensing, drug quantity, dose, number of days of supply prescription, daily dosage, prescriber)	☒	☐	☐	8.8.3
9.2.2 Outcomes? (e.g. date of occurrence, multiple event, severity measures related to event)	☐	☐	☒	
9.2.3 Covariates and other characteristics? (e.g. age, sex, clinical and drug use history, co-morbidity, co-medications, lifestyle)	☒	☐	☐	8.8.3
9.3 Is a coding system described for:				
9.3.1 Exposure? (e.g. WHO Drug Dictionary, Anatomical Therapeutic Chemical (ATC) Classification System)	☒	☐	☐	ANNEX IV
9.3.2 Outcomes? (e.g. International Classification of Diseases (ICD), Medical Dictionary for Regulatory Activities (MedDRA))	☐	☐	☒	
9.3.3 Covariates and other characteristics?	☒	☐	☐	ANNEX IV
9.4 Is a linkage method between data sources described? (e.g. based on a unique identifier or other)	☐	☐	☒	

Comments:

Section 10: Analysis plan	Yes	No	N/A	Section Number
10.1 Are the statistical methods and the reason for their choice described?	☒	☐	☐	8.8
10.2 Is study size and/or statistical precision estimated?	☒	☐	☐	8.7
10.3 Are descriptive analyses included?	☒	☐	☐	8.8

Section 10: Analysis plan	**Yes**	**No**	**N/A**	**Section Number**
10.4 Are stratified analyses included?	☒	☐	☐	8.8
10.5 Does the plan describe methods for analytic control of confounding?	☒	☐	☐	8.8
10.6 Does the plan describe methods for analytic control of outcome misclassification?	☐	☐	☒	
10.7 Does the plan describe methods for handling missing data?	☒	☐	☐	8.8.3
10.8 Are relevant sensitivity analyses described?	☒	☐	☐	8.8.3

Comments:

Section 11: Data management and quality control	**Yes**	**No**	**N/A**	**Section Number**
11.1 Does the protocol provide information on data storage? (e.g. software and IT environment, data source maintenance and anti-fraud protection, archiving)	☒	☐	☐	Annex III
11.2 Are methods of quality assurance described?	☒	☐	☐	Annex III
11.3 Is there a system in place for independent review of study results?	☐	☒	☐	

Comments:

Section 12: Limitations	**Yes**	**No**	**N/A**	**Section Number**
12.1 Does the protocol discuss the impact on the study results of:				
12.1.1 Selection bias?	☒	☐	☐	9
12.1.2 Information bias?	☒	☐	☐	9
12.1.3 Residual/unmeasured confounding? (e.g. anticipated direction and magnitude of such biases, validation sub-study, use of validation and external data, analytical methods).	☐	☐	☐	9
12.2 Does the protocol discuss study feasibility? (e.g. study size, anticipated exposure uptake, duration of follow-up in a cohort study, patient recruitment, precision of the estimates)	☒	☐	☐	8.7

Comments:

Section 13: Ethical/data protection issues	**Yes**	**No**	**N/A**	**Section Number**
13.1 Have requirements of Ethics Committee/ Institutional Review Board been described?	☐	☐	☒	

Section 13: Ethical/data protection issues	**Yes**	**No**	**N/A**	**Section Number**
13.2 Has any outcome of an ethical review procedure been addressed?	☐	☐	☒	
13.3 Have data protection requirements been described?	☒	☐	☐	Annex III

Comments:

Section 14: Amendments and deviations	**Yes**	**No**	**N/A**	**Section Number**
14.1 Does the protocol include a section to document amendments and deviations?	☐	☐	☒	

Comments:

Section 15: Plans for communication of study results	**Yes**	**No**	**N/A**	**Section Number**
15.1 Are plans described for communicating study results (e.g. to regulatory authorities)?	☒	☐	☐	Annex III
15.2 Are plans described for disseminating study results externally, including publication?	☒	☐	☐	Annex III

Comments:

Name of the main author of the protocol: Anum Zahra

Date: 18/11/2025

Signature: Anum Zahra

ANNEX VII. Glossary

Additional definitions are available in the EMA Glossary of terms https://www.ema.europa.eu/en/about-us/glossaries.

