Relative Risk of Cervical Neoplasms Associated with Copper and Levonorgestrel Secreting Intrauterine Devices: Real World Evidence from the OHDSI Network

**Version:** 1.0

Authors

|  |  |  |
| --- | --- | --- |
| Name | Email address | Affiliation |
| Matthew E. Spotnitz | mes2165@cumc.columbia.edu | Columbia University Medical Center |
| Karthik Natarajan | kn2174@cumc.columbia.edu | Columbia University Medical Center |
| Patrick Ryan | ryan@ohdsi.org | Columbia University Medical Center |
| Carolyn L. Westhoff | clw3@cumc.columbia.edu | Columbia University Medical Center |

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# List of abbreviations

IUD Intrauterine Device

LNG Levonorgestrel

Cu-IUDs Copper Intrauterine Devices

LNG-IUDs Levonorgestrel Intrauterine Devices

EC Emergency Contraception

CYCLOPS Cyclic coordinate descent for logistic, Poisson and survival analysis

SNOMED Systematized Nomenclature of Medicine

OHDSI Observational Health Data Sciences and Informatics

OMOP Observational Medical Outcomes Partnership

T Target cohort

C Comparator cohort

O Outcome cohort

PS Propensity Scores

LASSO Least absolute shrinkage and selection operator

CI Confidence Interval

# Abstract

Intrauterine devices (IUDs) are a form of contraception that is commonly used worldwide. We are interested in large scale, international, observational data about the comparative effectiveness of copper IUDs (Cu-IUDs) compared to levonorgestrel secreting intrauterine systems (LNG-IUSs) in preventing high grade cervical neoplasms.

# Amendments and Updates

|  |  |  |  |
| --- | --- | --- | --- |
| 1 | 10/29/2019 |  | We will do custom characterization of the patient population with an R code we developed. |
| 2 | 1/2/2020 |  | We have added new definition of Copper and LNG IUD exposure that were optimized on claims data. Negative controls have been updated. The Medicare database will not be included in our analysis. |
|  |  |  |  |
|  |  |  |  |

# Milestones

|  |  |
| --- | --- |
| Milestone | Planned / Estimated Date |
| Start of analysis | 06/10/19 |
| Single Site Manuscript Submission | 08/18/2019 |
| Start of Network Study | 09/23/2019 |
| End of Network Study | 11/15/2019 |
| Presentation of results | 1/10/2020 |

# Rationale and Background

As early as the 1980’s studies suggested a reduced risk of cervical cancer among women who has used an intrauterine contraceptive. A 2017 systematic review of 17 case-control studies found that intrauterine devices (IUDs) were protective against cervical cancer. The summary odds ratio was 0.64 (95% confidence interval 0.53, 0.77). Those authors suggested that the traumatic manipulation of the cervical canal may clear human papillomavirus (HPV) infection from a combination of acute and chronic inflammatory effects. [1]. That study did not differentiate users of a copper intrauterine device (Cu-IUD) from users of hormonal intrauterine devices. A progesterone-containing IUD (Progestasert®) was registered in the U.S. from 1976-2001. A levonorgestrel intrauterine system (LNG-IUS, Mirena®) was first registered in Finland in 1990 and in the U.S. in 2000. The LNG-IUS is now widely used, but the earlier studies of the association between IUDs and cervical cancer do not report on IUD type, and were unlikely to have included many women using a hormonal type device; most of the devices reported in those earlier studies were likely to be copper-bearing IUDs.

Intrauterine levonorgestrel exposure may predispose the cervix to HPV infection, which is a precursor of cervical malignancy. Specifically, a decrease in prostaglandin production may suppress local immunity and render the uterus more susceptible to viral infection [2]. The angiogenesis and increase in matrix metalloproteinase (MMP) activity that follow approximately 6 months following LNG-IUS placement may accelerate the growth of dysplasia [3,4]. In contrast, the copper ions in Cu-IUDs may increase the clearance rate of HPV. This analysis evaluates the association between LNG-IUS use versus Cu-IUD use and high-grade cervical neoplasms.

# Research Questions and Objectives

## Research Questions

We will study the comparative effectiveness of Cu-IUDs and LNG-IUDs in preventing high grade cervical neoplasms.

# Research methods

## Study Design

This study will be a set of retrospective, observational, cohort studies. By ‘retrospective’ we mean the study will use data already collected at the start of the study. By ‘observational’ we mean no intervention will take place in the course of this study. By ‘cohort study’ we mean two cohorts, a target and comparator cohort, will be followed from index date (start of first exposure) to some end date, and assessed for the occurrence of the outcomes of interest.

Women greater than 45 years of age, or with a history of endometrial or cervical neoplasms are excluded. The outcome is a cervical neoplasm diagnosis. The time at risk is from 30 days to 15 years after IUD implantation. A subgroup analysis from 365 days to 15 years will be performed.

The analyses will be performed across a network of observational healthcare databases. All databases have been transformed into the OMOP Common Data Model, version 5. The complete specification for OMOP Common Data Model, version 5 is available at: <https://github.com/OHDSI/CommonDataModel>. The following databases will be included in this analysis following successful feasibility and passing all study diagnostics:

### Columbia University Irving Medical Center (CUIMC)

Columbia University Irving Medical Center (CUIMC) has an anonymized electronic health record data from the Columbia University Irving Medical Center and New York-Presbyterian Hospital clinical transaction-based data repository. The data are derived from a mixture of inpatient and outpatient visits, span a time period of 4 decades (1980s-present), and represent a population of 4 million patients.

### IBM MarketScan Commercial Claims and Encounters (CCAE)

IBM Health MarketScan® Commercial Claims and Encounters Database (CCAE) represent data from individuals enrolled in United States employer-sponsored insurance health plans. The data includes adjudicated health insurance claims (e.g. inpatient, outpatient, and outpatient pharmacy) as well as enrollment data from large employers and health plans who provide private healthcare coverage to employees, their spouses, and dependents. Additionally, it captures laboratory tests for a subset of the covered lives. This administrative claims database includes a variety of fee-for-service, preferred provider organizations, and capitated health plans.

### IBM MarketScan Multi-state Medicaid (MDCD)

IBM Health MarketScan® Multi-State Medicaid Database (MDCD) adjudicated US health insurance claims for Medicaid enrollees from multiple states and includes hospital discharge diagnoses, outpatient diagnoses and procedures, and outpatient pharmacy claims as well as ethnicity and Medicare eligibility. Members maintain their same identifier even if they leave the system for a brief period however the dataset lacks lab data. [For further information link to RWE site for IBM MDCD.

### Optum ClinFormatics (Optum)

Optum Clinformatics Extended DataMart is an adjudicated US administrative health claims database for members of private health insurance, who are fully insured in commercial plans or in administrative services only (ASOs), Legacy Medicare Choice Lives (prior to January 2006), and Medicare Advantage (Medicare Advantage Prescription Drug coverage starting January 2006). The population is primarily representative of commercial claims patients (0-65 years old) with some Medicare (65+ years old) however ages are capped at 90 years. It includes data captured from administrative claims processed from inpatient and outpatient medical services and prescriptions as dispensed, as well as results for outpatient lab tests processed by large national lab vendors who participate in data exchange with Optum. This dataset also provides date of death (month and year only) for members with both medical and pharmacy coverage from the Social Security Death Master File (however after 2011 reporting frequency changed due to changes in reporting requirements) and location information for patients is at the US state level.

### The Health Improvement Network (THIN)

The Health Improvement Network (THIN) is a UK primary care database. THIN contains pseudonymized primary care medical records from over 16 million patients including their year of birth, of whom over 3.2 million were active (i.e. alive and still in practice) representing almost 5% of the UK population.

## Study population

Study cohorts will be created using ATLAS using previously tested parameters and code lists implemented in previously conducted analyses of OMOP-mapped US claims data. We will use the date of IUD placement as the index date for the study.

## Exposures

In this study, we are interested in comparisons between target cohorts of persons who had an IUD placement. Comparisons will be made with respect to Cu-IUDs and LNG-IUDs for definitions that were optimized on electronic health record (EHR) and claims databases.

### Copper IUD Cohort (Cu-IUD) - EHR

Initial Event Cohort: The index event is a procedure of an IUD placement for the first time in the patient’s history. Patients will have medical records for 365 days prior to the index event and 365 days after the index event. Limit initial events to: **earliest event per person**.

Inclusion Rules

Inclusion Criteria#1: Exactly 0 IUD replacement procedures between all days and 1 day before the index event.

Inclusion Criteria#2: Exactly 0 prior IUD observations between all days before and 1 day before the index event.

Inclusion Criteria#3: Less than or equal to 45 years of age.

Inclusion Criteria#4: “FEMALE” or “Feminine gender.”

Inclusion Criteria#5: Exactly 0 drug exposures of a Levonorgestrel Intrauterine System between 0 and all days after the index event.

Inclusion Criteria#6: Exactly 0 conditions of cervical or endometrial neoplasms between all days and 0 days prior to the index event.

### Levonorgestrel IUS cohort (LNG-IUS) - EHR

Initial Event Cohort: The index event is a procedure of an IUD placement for the first time in the patient’s history. Patients will have medical records for 365 days prior to the index event and 365 days after the index event. Limit initial events to: **earliest event per person**.

Inclusion Rules

Inclusion Criteria#1: Exactly 0 IUD replacement procedures between all days and 1 day before the index event.

Inclusion Criteria#2: Exactly 0 prior IUD observations between all days before and 1 day before the index event.

Inclusion Criteria#3: Less than or equal to 45 years of age.

Inclusion Criteria#4: “FEMALE” or “Feminine gender.”

Inclusion Criteria#5: At least 1 drug exposure of a Levonorgestrel Intrauterine System between 0 and all days after the index event.

Inclusion Criteria#6: Exactly 0 conditions of cervical or endometrial neoplasms between all days and 0 days prior to the index event.

### Copper IUD Cohort (Cu-IUD) - Claims

Initial Event Cohort: The index event is a procedure or drug exposure of an IUD placement with copper for the first time in the patient’s history. Patients will have medical records for 365 days prior to the index event and 365 days after the index event. Limit initial events to: **earliest event per person**.

Inclusion Rules

Inclusion Criteria#1: Exactly 0 IUD observations before the index event.

Inclusion Criteria#2: Less than or equal to 45 years of age.

Inclusion Criteria#3: “FEMALE” or “Feminine gender.”

Inclusion Criteria#4: No history of malignancy prior to the index event.

### Levonorgestrel IUS cohort (LNG-IUS) - Claims

Initial Event Cohort: The index event is a procedure or drug exposure of an IUD placement with levonorgestrel for the first time in the patient’s history. Patients will have medical records for 365 days prior to the index event and 365 days after the index event. Limit initial events to: **earliest event per person**.

Inclusion Rules

Inclusion Criteria#1: Exactly 0 IUD observations before the index event.

Inclusion Criteria#2: Less than or equal to 45 years of age.

Inclusion Criteria#3: “FEMALE” or “Feminine gender.”

Inclusion Criteria#4: No history of malignancy prior to the index event.

## Outcomes

### Cervical Neoplasms

Cervical neoplasms will be identified by a collection of procedure or billing codes. The proportion of patients who had a cervical neoplasm and time to event will be studied.

### Negative Control Outcomes

Negative controls are concepts known to not be associated with the target or comparator cohorts, such that we can assume the true relative risk between the two cohorts is 1. Once potential negative control candidates were selected, manual clinical review to exclude any pairs that may still be in a causal relationship or similar to the study outcome was be performed to select the top concepts by patient exposure. The final list can be found in Table 1.

|  |  |  |  |
| --- | --- | --- | --- |
| Concept Id | Concept Code | Name | Vocabulary |
| 45768910 | 7.07E+08 | Uncomplicated asthma | SNOMED |
| 40483107 | 4.42E+08 | Inflamed seborrheic keratosis | SNOMED |
| 4311591 | 4.25E+08 | Cramp in limb | SNOMED |
| 4308509 | 3.91E+08 | Impaired fasting glycaemia | SNOMED |
| 4305080 | 3.87E+08 | Abnormal breathing | SNOMED |
| 4211231 | 56576003 | Panic disorder without agoraphobia | SNOMED |
| 4209423 | 56294008 | Nicotine dependence | SNOMED |
| 4193704 | 3.13E+08 | Type 2 diabetes mellitus without complication | SNOMED |
| 4172432 | 49765009 | Hyperpigmentation of skin | SNOMED |
| 4168217 | 2.75E+08 | Generalized hyperhidrosis | SNOMED |
| 4110815 | 1.94E+08 | Sensorineural hearing loss, bilateral | SNOMED |
| 4103703 | 2901004 | Melena | SNOMED |
| 4098604 | 1.91E+08 | Hypomagnesemia | SNOMED |
| 4084229 | 24595009 | Primary gout | SNOMED |
| 4033837 | 1.09E+08 | Melanocytic nevus of trunk | SNOMED |
| 444367 | 70342003 | Cholelithiasis without obstruction | SNOMED |
| 443731 | 4.2E+08 | Renal disorder due to type 2 diabetes mellitus | SNOMED |
| 443597 | 4.33E+08 | Chronic kidney disease stage 3 | SNOMED |
| 441417 | 2.81E+08 | Incoordination | SNOMED |
| 440129 | 17467004 | Hypertrophy of nasal turbinates | SNOMED |
| 439147 | 48167000 | Amnesia | SNOMED |
| 438409 | 4.07E+08 | Attention deficit hyperactivity disorder | SNOMED |
| 438120 | 75544000 | Opioid dependence | SNOMED |
| 437851 | 35472004 | Open angle with borderline intraocular pressure | SNOMED |
| 437833 | 43339004 | Hypokalemia | SNOMED |
| 437264 | 89765005 | Tobacco dependence syndrome | SNOMED |
| 437246 | 47903000 | Vitamin B deficiency | SNOMED |
| 436962 | 1.93E+08 | Insomnia | SNOMED |
| 436940 | 2.38E+08 | Metabolic syndrome X | SNOMED |
| 436375 | 28560003 | Hypovolemia | SNOMED |
| 436246 | 8357008 | Reduced libido | SNOMED |
| 436118 | 1.94E+08 | After-cataract with vision obscured | SNOMED |
| 436070 | 34713006 | Vitamin D deficiency | SNOMED |
| 435796 | 34095006 | Dehydration | SNOMED |
| 435515 | 2.67E+08 | Hypo-osmolality and or hyponatremia | SNOMED |
| 435511 | 66931009 | Hypercalcemia | SNOMED |
| 435510 | 5291005 | Hypocalcemia | SNOMED |
| 435243 | 66590003 | Alcohol dependence | SNOMED |
| 434613 | 21897009 | Generalized anxiety disorder | SNOMED |
| 434610 | 14140009 | Hyperkalemia | SNOMED |
| 434005 | 2.38E+08 | Morbid obesity | SNOMED |
| 434004 | 21639008 | Hypervolemia | SNOMED |
| 433811 | 43064006 | Hydronephrosis | SNOMED |
| 433753 | 15167005 | Alcohol abuse | SNOMED |
| 433440 | 78667006 | Dysthymia | SNOMED |
| 433316 | 2.72E+08 | Dizziness and giddiness | SNOMED |
| 433163 | 2.38E+08 | Deficiency of macronutrients | SNOMED |
| 432883 | 1.92E+08 | Recurrent major depressive episodes, moderate | SNOMED |
| 432798 | 5285008 | Mechanical complication of internal orthopedic device, implant AND/OR graft | SNOMED |
| 432738 | 52702003 | Chronic fatigue syndrome | SNOMED |
| 432730 | 47004009 | Difficulty speaking | SNOMED |
| 381877 | 56713002 | Dysfunction of eustachian tube | SNOMED |
| 381295 | 39450006 | Age-related cataract | SNOMED |
| 381292 | 26045000 | Chronic allergic conjunctivitis | SNOMED |
| 379805 | 57190000 | Myopia | SNOMED |
| 377910 | 1.27E+08 | Deviated nasal septum | SNOMED |
| 377575 | 60862001 | Tinnitus | SNOMED |
| 376382 | 3.98E+08 | Tension-type headache | SNOMED |
| 376065 | 4.21E+08 | Neurological disorder with diabetes type 2 | SNOMED |
| 375806 | 22722001 | Idiopathic peripheral neuropathy | SNOMED |
| 374375 | 18070006 | Impacted cerumen | SNOMED |
| 373478 | 41256004 | Presbyopia | SNOMED |
| 321596 | 20696009 | Peripheral venous insufficiency | SNOMED |
| 318800 | 2.36E+08 | Gastroesophageal reflux disease | SNOMED |
| 318736 | 37796009 | Migraine | SNOMED |
| 316127 | 4.22E+08 | Vitreous opacities | SNOMED |
| 313459 | 73430006 | Sleep apnea | SNOMED |
| 312950 | 4.25E+08 | IgE-mediated allergic asthma | SNOMED |
| 261325 | 87433001 | Pulmonary emphysema | SNOMED |
| 257004 | 1.96E+08 | Acute exacerbation of chronic obstructive airways disease | SNOMED |
| 201826 | 44054006 | Type 2 diabetes mellitus | SNOMED |
| 201620 | 95570007 | Kidney stone | SNOMED |
| 201418 | 2.72E+08 | Flatulence, eructation and gas pain | SNOMED |
| 201322 | 38214006 | Internal hemorrhoids without complication | SNOMED |
| 201254 | 46635009 | Type 1 diabetes mellitus | SNOMED |
| 201061 | 39839004 | Diaphragmatic hernia | SNOMED |
| 200528 | 3.89E+08 | Ascites | SNOMED |
| 199866 | 25458004 | Acute gastritis | SNOMED |
| 198400 | 2.71E+08 | Hemangioma of skin and subcutaneous tissue | SNOMED |
| 198101 | 1.89E+08 | Lipoma of skin and subcutaneous tissue | SNOMED |
| 197381 | 79922009 | Epigastric pain | SNOMED |
| 197006 | 31704005 | Residual hemorrhoidal skin tags | SNOMED |
| 196456 | 2.36E+08 | Gallstone | SNOMED |
| 195562 | 70153002 | Hemorrhoids | SNOMED |
| 194686 | 1.06E+08 | Acquired renal cystic disease | SNOMED |
| 141932 | 3.99E+08 | Senile hyperkeratosis | SNOMED |
| 141375 | 24782002 | Hypertrophic condition of skin | SNOMED |
| 139099 | 4E+08 | Ingrowing nail | SNOMED |
| 138825 | 2.01E+08 | Actinic keratosis | SNOMED |
| 138384 | 1.12E+08 | Acquired hypothyroidism | SNOMED |
| 137951 | 4E+08 | Acquired keratoderma | SNOMED |
| 137351 | 4.2E+08 | Epidermoid cyst of skin | SNOMED |
| 136773 | 3.99E+08 | Rosacea | SNOMED |
| 136661 | 1.9E+08 | Non-toxic nodular goiter | SNOMED |
| 136184 | 2.79E+08 | Pruritus of skin | SNOMED |
| 136057 | 92380000 | Benign neoplasm of skin of trunk | SNOMED |
| 133729 | 66999008 | Hyperparathyroidism | SNOMED |
| 81151 | 44465007 | Sprain of ankle | SNOMED |
| 80824 | 18040001 | Senile osteoporosis | SNOMED |
| 79864 | 53298000 | Hematuria syndrome | SNOMED |
| 78162 | 50438001 | Peripheral vertigo | SNOMED |
| 77139 | 2630008 | Open wound of finger without complication | SNOMED |
| 76161 | 1.98E+08 | Impotence of organic origin | SNOMED |
| 75860 | 14760008 | Constipation | SNOMED |
| 74725 | 85216006 | Displacement of cervical intervertebral disc without myelopathy | SNOMED |
| 73575 | 3E+08 | Deformity of toe | SNOMED |
| 72715 | 4.16E+08 | Exostosis | SNOMED |
| 31317 | 40739000 | Dysphagia | SNOMED |
| 30753 | 16761005 | Esophagitis | SNOMED |
| 30234 | 2.1E+08 | Neck sprain | SNOMED |

Table 1: Negative controls for IUD Analysis.