Aggregated Data

Data collected and combined from multiple sources to generate summary information, typically anonymised.

Benefit-Risk Assessment

Evaluation of the positive therapeutic effects of a medicine compared to its risks (e.g., side effects).

Common Data Model (CDM)

A standardized data structure that enables data from multiple sources to be harmonized, making analysis consistent and reproducible. DARWIN EU® utilises the OMOP CDM maintained by the OHDSI community.

Complex Studies (C3)

Studies requiring the development or customisation of specific study designs, protocols, and Statistical Analysis Plans (SAPs), with extensive collection or extraction of data. Examples include etiological studies measuring the strength and determinants of an association between an exposure and the occurrence of a health outcome in a defined population considering sources of bias, potential confounding factors, and effect modifiers.

Coordination Centre (CC)

The central hub responsible for managing and overseeing the activities within DARWIN EU®. It is based at Erasmus University Medical Centre in Rotterdam, the Netherlands.

Data Access

The process of obtaining permission to use specific datasets for regulatory or scientific studies.

Data Quality Framework

A set of standards and procedures to ensure accuracy, completeness, timeliness, and consistency of data used in DARWIN EU®.

Data Source

A data source or repository of structured health-related data, such as electronic health records (EHRs), insurance claims, or registries.

DARWIN EU®

The European Medicines Agency's (EMA) federated network of real-world data sources designed to generate evidence to support regulatory decision-making.

EMA (European Medicines Agency)

The regulatory body responsible for the evaluation and supervision of medicinal products in the EU, overseeing DARWIN EU®.

Evidence Generation

The process of analysing real-world data to produce scientific information that can inform healthcare or regulatory decisions.

Federated Network

A data infrastructure where data remain at their original location but can be analysed in a harmonised way across multiple partners using a common model and tools.

GDPR (General Data Protection Regulation)

The EU regulation governing the protection of personal data and privacy, crucial to how DARWIN EU® handles health data.

Health Technology Assessment (HTA)

A systematic evaluation of properties and impacts of health technology, often using DARWIN EU® data to support assessments.

Metadata

Descriptive information about a data source (e.g., its content, quality, and structure), essential for identifying relevant data sources in DARWIN EU® studies.

Off-the-Shelf Studies (OTS)

Studies for which a standard protocol per study/analysis type and standardised analytics may be developed and applied or adapted, typically relating to a descriptive research question. This includes studies on disease epidemiology, for example, the estimation of the prevalence or incidence of health outcomes in defined time periods and population groups, or drug utilisation studies at the population or patient level.

OHDSI (Observational Health Data Sciences and Informatics)

An open-science collaborative community that develops tools and standards (including the OMOP CDM) to enable large-scale analytics of observational health data. OHDSI provides the technical and scientific foundation for DARWIN EU®'s analytical ecosystem.

Patient-Level Data

Data related to individuals, de-identified, used for longitudinal or detailed analyses.

OMOP (Observational Medical Outcomes Partnership)

A common data model (CDM) that standardises the structure and content of observational healthcare data, enabling systematic analysis across disparate datasets. DARWIN EU® uses the OMOP CDM to ensure interoperability and consistency in real-world evidence generation.

Real-World Data (RWD)

Data relating to individual health status or healthcare delivery that is collected from routine clinical practice rather than from randomised controlled trials.

Real-World Evidence (RWE)

Clinical evidence derived from the analysis of RWD, used to inform decisions by regulators, payers, or clinicians.

Regulatory Decision-Making

The process by which authorities like EMA assess data to authorise, monitor, or modify the use of medicines in the EU.

Routine Repeated Studies (RR)

Studies that are either Off-the-Shelf or Complex studies repeated on a regular basis, following the same protocol and study code, but with updated data and/or different data partners.

Study Protocol

A detailed plan describing how a specific real-world study will be conducted, including objectives, design, data sources, and analyses.

Very Complex Studies (C4)

Studies which cannot rely only on electronic health care data sources, or which would require complex methodological work, for example, due to the occurrence of events that cannot be defined by existing diagnosis codes, including events that do not yet have a diagnosis code, where it may be necessary to combine a diagnosis code with other data such as results of laboratory investigations. These studies might require the collection of data prospectively, or the inclusion of new (not previously onboarded) data sources.