For each negative control outcome, a patient enters the negative control outcome cohort at the occurrence of a diagnosis code identified by the concepts listed above, or any one of its descendant codes.

## Covariates

### Propensity score covariates

Propensity scores (PS) will be used as an analytic strategy to reduce potential confounding due to imbalance between the target and comparator cohorts in baseline covariates. The propensity score is the probability of a patient being classified in the target cohort vs. the comparator cohort, given a set of observed covariates.

Tens of thousands of baseline covariates will be included in the propensity score model representing demographics (sex, age, index month and year), all conditions and drug dispensing observed in the 30, 365, 1095 days, and any time prior to index, all procedures in the 365 days and any time prior to index, visit counts in the 365 and 1095 days prior to index, and the CHADS2, CHA2DS2VASc, DCSI, and Charlson indices. A large-scale regularized logistic regression will be fit with a LaPlace prior (LASSO) with the optimal hyperparameter determined through 10-fold cross validation [5], a method with demonstrated superior covariate balancing properties than other popular methods for high-dimensional data [6].

# Data Analysis Plan

## Calculation of time-at risk

Time-at-risk periods will be specified dependent on the outcome. The primary time-at-risk for cervical neoplasm will be from 30 days following the index date (day 1) through the 15 years. The study window will be from 01/01/2003 through the end of the study period. The study will be an intent to treat design. A subgroup analysis from 365 days to 15 years will be performed.

## Model Specification

In this study, we compare the target cohort with the comparator cohort for the hazards of outcome during the time-at-risk by applying a Cox proportional hazards model.

The time-to-event of outcome among patients in the target and comparator cohorts is determined by calculating the number of days from the start of the time-at-risk window (the cohort start date), until the earliest event among 1) the first occurrence of the outcome, 2) the end of the time-at-risk window as defined in section 9.1, and 3) the end of the observation period that spans the time-at-risk start.

Patients with the outcome observed prior to target or comparator cohort entry are not excluded from consideration.

Propensity scores will be used as an analytic strategy to reduce potential confounding due to imbalance between the target and comparator cohorts in baseline covariates. The propensity score is the probability of a patient being classified in the target cohort vs. the comparator cohort, given a set of observed covariates. In this study, the propensity score is estimated for each patient, using the predicted probability from a regularized logistic regression model, fit with a Laplace prior (LASSO) and the regularization hyperparameter selected by optimizing the likelihood in a 10-fold cross, a starting variance of 0.01 and a tolerance of 2e-7. Covariates to be used in the propensity score model are listed in section 8.6.

Patients are matched on the propensity score by two methods. A final propensity score adjustment sensitivity analysis is to trim the upper and lower extremes of the propensity score distribution overlap by 5%.

### Pooling effect estimates across databases

Effects will be pooled across databases using a random-effects meta-analysis if there is sufficient homogeneity across populations (I2 < 40%). Estimates for negative and positive controls will be pooled before performing empirical calibration on the pooled estimates.

## Output

For each analysis, we will produce 1) covariate summary before and after propensity score adjustment, 2) propensity score distribution, 3) covariate balance summary, 4) estimation for negative and positive controls, to assess residual error, 5) summary of outcome incidence, 6) hazard ratio estimates – pre- and post-calibration, and 7) Kaplan-Meier plot.

## Evidence Evaluation

We have executed diagnostics to determine if the analysis can be appropriately conducted. The diagnostics include:

* Propensity score distribution
* Covariate balance before and after propensity score matching
* Estimation for negative and positive controls, to assess residual error
* Negative and positive control exposures and outcomes will be used to evaluate the potential impact of residual systematic error in the study design, and to facilitate empirical calibration of the p-value and confidence interval for the exposures and outcome of interest.

Negative control outcomes in the context of this study are outcomes that are not believed to be caused by neither exposure in any comparison and where therefore the true hazard ratio is equal to 1. We will execute the same analysis used for the primary hypotheses to produce hazard ratio estimates for the negative controls. The distribution of effect estimates across all negative controls will be used to fit an empirical null distribution which models the observed residual systematic error. The empirical null distribution will then be applied to the target exposures and outcome of interest to calibrate the p-value [7].

Positive control exposures and outcomes are pairs of exposures and outcomes where the hazard ratio is known to be of some magnitude greater than 1. We will synthesize positive controls by starting with the negative controls defined earlier, and adding additional, simulated outcomes during the time-at-risk until the desired true hazard ratio is achieved. The target hazard ratios are 1.5, 2 and 4. The negative and positive controls together will be used to estimate an empirical systematic error model, which will inform whether systematic error changes as a function of true effect size. The empirical systematic error model will then be applied to the target the target exposures and outcome of interest to calibrate the confidence interval [8].

Empirical calibration serves as an important diagnostic tool to evaluate if the residual systematic error is sufficient to cast doubt on the accuracy of the unknown effect estimate. The calibration effect plot and calibration probability plots will be generated for review. We will report the traditional and empirically calibrated p-value and confidence interval for each negative control, as well as the hypothesis of interest.

# Study Diagnostics

## Sample Size and Study Power

XXX. Sample size and power are reported in the OHDSI Shiny application (<http://data.ohdsi.org>).

## Cohort Comparability

XXX all achieved sufficient comparability, as seen in the propensity score distributions on the OHDSI Shiny application (<http://data.ohdsi.org>).

## Systematic Error Assessment

XXX failed study diagnostics and will not be used for final analyses. Baseline covariates could not be made sufficient balanced, and unbalanced covariates were determined to be likely confounders important to the analysis.

# Strengths and Limitations of the Research Methods

Strength

* Cohort studies allow direct estimation of incidence rates following exposure of interest, and the new-user design can capture early events following treatment exposures while avoiding confounding from previous treatment effects. New use allows for a clear exposure index date.
* PS matching allow balancing on a large number of baseline potential confounders.
* Use of negative and positive control outcomes allow for evaluating the study design as a whole in terms of residual bias.

Limitations

* Even though many potential confounders will be included in this study, there may be residual bias due to unmeasured or misspecified confounders.

# Protection of Human Subjects

The study is using only de-identified data. Confidentiality of patient records will be maintained at all times. All study reports will contain aggregate data only and will not identify individual patients or physicians.

# Management and Reporting of Adverse Events and Adverse Reactions

This study uses coded data that already exist in an electronic database. In this type of database, it is not possible to link (i.e., identify a potential causal association between) a particular product and medical event for any individual. Thus, the minimum criteria for reporting an adverse event (i.e., identifiable patient, identifiable reporter, a suspect product, and event) are not available and adverse events are not reportable as individual adverse events reports. The study results will be assessed for medically important results.

# Plans for Disseminating and Communicating Study Results

The study results will be posted on the OHDSI website after completion of the study. At least one paper describing the study and its results will be written and submitted for publication to a peer-reviewed scientific journal.

# References

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Appendix 1: Concept Set Definitions

IUD Placement Procedure

|  |  |  |  |
| --- | --- | --- | --- |
| Concept Id | Code | Name | Vocabulary |
| 4275113 | 65200003 | Insertion of intrauterine contraceptive device | SNOMED |
| 2110194 | 58300 | Insertion of intrauterine device (IUD) | CPT4 |
| 2004529 | 69.7 | Insertion of intrauterine contraceptive device | ICD9Proc |
| 44792289 | 3.41E+14 | Insertion of T shaped 380 millimetres squared copper coated intrauterine contraceptive device | SNOMED |
| 44792288 | 3.41E+14 | Insertion of T shaped 375 millimetres squared copper coated intrauterine contraceptive device | SNOMED |
| 44792287 | 3.41E+14 | Insertion of frameless 330 millimetres squared copper coated intrauterine contraceptive device | SNOMED |
| 43020952 | 4.73E+08 | Insertion of hormone releasing intrauterine contraceptive device | SNOMED |

Levonorgestrel Releasing Intrauterine Device (EHR Optimized)

|  |  |  |  |
| --- | --- | --- | --- |
| Concept Id | Code | Name | Vocabulary |
| 19132304 | 807283 | Levonorgestrel 0.000833 MG/HR Intrauterine System [Mirena] | RxNorm |
| 19131647 | 804156 | Levonorgestrel 0.000833 MG/HR Intrauterine System | RxNorm |
| 46221626 | 1605257 | Levonorgestrel 0.000775 MG/HR Intrauterine System [Liletta] | RxNorm |
| 43012751 | 1366339 | Levonorgestrel 0.000583 MG/HR Intrauterine System [Skyla] | RxNorm |
| 46221622 | 1605252 | Levonorgestrel 0.000775 MG/HR Intrauterine System | RxNorm |
| 43012750 | 1366334 | Levonorgestrel 0.000583 MG/HR Intrauterine System | RxNorm |
| 1718994 | 1811886 | Levonorgestrel 0.000729 MG/HR Intrauterine System | RxNorm |
| 1718412 | 1856546 | Levonorgestrel 0.000729 MG/HR Intrauterine System [Kyleena] | RxNorm |
| 1718405 | 1856535 | Levonorgestrel Intrauterine System [Kyleena] | RxNorm |
| 1718403 | 1856528 | Levonorgestrel Intrauterine System [Mirena] | RxNorm |
| 1718402 | 1856524 | Levonorgestrel Intrauterine System [Liletta] | RxNorm |
| 1718401 | 1856517 | Levonorgestrel Intrauterine System [Skyla] | RxNorm |
| 1718400 | 1856515 | Levonorgestrel Intrauterine System | RxNorm |

IUD Placement With Copper (Claims Optimized)

|  |  |  |  |
| --- | --- | --- | --- |
| Concept Id | Concept Code | Name | Vocabulary |
| 2718682 | J7300 | Intrauterine copper contraceptive | HCPCS |

IUD Placement With Levonorgestrel (Claims Optimized)

|  |  |  |  |
| --- | --- | --- | --- |
| Concept Id | Concept Code | Name | Vocabulary |
| 44786600 | Q0090 | Levonorgestrel-releasing intrauterine contraceptive system, (skyla), 13.5 mg | HCPCS |
| 44786565 | J7301 | Levonorgestrel-releasing intrauterine contraceptive system (skyla), 13.5 mg | HCPCS |
| 44127810 | OMOP1122441 | Levonorgestrel 19.5 MG Drug Implant [Kyleena] by Bayer | RxNorm Extension |
| 44123197 | OMOP1117828 | Levonorgestrel 13.5 MG Drug Implant | RxNorm Extension |
| 44121637 | OMOP1116268 | Levonorgestrel Drug Implant [Jaydess] | RxNorm Extension |
| 44101836 | OMOP1096467 | Levonorgestrel 13.5 MG Drug Implant [Jaydess] by Bayer | RxNorm Extension |
| 44097167 | OMOP1091798 | Levonorgestrel 19.5 MG Drug Implant | RxNorm Extension |
| 44086126 | OMOP1080757 | Levonorgestrel 19.5 MG Drug Implant [Kyleena] | RxNorm Extension |
| 44082723 | OMOP1077354 | Levonorgestrel Drug Implant [Kyleena] | RxNorm Extension |
| 44073214 | OMOP1067845 | Levonorgestrel 52 MG Drug Implant [Mirena] | RxNorm Extension |
| 44060436 | OMOP1055067 | Levonorgestrel 13.5 MG Drug Implant [Jaydess] | RxNorm Extension |
| 44050232 | OMOP1044863 | Levonorgestrel 52 MG Drug Implant [Mirena] by Bayer | RxNorm Extension |
| 44045536 | OMOP1040167 | Levonorgestrel 52 MG Drug Implant | RxNorm Extension |
| 44045535 | OMOP1040166 | Levonorgestrel 36 MG Drug Implant | RxNorm Extension |
| 44025740 | OMOP1020371 | Levonorgestrel Drug Implant [Mirena] | RxNorm Extension |
| 43020952 | 4.73E+08 | Insertion of hormone releasing intrauterine contraceptive device | SNOMED |
| 43012754 | 1366343 | Levonorgestrel 0.00354 MG/HR Drug Implant | RxNorm |
| 40001198 | 378923 | Levonorgestrel Drug Implant | RxNorm |
| 19123248 | 608565 | Levonorgestrel 75 MG Drug Implant | RxNorm |
| 2721260 | S4981 | Insertion of levonorgestrel-releasing intrauterine system | HCPCS |
| 2718683 | J7302 | Levonorgestrel-releasing intrauterine contraceptive system, 52 mg | HCPCS |
| 937612 | Q9984 | Levonorgestrel-releasing intrauterine contraceptive system (kyleena), 19.5 mg | HCPCS |
| 937575 | J7296 | Levonorgestrel-releasing intrauterine contraceptive system, (kyleena), 19.5 mg | HCPCS |
| 915801 | J7298 | Levonorgestrel-releasing intrauterine contraceptive system (mirena), 52 mg | HCPCS |
| 915800 | J7297 | Levonorgestrel-releasing intrauterine contraceptive system (liletta), 52 mg | HCPCS |

Cervical Neoplasm

|  |  |  |  |
| --- | --- | --- | --- |
| Concept Id | Concept Code | Name | Vocabulary |
| 196359 | 372024009 | Primary malignant neoplasm of uterine cervix | SNOMED |
| 192676 | 285836003 | Cervical intraepithelial neoplasia grade 1 | SNOMED |
| 198984 | 363354003 | Malignant tumor of cervix | SNOMED |
| 194611 | 92564006 | Carcinoma in situ of uterine cervix | SNOMED |
| 4157449 | 372097009 | Malignant neoplasm of endocervix | SNOMED |
| 199877 | 55310007 | Mucous polyp of cervix | SNOMED |
| 196165 | 285838002 | Cervical intraepithelial neoplasia grade 2 | SNOMED |
| 4162876 | 372099007 | Malignant neoplasm of exocervix | SNOMED |
| 4280498 | 65576009 | Polyp of cervix | SNOMED |
| 196364 | 92056006 | Benign neoplasm of uterine cervix | SNOMED |
| 4092515 | 188180002 | Malignant neoplasm, overlapping lesion of cervix uteri | SNOMED |
| 4243120 | 92580001 | Carcinoma in situ of endocervix | SNOMED |
| 4243874 | 92588008 | Carcinoma in situ of exocervix | SNOMED |
| 45885701 | 10074909 | Clear cell carcinoma of cervix | MedDRA |
| 44503140 | 8077/2-C53.0 | Squamous intraepithelial neoplasia, high grade of Endocervix | ICDO3 |
| 44503108 | 8935/3-C53.0 | Stromal sarcoma of Endocervix | ICDO3 |
| 44502927 | 8072/3-C53.9 | Squamous cell carcinoma, large cell, nonkeratinizing of Cervix uteri | ICDO3 |
| 44502813 | 8120/2-C53.9 | Transitional cell carcinoma in situ of Cervix uteri | ICDO3 |
| 44502690 | 8070/3-C53.0 | Squamous cell carcinoma of Endocervix | ICDO3 |
| 44502645 | 8933/3-C53.0 | Adenosarcoma of Endocervix | ICDO3 |
| 44502600 | 8015/3-C53.9 | Glassy cell carcinoma of Cervix uteri | ICDO3 |
| 44502575 | 8560/3-C53.0 | Adenosquamous carcinoma of Endocervix | ICDO3 |
| 44502558 | 8950/3-C53.9 | Mullerian mixed tumor of Cervix uteri | ICDO3 |
| 44502521 | 8073/3-C53.9 | Squamous cell carcinoma, small cell, nonkeratinizing of Cervix uteri | ICDO3 |
| 44502520 | 8071/3-C53.0 | Squamous cell carcinoma, keratinizing of Endocervix | ICDO3 |
| 44502472 | 8461/3-C53.9 | Serous surface papillary carcinoma of Cervix uteri | ICDO3 |
| 44502450 | 8070/2-C53.0 | Squamous cell carcinoma in situ of Endocervix | ICDO3 |
| 44502445 | 8380/3-C53.9 | Endometrioid adenocarcinoma of Cervix uteri | ICDO3 |
| 44502442 | 8210/2-C53.0 | Adenocarcinoma in situ in adenomatous polyp of Endocervix | ICDO3 |
| 44502392 | 8310/3-C53.0 | Clear cell adenocarcinoma of Endocervix | ICDO3 |
| 44502310 | 9680/3-C53.9 | Malignant lymphoma, large B-cell, diffuse of Cervix uteri | ICDO3 |
| 44502249 | 8933/3-C53.9 | Adenosarcoma of Cervix uteri | ICDO3 |
| 44502247 | 8910/3-C53.9 | Embryonal rhabdomyosarcoma of Cervix uteri | ICDO3 |
| 44502096 | 8144/3-C53.9 | Adenocarcinoma, intestinal type of Cervix uteri | ICDO3 |
| 44502012 | 8077/2-C53.1 | Squamous intraepithelial neoplasia, high grade of Exocervix | ICDO3 |
| 44501964 | 8745/3-C53.9 | Desmoplastic melanoma, malignant of Cervix uteri | ICDO3 |
| 44501939 | 8323/3-C53.0 | Mixed cell adenocarcinoma of Endocervix | ICDO3 |
| 44501802 | 8384/3-C53.0 | Adenocarcinoma, endocervical type of Endocervix | ICDO3 |
| 44501784 | 8083/3-C53.9 | Basaloid squamous cell carcinoma of Cervix uteri | ICDO3 |
| 44501641 | 8263/3-C53.9 | Adenocarcinoma in tubulovillous adenoma of Cervix uteri | ICDO3 |
| 44501637 | 8246/3-C53.9 | Neuroendocrine carcinoma of Cervix uteri | ICDO3 |
| 44501580 | 8482/3-C53.9 | Mucinous adenocarcinoma, endocervical type of Cervix uteri | ICDO3 |
| 44501517 | 8074/3-C53.9 | Squamous cell carcinoma, spindle cell of Cervix uteri | ICDO3 |
| 44501441 | 8441/3-C53.0 | Serous cystadenocarcinoma of Endocervix | ICDO3 |
| 44501420 | 8806/3-C53.9 | Desmoplastic small round cell tumor of Cervix uteri | ICDO3 |
| 44501401 | 8140/2-C54.9 | Adenocarcinoma in situ of Corpus uteri | ICDO3 |
| 44501396 | 8070/3-C53.1 | Squamous cell carcinoma of Exocervix | ICDO3 |
| 44501336 | 8077/2-C53.9 | Squamous intraepithelial neoplasia, high grade of Cervix uteri | ICDO3 |
| 44501289 | 8951/3-C53.9 | Mesodermal mixed tumor of Cervix uteri | ICDO3 |
| 44501255 | 8073/3-C53.0 | Squamous cell carcinoma, small cell, nonkeratinizing of Endocervix | ICDO3 |
| 44501228 | 8890/3-C53.0 | Leiomyosarcoma of Endocervix | ICDO3 |
| 44501193 | 8076/3-C53.0 | Squamous cell carcinoma, microinvasive of Endocervix | ICDO3 |
| 44501182 | 8052/3-C53.9 | Papillary squamous cell carcinoma of Cervix uteri | ICDO3 |
| 44501133 | 8144/3-C53.0 | Adenocarcinoma, intestinal type of Endocervix | ICDO3 |
| 44501016 | 8460/3-C53.9 | Papillary serous cystadenocarcinoma of Cervix uteri | ICDO3 |
| 44500998 | 8098/3-C53.0 | Adenoid basal carcinoma of Endocervix | ICDO3 |
| 44500990 | 8076/3-C53.1 | Squamous cell carcinoma, microinvasive of Exocervix | ICDO3 |
| 44500980 | 8052/3-C53.1 | Papillary squamous cell carcinoma of Exocervix | ICDO3 |
| 44500817 | 9150/3-C53.9 | Hemangiopericytoma, malignant of Cervix uteri | ICDO3 |
| 44500545 | 8070/3-C53.9 | Squamous cell carcinoma of Cervix uteri | ICDO3 |
| 44500540 | 8020/3-C53.0 | Carcinoma, undifferentiated of Endocervix | ICDO3 |
| 44500521 | 9110/3-C53.9 | Mesonephroma, malignant of Cervix uteri | ICDO3 |
| 44500513 | 8800/3-C53.9 | Sarcoma of Cervix uteri | ICDO3 |
| 44500492 | 8076/3-C53.9 | Squamous cell carcinoma, microinvasive of Cervix uteri | ICDO3 |
| 44500434 | 8072/3-C53.0 | Squamous cell carcinoma, large cell, nonkeratinizing of Endocervix | ICDO3 |
| 44500377 | 8910/3-C53.0 | Embryonal rhabdomyosarcoma of Endocervix | ICDO3 |
| 44500297 | 8260/3-C53.9 | Papillary adenocarcinoma of Cervix uteri | ICDO3 |
| 44500296 | 8255/3-C53.9 | Adenocarcinoma with mixed subtypes of Cervix uteri | ICDO3 |
| 44500269 | 8951/3-C53.0 | Mesodermal mixed tumor of Endocervix | ICDO3 |
| 44500258 | 8482/3-C53.0 | Mucinous adenocarcinoma, endocervical type of Endocervix | ICDO3 |
| 44500232 | 8013/3-C53.9 | Large cell neuroendocrine carcinoma of Cervix uteri | ICDO3 |
| 44500146 | 8480/3-C53.0 | Mucinous adenocarcinoma of Endocervix | ICDO3 |
| 44500143 | 8384/3-C53.9 | Adenocarcinoma, endocervical type of Cervix uteri | ICDO3 |
| 44500091 | 8950/3-C53.0 | Mullerian mixed tumor of Endocervix | ICDO3 |
| 44499916 | 8310/3-C53.9 | Clear cell adenocarcinoma of Cervix uteri | ICDO3 |
| 44499910 | 9110/3-C53.0 | Mesonephroma, malignant of Endocervix | ICDO3 |
| 44499817 | 8490/3-C53.0 | Signet ring cell carcinoma of Endocervix | ICDO3 |
| 44499752 | 8520/2-C53.9 | Lobular carcinoma in situ of Cervix uteri | ICDO3 |
| 44499749 | 8480/3-C53.9 | Mucinous adenocarcinoma of Cervix uteri | ICDO3 |
| 44499746 | 8441/3-C53.9 | Serous cystadenocarcinoma of Cervix uteri | ICDO3 |
| 44499713 | 8032/3-C53.9 | Spindle cell carcinoma of Cervix uteri | ICDO3 |
| 44499680 | 8052/2-C53.9 | Papillary squamous cell carcinoma, non-invasive of Cervix uteri | ICDO3 |
| 44499679 | 8041/3-C53.9 | Small cell carcinoma of Cervix uteri | ICDO3 |
| 44499647 | 8460/3-C53.0 | Papillary serous cystadenocarcinoma of Endocervix | ICDO3 |
| 44499644 | 8323/3-C53.9 | Mixed cell adenocarcinoma of Cervix uteri | ICDO3 |
| 44499568 | 8801/3-C53.9 | Spindle cell sarcoma of Cervix uteri | ICDO3 |
| 44499509 | 8380/3-C53.0 | Endometrioid adenocarcinoma of Endocervix | ICDO3 |
| 44499507 | 8260/3-C53.0 | Papillary adenocarcinoma of Endocervix | ICDO3 |
| 44499485 | 8070/2-C53.1 | Squamous cell carcinoma in situ of Exocervix | ICDO3 |
| 44499458 | 8890/3-C53.9 | Leiomyosarcoma of Cervix uteri | ICDO3 |
| 44499445 | 8481/3-C53.0 | Mucin-producing adenocarcinoma of Endocervix | ICDO3 |
| 44499013 | 8071/3-C53.9 | Squamous cell carcinoma, keratinizing of Cervix uteri | ICDO3 |
| 44498939 | 8042/3-C53.9 | Oat cell carcinoma of Cervix uteri | ICDO3 |
| 42689509 | 1.06468E+15 | CGIN - cervical glandular intraepithelial neoplasia | SNOMED |
| 40493012 | 449059000 | Follicular non-Hodgkin's lymphoma of uterine cervix | SNOMED |
| 40491512 | 448774004 | Non-Hodgkin's lymphoma of uterine cervix | SNOMED |
| 40490518 | 448607004 | Diffuse non-Hodgkin's lymphoma of uterine cervix | SNOMED |
| 40486538 | 447760009 | Endocervical adenocarcinoma in situ | SNOMED |
| 37116830 | 733834006 | Invasive carcinoma of uterine cervix co-occurrent with human immunodeficiency virus infection | SNOMED |
| 37103694 | 10029109 | Cervix neoplasms | MedDRA |
| 37016242 | 2.08041E+14 | Primary adenocarcinoma of endocervix | SNOMED |
| 37016238 | 1.84781E+14 | Primary adenocarcinoma of cervix uteri | SNOMED |
| 36716617 | 722683006 | Primary neuroendocrine carcinoma of cervix uteri | SNOMED |
| 36672714 | 10029103 | Neoplasm uterine cervix | MedDRA |
| 36672713 | 10028986 | Neoplasm cervix | MedDRA |
| 36672711 | 10008290 | Cervical neoplasm NOS | MedDRA |
| 36672591 | 10065355 | Lymphoepithelioma-like carcinoma of cervix stage IV | MedDRA |
| 36672590 | 10028991 | Neoplasm cervix stage IV | MedDRA |
| 36672589 | 10026271 | Malignant neoplasm of other specified sites of cervix stage IV | MedDRA |
| 36672588 | 10025908 | Malignant neoplasm of exocervix stage IV | MedDRA |
| 36672587 | 10025896 | Malignant neoplasm of endocervix stage IV | MedDRA |
| 36672586 | 10025836 | Malignant neoplasm of cervix uteri stage IV | MedDRA |
| 36672585 | 10008367 | Cervix uteri cancer stage IV | MedDRA |
| 36672584 | 10008359 | Cervix neoplasm stage IV | MedDRA |
| 36672582 | 10008249 | Cervical carcinoma stage IVB | MedDRA |
| 36672581 | 10008248 | Cervical carcinoma stage IVA | MedDRA |
| 36672580 | 10008247 | Cervical carcinoma stage IV | MedDRA |
| 36672579 | 10008236 | Cervical cancer stage IV | MedDRA |
| 36672578 | 10007499 | Carcinoma uterine cervix stage IV | MedDRA |
| 36672576 | 10007329 | Carcinoma cervix stage IV | MedDRA |
| 36672574 | 10065354 | Lymphoepithelioma-like carcinoma of cervix stage III | MedDRA |
| 36672573 | 10028990 | Neoplasm cervix stage III | MedDRA |
| 36672572 | 10026270 | Malignant neoplasm of other specified sites of cervix stage III | MedDRA |
| 36672571 | 10025907 | Malignant neoplasm of exocervix stage III | MedDRA |
| 36672570 | 10025895 | Malignant neoplasm of endocervix stage III | MedDRA |
| 36672569 | 10025835 | Malignant neoplasm of cervix uteri stage III | MedDRA |
| 36672568 | 10008366 | Cervix uteri cancer stage III | MedDRA |
| 36672567 | 10008358 | Cervix neoplasm stage III | MedDRA |
| 36672565 | 10008246 | Cervical carcinoma stage III | MedDRA |
| 36672564 | 10008235 | Cervical cancer stage III | MedDRA |
| 36672563 | 10007498 | Carcinoma uterine cervix stage III | MedDRA |
| 36672561 | 10007328 | Carcinoma cervix stage III | MedDRA |
| 36672559 | 10065353 | Lymphoepithelioma-like carcinoma of cervix stage II | MedDRA |
| 36672558 | 10028989 | Neoplasm cervix stage II | MedDRA |
| 36672557 | 10026269 | Malignant neoplasm of other specified sites of cervix stage II | MedDRA |
| 36672556 | 10025906 | Malignant neoplasm of exocervix stage II | MedDRA |
| 36672555 | 10025894 | Malignant neoplasm of endocervix stage II | MedDRA |
| 36672554 | 10025834 | Malignant neoplasm of cervix uteri stage II | MedDRA |
| 36672553 | 10008365 | Cervix uteri cancer stage II | MedDRA |
| 36672552 | 10008357 | Cervix neoplasm stage II | MedDRA |
| 36672550 | 10008245 | Cervical carcinoma stage IIB | MedDRA |
| 36672549 | 10008244 | Cervical carcinoma stage IIA | MedDRA |
| 36672548 | 10008243 | Cervical carcinoma stage II | MedDRA |
| 36672547 | 10008234 | Cervical cancer stage II | MedDRA |
| 36672546 | 10007497 | Carcinoma uterine cervix stage II | MedDRA |
| 36672544 | 10007327 | Carcinoma cervix stage II | MedDRA |
| 36672542 | 10067069 | Microinvasive cervix cancer | MedDRA |
| 36672541 | 10065352 | Lymphoepithelioma-like carcinoma of cervix stage I | MedDRA |
| 36672540 | 10028988 | Neoplasm cervix stage I | MedDRA |
| 36672539 | 10026268 | Malignant neoplasm of other specified sites of cervix stage I | MedDRA |
| 36672538 | 10025905 | Malignant neoplasm of exocervix stage I | MedDRA |
| 36672537 | 10025893 | Malignant neoplasm of endocervix stage I | MedDRA |
| 36672536 | 10025833 | Malignant neoplasm of cervix uteri stage I | MedDRA |
| 36672535 | 10008364 | Cervix uteri cancer stage I | MedDRA |
| 36672534 | 10008356 | Cervix neoplasm stage I | MedDRA |
| 36672532 | 10008242 | Cervical carcinoma stage IB | MedDRA |
| 36672531 | 10008241 | Cervical carcinoma stage IA | MedDRA |
| 36672530 | 10008240 | Cervical carcinoma stage I | MedDRA |
| 36672529 | 10008233 | Cervical cancer stage I | MedDRA |
| 36672528 | 10007496 | Carcinoma uterine cervix stage I | MedDRA |
| 36672526 | 10007326 | Carcinoma cervix stage I | MedDRA |
| 36672524 | 10065697 | Papanicolaou smear abnormal, class IV b | MedDRA |
| 36672523 | 10065696 | Papanicolaou smear abnormal, class IV a | MedDRA |
| 36672522 | 10065351 | Lymphoepithelioma-like carcinoma of cervix stage 0 | MedDRA |
| 36672520 | 10059383 | Cervical carcinoma stage 0 | MedDRA |
| 36672519 | 10046771 | Uterine cervix carcinoma stage 0 | MedDRA |
| 36672518 | 10021571 | In situ cancer of cervix | MedDRA |
| 36672517 | 10009215 | CIS of cervix | MedDRA |
| 36672516 | 10008343 | Cervix carcinoma in situ | MedDRA |
| 36672515 | 10008237 | Cervical carcinoma in situ | MedDRA |
| 36672514 | 10008232 | Cervical cancer stage 0 | MedDRA |
| 36672513 | 10007494 | Carcinoma uterine cervix in situ | MedDRA |
| 36672512 | 10007364 | Carcinoma in situ of cervix uteri | MedDRA |
| 36672511 | 10007363 | Carcinoma in situ of cervix | MedDRA |
| 36672510 | 10007324 | Carcinoma cervix in situ | MedDRA |
| 36672509 | 10065592 | Lymphoepithelioma-like carcinoma of cervix recurrent | MedDRA |
| 36672508 | 10028987 | Neoplasm cervix recurrent | MedDRA |
| 36672507 | 10026267 | Malignant neoplasm of other specified sites of cervix recurrent | MedDRA |
| 36672506 | 10025904 | Malignant neoplasm of exocervix recurrent | MedDRA |
| 36672505 | 10025892 | Malignant neoplasm of endocervix recurrent | MedDRA |
| 36672504 | 10025832 | Malignant neoplasm of cervix uteri recurrent | MedDRA |
| 36672503 | 10008363 | Cervix uteri cancer recurrent | MedDRA |
| 36672502 | 10008355 | Cervix neoplasm recurrent | MedDRA |
| 36672500 | 10008239 | Cervical carcinoma recurrent | MedDRA |
| 36672499 | 10008231 | Cervical cancer recurrent | MedDRA |
| 36672498 | 10007495 | Carcinoma uterine cervix recurrent | MedDRA |
| 36672496 | 10007325 | Carcinoma cervix recurrent | MedDRA |
| 36672494 | 10065698 | Papanicolaou smear abnormal, class V | MedDRA |
| 36672493 | 10065350 | Lymphoepithelioma-like carcinoma of cervix | MedDRA |
| 36672492 | 10064444 | Invasive cervix cancer | MedDRA |
| 36672490 | 10025903 | Malignant neoplasm of exocervix | MedDRA |
| 36672489 | 10025891 | Malignant neoplasm of endocervix | MedDRA |
| 36672488 | 10025837 | Malignant neoplasm of cervix uteri, unspecified | MedDRA |
| 36672487 | 10025831 | Malignant neoplasm of cervix uteri | MedDRA |
| 36672486 | 10008362 | Cervix uteri cancer | MedDRA |
| 36672484 | 10008238 | Cervical carcinoma NOS | MedDRA |
| 36672483 | 10008229 | Cervical cancer | MedDRA |
| 36672482 | 10007493 | Carcinoma uterine cervix | MedDRA |
| 36672480 | 10007323 | Carcinoma cervix | MedDRA |
| 36672478 | 10065593 | Lymphoepithelioma-like carcinoma of cervix metastatic | MedDRA |
| 36672476 | 10008226 | Cervical adenosquamous carcinoma | MedDRA |
| 36672474 | 10008224 | Cervical adenocarcinoma | MedDRA |
| 36672364 | 10036125 | Polyp of cervix adenomatous | MedDRA |
| 36672362 | 10008225 | Cervical adenomatous polyp | MedDRA |
| 36672361 | 10001239 | Adenomatous polyp of cervix (excl mucous polyp) | MedDRA |
| 36672360 | 10066346 | Portio polyp | MedDRA |
| 36672359 | 10050072 | Endocervical polyp | MedDRA |
| 36672358 | 10036124 | Polyp of cervix | MedDRA |
| 36672357 | 10028138 | Mucous polyp of cervix | MedDRA |
| 36672356 | 10008320 | Cervical uterine polyp | MedDRA |
| 36672354 | 10028673 | Nabothian cyst | MedDRA |
| 36672352 | 10048864 | Benign cervical tumor | MedDRA |
| 36672350 | 10004247 | Benign cervix uteri neoplasm NOS | MedDRA |
| 36672349 | 10004246 | Benign cervical tumour | MedDRA |
| 36617601 | 10008354 | Cervix neoplasm | MedDRA |
| 36617573 | 10041848 | Squamous cell carcinoma of the cervix | MedDRA |
| 36617572 | 10041057 | Small cell carcinoma of the cervix | MedDRA |
| 36617571 | 10008348 | Cervix carcinoma stage IV | MedDRA |
| 36617570 | 10008347 | Cervix carcinoma stage III | MedDRA |
| 36617569 | 10008346 | Cervix carcinoma stage II | MedDRA |
| 36617568 | 10008345 | Cervix carcinoma stage I | MedDRA |
| 36617567 | 10061809 | Cervix carcinoma stage 0 | MedDRA |
| 36617566 | 10008344 | Cervix carcinoma recurrent | MedDRA |
| 36617565 | 10008342 | Cervix carcinoma | MedDRA |
| 36617564 | 10055094 | Cervix cancer metastatic | MedDRA |
| 36617563 | 10001244 | Adenosquamous carcinoma of the cervix | MedDRA |
| 36617562 | 10001197 | Adenocarcinoma of the cervix | MedDRA |
| 36617533 | 10008338 | Cervix adenomatous polyp | MedDRA |
| 36617532 | 10008297 | Cervical polyp | MedDRA |
| 36617531 | 10008254 | Cervical cyst | MedDRA |
| 36617530 | 10004312 | Benign neoplasm of cervix uteri | MedDRA |
| 4319273 | 22288000 | Tumor of cervix affecting pregnancy | SNOMED |
| 4314644 | 94819002 | Neoplasm of uncertain behavior of endocervix | SNOMED |
| 4314638 | 94792004 | Neoplasm of uncertain behavior of uterine cervix | SNOMED |
| 4313498 | 94829009 | Neoplasm of uncertain behavior of exocervix | SNOMED |
| 4311881 | 94290006 | Secondary malignant neoplasm of exocervix | SNOMED |
| 4310575 | 423973006 | Carcinoma of uterine cervix, invasive | SNOMED |
| 4294181 | 385478001 | Adenoma malignum | SNOMED |
| 4289673 | 369497003 | Malignant tumor involving uterine cervix by direct extension from fallopian tube | SNOMED |
| 4289386 | 369501008 | Malignant tumor involving uterine cervix by separate metastasis from ovary | SNOMED |
| 4283743 | 369500009 | Malignant tumor involving uterine cervix by separate metastasis from fallopian tube | SNOMED |
| 4283742 | 369499000 | Malignant tumor involving uterine cervix by direct extension from vagina | SNOMED |
| 4281162 | 369574004 | Malignant tumor involving uterine cervix by separate metastasis from vagina | SNOMED |
| 4281020 | 369498008 | Malignant tumor involving uterine cervix by direct extension from ovary | SNOMED |
| 4247949 | 94279001 | Secondary malignant neoplasm of endocervix | SNOMED |
| 4247367 | 406103009 | Squamous cell carcinoma in situ of uterine cervix | SNOMED |
| 4239880 | 92095007 | Benign neoplasm of exocervix | SNOMED |
| 4239878 | 92084001 | Benign neoplasm of endocervix | SNOMED |
| 4239635 | 58881007 | Polyp of cervix affecting pregnancy | SNOMED |
| 4220210 | 8220004 | Endocervical polyp | SNOMED |
| 4219339 | 81956008 | Cyst of cervix | SNOMED |
| 4216500 | 80914001 | Anaplasia of cervix | SNOMED |
| 4201484 | 314970000 | Local recurrence of malignant tumor of cervix | SNOMED |
| 4162134 | 372098004 | Carcinoma of endocervix | SNOMED |
| 4157450 | 372100004 | Carcinoma of exocervix | SNOMED |
| 4131759 | 126913006 | Neoplasm of exocervix | SNOMED |
| 4131009 | 126912001 | Neoplasm of endocervix | SNOMED |
| 4116358 | 255196008 | Adenomatous polyp of cervix | SNOMED |
| 4116083 | 254891007 | Cervical fibroid | SNOMED |
| 4116082 | 254889004 | Carcinoma of cervix stage 0 | SNOMED |
| 4116081 | 254888007 | Adenosquamous carcinoma of cervix | SNOMED |
| 4116080 | 254886006 | Squamous cell carcinoma of cervix | SNOMED |
| 4112876 | 254892000 | Fibroid polyp of cervix | SNOMED |
| 4112875 | 254890008 | Adenocarcinoma in situ of cervix | SNOMED |
| 4112314 | 285432005 | Carcinoma of cervix | SNOMED |
| 4110872 | 254887002 | Adenocarcinoma of cervix | SNOMED |
| 4108901 | 253833001 | Embryonic cyst of cervix | SNOMED |
| 4098948 | 252991009 | Cervical intraepithelial neoplasia grade III with severe dysplasia | SNOMED |
| 4095927 | 248936004 | Polyp at cervical os | SNOMED |
| 4095746 | 188183000 | Malignant neoplasm of cervical stump | SNOMED |
| 4095158 | 188184006 | Malignant neoplasm of squamocolumnar junction of cervix | SNOMED |
| 4095156 | 188176007 | Malignant neoplasm of endocervical canal | SNOMED |
| 4092514 | 188177003 | Malignant neoplasm of endocervical gland | SNOMED |
| 4091766 | 188469005 | Secondary malignant neoplasm of cervix uteri | SNOMED |
| 4077230 | 24565001 | Nabothian follicles on cervix | SNOMED |
| 4061209 | 198203009 | Cervicitis with Nabothian cyst | SNOMED |
| 4061049 | 198206001 | Endocervicitis with Nabothian cyst | SNOMED |
| 4047649 | 123842006 | Endocervical adenocarcinoma | SNOMED |
| 4047648 | 123841004 | Neoplasm of uterine cervix | SNOMED |
| 4023453 | 19372002 | Chronic cystic cervicitis | SNOMED |
| 4003682 | 109880006 | Overlapping malignant neoplasm of uterine cervix | SNOMED |
| 506725 | 1.054E+15 | Invasive carcinoma of uterine cervix co-occurrent with human immunodeficiency virus infection | SNOMED |
| 441805 | 93779009 | Primary malignant neoplasm of endocervix | SNOMED |
| 436358 | 93789008 | Primary malignant neoplasm of exocervix | SNOMED |
| 198572 | 285636001 | Cervical intraepithelial neoplasia | SNOMED |

Endometrial Neoplasm

|  |  |  |  |
| --- | --- | --- | --- |
| Concept Id | Concept Code | Name | Vocabulary |
| 4048225 | 123844007 | Neoplasm of endometrium | SNOMED |
| 4303970 | 419327006 | Endometrial intraepithelial neoplasia | SNOMED |
| 44783287 | 699358009 | High grade endometrial stromal sarcoma | SNOMED |
| 44783286 | 699357004 | Low grade endometrial stromal sarcoma | SNOMED |
| 44783285 | 699356008 | Endometrial stromal sarcoma | SNOMED |
| 44503554 | 8490/3-C54.1 | Signet ring cell carcinoma of Endometrium | ICDO3 |
| 44503094 | 8481/3-C54.1 | Mucin-producing adenocarcinoma of Endometrium | ICDO3 |
| 44503024 | 8482/3-C54.1 | Mucinous adenocarcinoma, endocervical type of Endometrium | ICDO3 |
| 44503016 | 8201/3-C54.1 | Cribriform carcinoma of Endometrium | ICDO3 |
| 44502725 | 8935/3-C54.1 | Stromal sarcoma of Endometrium | ICDO3 |
| 44502648 | 8951/3-C54.1 | Mesodermal mixed tumor of Endometrium | ICDO3 |
| 44502629 | 8461/3-C54.1 | Serous surface papillary carcinoma of Endometrium | ICDO3 |
| 44502430 | 8070/2-C54.1 | Squamous cell carcinoma in situ of Endometrium | ICDO3 |
| 44502407 | 8981/3-C54.1 | Carcinosarcoma, embryonal of Endometrium | ICDO3 |
| 44502362 | 9473/3-C54.1 | Primitive neuroectodermal tumor of Endometrium | ICDO3 |
| 44502297 | 8940/3-C54.1 | Mixed tumor, malignant of Endometrium | ICDO3 |
| 44502184 | 8803/3-C54.1 | Small cell sarcoma of Endometrium | ICDO3 |
| 44502083 | 8070/3-C54.1 | Squamous cell carcinoma of Endometrium | ICDO3 |
| 44502010 | 8071/3-C54.1 | Squamous cell carcinoma, keratinizing of Endometrium | ICDO3 |
| 44502002 | 8010/3-C54.1 | Carcinoma of Endometrium | ICDO3 |
| 44501895 | 8480/3-C54.1 | Mucinous adenocarcinoma of Endometrium | ICDO3 |
| 44501876 | 8041/3-C54.1 | Small cell carcinoma of Endometrium | ICDO3 |
| 44501852 | 8380/3-C54.1 | Endometrioid adenocarcinoma of Endometrium | ICDO3 |
| 44501801 | 8381/3-C54.1 | Endometrioid adenofibroma, malignant of Endometrium | ICDO3 |
| 44501741 | 8980/3-C54.1 | Carcinosarcoma of Endometrium | ICDO3 |
| 44501536 | 8891/3-C54.1 | Epithelioid leiomyosarcoma of Endometrium | ICDO3 |
| 44501496 | 8255/3-C54.1 | Adenocarcinoma with mixed subtypes of Endometrium | ICDO3 |
| 44501450 | 8890/3-C54.1 | Leiomyosarcoma of Endometrium | ICDO3 |
| 44500915 | 8005/3-C54.1 | Malignant tumor, clear cell type of Endometrium | ICDO3 |
| 44500868 | 8120/3-C54.1 | Transitional cell carcinoma of Endometrium | ICDO3 |
| 44500815 | 9100/3-C54.1 | Choriocarcinoma of Endometrium | ICDO3 |
| 44500806 | 8801/3-C54.1 | Spindle cell sarcoma of Endometrium | ICDO3 |
| 44500692 | 9105/3-C54.1 | Trophoblastic tumor, epithelioid of Endometrium | ICDO3 |
| 44500519 | 8910/3-C54.1 | Embryonal rhabdomyosarcoma of Endometrium | ICDO3 |
| 44500503 | 8384/3-C54.1 | Adenocarcinoma, endocervical type of Endometrium | ICDO3 |
| 44500399 | 8050/3-C54.1 | Papillary carcinoma of Endometrium | ICDO3 |
| 44500299 | 8382/3-C54.1 | Endometrioid adenocarcinoma, secretory variant of Endometrium | ICDO3 |
| 44500253 | 8380/1-C54.1 | Endometrioid adenoma, borderline malignancy of Endometrium | ICDO3 |
| 44500159 | 8933/3-C54.1 | Adenosarcoma of Endometrium | ICDO3 |
| 44500084 | 8800/3-C54.1 | Sarcoma of Endometrium | ICDO3 |
| 44500066 | 8441/3-C54.1 | Serous cystadenocarcinoma of Endometrium | ICDO3 |
| 44499901 | 8570/3-C54.1 | Adenocarcinoma with squamous metaplasia of Endometrium | ICDO3 |
| 44499887 | 8210/2-C54.1 | Adenocarcinoma in situ in adenomatous polyp of Endometrium | ICDO3 |
| 44499812 | 8323/3-C54.1 | Mixed cell adenocarcinoma of Endometrium | ICDO3 |
| 44499709 | 8012/3-C54.1 | Large cell carcinoma of Endometrium | ICDO3 |
| 44499653 | 8523/3-C54.1 | Infiltrating duct mixed with other types of carcinoma of Endometrium | ICDO3 |
| 44499546 | 8260/3-C54.1 | Papillary adenocarcinoma of Endometrium | ICDO3 |
| 44498953 | 8210/3-C54.1 | Adenocarcinoma in adenomatous polyp of Endometrium | ICDO3 |
| 40491873 | 447266004 | Sarcoma of endometrium | SNOMED |
| 40489883 | 446887007 | Endometrial stromal tumor | SNOMED |
| 37395565 | 1.07781E+14 | Primary papillary serous cystadenocarcinoma of endometrium | SNOMED |
| 37116597 | 733360000 | Primary undifferentiated carcinoma of endometrium | SNOMED |
| 37116596 | 733359005 | Primary squamous cell carcinoma of endometrium | SNOMED |
| 37115735 | 732201008 | Carcinosarcoma of endometrium | SNOMED |
| 37016125 | 1.07791E+14 | Primary adenosquamous carcinoma of endometrium | SNOMED |
| 37016124 | 1.07771E+14 | Primary malignant clear cell neoplasm of endometrium | SNOMED |
| 37016123 | 1.07751E+14 | Primary malignant mixed Mullerian neoplasm of endometrium | SNOMED |
| 36717227 | 722680009 | Primary serous adenocarcinoma of endometrium | SNOMED |
| 36716616 | 722682001 | Primary small cell carcinoma of endometrium | SNOMED |
| 36716615 | 722681008 | Primary mixed adenocarcinoma of endometrium | SNOMED |
| 36716614 | 722679006 | Primary mucinous adenocarcinoma of endometrium | SNOMED |
| 36672718 | 10028993 | Neoplasm endometrium | MedDRA |
| 36672717 | 10014768 | Endometrial neoplasm NOS | MedDRA |
| 36672715 | 10014758 | Endometrial neoplasia | MedDRA |
| 36617602 | 10014759 | Endometrial neoplasm | MedDRA |
| 4313495 | 94821007 | Neoplasm of uncertain behavior of endometrium | SNOMED |
| 4311879 | 94281004 | Secondary malignant neoplasm of endometrium | SNOMED |
| 4247238 | 93781006 | Primary malignant neoplasm of endometrium | SNOMED |
| 4241777 | 92582009 | Carcinoma in situ of endometrium | SNOMED |
| 4241030 | 92086004 | Benign neoplasm of endometrium | SNOMED |
| 4110871 | 254878006 | Endometrial carcinoma | SNOMED |
| 4095749 | 188192002 | Malignant neoplasm of endometrium of corpus uteri | SNOMED |
| 4048226 | 123845008 | Adenocarcinoma of endometrium | SNOMED |

High Grade Cervical Neoplasm Outcome

|  |  |  |  |
| --- | --- | --- | --- |
| Id | Code | Name | Vocabulary |
| 196359 | 372024009 | Primary malignant neoplasm of uterine cervix | SNOMED |
| 198984 | 363354003 | Malignant tumor of cervix | SNOMED |
| 194611 | 92564006 | Carcinoma in situ of uterine cervix | SNOMED |
| 4157449 | 372097009 | Malignant neoplasm of endocervix | SNOMED |
| 196165 | 285838002 | Cervical intraepithelial neoplasia grade 2 | SNOMED |
| 4162876 | 372099007 | Malignant neoplasm of exocervix | SNOMED |
| 4092515 | 188180002 | Malignant neoplasm, overlapping lesion of cervix uteri | SNOMED |
| 4243120 | 92580001 | Carcinoma in situ of endocervix | SNOMED |
| 4243874 | 92588008 | Carcinoma in situ of exocervix | SNOMED |
| 45885701 | 10074909 | Clear cell carcinoma of cervix | MedDRA |
| 44503140 | 8077/2-C53.0 | Squamous intraepithelial neoplasia, high grade of Endocervix | ICDO3 |
| 44503108 | 8935/3-C53.0 | Stromal sarcoma of Endocervix | ICDO3 |
| 44502927 | 8072/3-C53.9 | Squamous cell carcinoma, large cell, nonkeratinizing of Cervix uteri | ICDO3 |
| 44502813 | 8120/2-C53.9 | Transitional cell carcinoma in situ of Cervix uteri | ICDO3 |
| 44502690 | 8070/3-C53.0 | Squamous cell carcinoma of Endocervix | ICDO3 |
| 44502645 | 8933/3-C53.0 | Adenosarcoma of Endocervix | ICDO3 |
| 44502600 | 8015/3-C53.9 | Glassy cell carcinoma of Cervix uteri | ICDO3 |
| 44502575 | 8560/3-C53.0 | Adenosquamous carcinoma of Endocervix | ICDO3 |
| 44502558 | 8950/3-C53.9 | Mullerian mixed tumor of Cervix uteri | ICDO3 |
| 44502521 | 8073/3-C53.9 | Squamous cell carcinoma, small cell, nonkeratinizing of Cervix uteri | ICDO3 |
| 44502520 | 8071/3-C53.0 | Squamous cell carcinoma, keratinizing of Endocervix | ICDO3 |
| 44502472 | 8461/3-C53.9 | Serous surface papillary carcinoma of Cervix uteri | ICDO3 |
| 44502450 | 8070/2-C53.0 | Squamous cell carcinoma in situ of Endocervix | ICDO3 |
| 44502445 | 8380/3-C53.9 | Endometrioid adenocarcinoma of Cervix uteri | ICDO3 |
| 44502392 | 8310/3-C53.0 | Clear cell adenocarcinoma of Endocervix | ICDO3 |
| 44502310 | 9680/3-C53.9 | Malignant lymphoma, large B-cell, diffuse of Cervix uteri | ICDO3 |
| 44502249 | 8933/3-C53.9 | Adenosarcoma of Cervix uteri | ICDO3 |
| 44502247 | 8910/3-C53.9 | Embryonal rhabdomyosarcoma of Cervix uteri | ICDO3 |
| 44502096 | 8144/3-C53.9 | Adenocarcinoma, intestinal type of Cervix uteri | ICDO3 |
| 44502012 | 8077/2-C53.1 | Squamous intraepithelial neoplasia, high grade of Exocervix | ICDO3 |
| 44501964 | 8745/3-C53.9 | Desmoplastic melanoma, malignant of Cervix uteri | ICDO3 |
| 44501939 | 8323/3-C53.0 | Mixed cell adenocarcinoma of Endocervix | ICDO3 |
| 44501802 | 8384/3-C53.0 | Adenocarcinoma, endocervical type of Endocervix | ICDO3 |
| 44501784 | 8083/3-C53.9 | Basaloid squamous cell carcinoma of Cervix uteri | ICDO3 |
| 44501641 | 8263/3-C53.9 | Adenocarcinoma in tubulovillous adenoma of Cervix uteri | ICDO3 |
| 44501637 | 8246/3-C53.9 | Neuroendocrine carcinoma of Cervix uteri | ICDO3 |
| 44501580 | 8482/3-C53.9 | Mucinous adenocarcinoma, endocervical type of Cervix uteri | ICDO3 |
| 44501517 | 8074/3-C53.9 | Squamous cell carcinoma, spindle cell of Cervix uteri | ICDO3 |
| 44501441 | 8441/3-C53.0 | Serous cystadenocarcinoma of Endocervix | ICDO3 |
| 44501420 | 8806/3-C53.9 | Desmoplastic small round cell tumor of Cervix uteri | ICDO3 |
| 44501401 | 8140/2-C54.9 | Adenocarcinoma in situ of Corpus uteri | ICDO3 |
| 44501396 | 8070/3-C53.1 | Squamous cell carcinoma of Exocervix | ICDO3 |
| 44501336 | 8077/2-C53.9 | Squamous intraepithelial neoplasia, high grade of Cervix uteri | ICDO3 |
| 44501289 | 8951/3-C53.9 | Mesodermal mixed tumor of Cervix uteri | ICDO3 |
| 44501255 | 8073/3-C53.0 | Squamous cell carcinoma, small cell, nonkeratinizing of Endocervix | ICDO3 |
| 44501228 | 8890/3-C53.0 | Leiomyosarcoma of Endocervix | ICDO3 |
| 44501193 | 8076/3-C53.0 | Squamous cell carcinoma, microinvasive of Endocervix | ICDO3 |
| 44501182 | 8052/3-C53.9 | Papillary squamous cell carcinoma of Cervix uteri | ICDO3 |
| 44501133 | 8144/3-C53.0 | Adenocarcinoma, intestinal type of Endocervix | ICDO3 |
| 44501016 | 8460/3-C53.9 | Papillary serous cystadenocarcinoma of Cervix uteri | ICDO3 |
| 44500998 | 8098/3-C53.0 | Adenoid basal carcinoma of Endocervix | ICDO3 |
| 44500990 | 8076/3-C53.1 | Squamous cell carcinoma, microinvasive of Exocervix | ICDO3 |
| 44500980 | 8052/3-C53.1 | Papillary squamous cell carcinoma of Exocervix | ICDO3 |
| 44500817 | 9150/3-C53.9 | Hemangiopericytoma, malignant of Cervix uteri | ICDO3 |
| 44500545 | 8070/3-C53.9 | Squamous cell carcinoma of Cervix uteri | ICDO3 |
| 44500540 | 8020/3-C53.0 | Carcinoma, undifferentiated of Endocervix | ICDO3 |
| 44500521 | 9110/3-C53.9 | Mesonephroma, malignant of Cervix uteri | ICDO3 |
| 44500513 | 8800/3-C53.9 | Sarcoma of Cervix uteri | ICDO3 |
| 44500492 | 8076/3-C53.9 | Squamous cell carcinoma, microinvasive of Cervix uteri | ICDO3 |
| 44500434 | 8072/3-C53.0 | Squamous cell carcinoma, large cell, nonkeratinizing of Endocervix | ICDO3 |
| 44500377 | 8910/3-C53.0 | Embryonal rhabdomyosarcoma of Endocervix | ICDO3 |
| 44500297 | 8260/3-C53.9 | Papillary adenocarcinoma of Cervix uteri | ICDO3 |
| 44500296 | 8255/3-C53.9 | Adenocarcinoma with mixed subtypes of Cervix uteri | ICDO3 |
| 44500269 | 8951/3-C53.0 | Mesodermal mixed tumor of Endocervix | ICDO3 |
| 44500258 | 8482/3-C53.0 | Mucinous adenocarcinoma, endocervical type of Endocervix | ICDO3 |
| 44500232 | 8013/3-C53.9 | Large cell neuroendocrine carcinoma of Cervix uteri | ICDO3 |
| 44500146 | 8480/3-C53.0 | Mucinous adenocarcinoma of Endocervix | ICDO3 |
| 44500143 | 8384/3-C53.9 | Adenocarcinoma, endocervical type of Cervix uteri | ICDO3 |
| 44500091 | 8950/3-C53.0 | Mullerian mixed tumor of Endocervix | ICDO3 |
| 44499916 | 8310/3-C53.9 | Clear cell adenocarcinoma of Cervix uteri | ICDO3 |
| 44499910 | 9110/3-C53.0 | Mesonephroma, malignant of Endocervix | ICDO3 |
| 44499817 | 8490/3-C53.0 | Signet ring cell carcinoma of Endocervix | ICDO3 |
| 44499752 | 8520/2-C53.9 | Lobular carcinoma in situ of Cervix uteri | ICDO3 |
| 44499749 | 8480/3-C53.9 | Mucinous adenocarcinoma of Cervix uteri | ICDO3 |
| 44499746 | 8441/3-C53.9 | Serous cystadenocarcinoma of Cervix uteri | ICDO3 |
| 44499713 | 8032/3-C53.9 | Spindle cell carcinoma of Cervix uteri | ICDO3 |
| 44499680 | 8052/2-C53.9 | Papillary squamous cell carcinoma, non-invasive of Cervix uteri | ICDO3 |
| 44499679 | 8041/3-C53.9 | Small cell carcinoma of Cervix uteri | ICDO3 |
| 44499647 | 8460/3-C53.0 | Papillary serous cystadenocarcinoma of Endocervix | ICDO3 |
| 44499644 | 8323/3-C53.9 | Mixed cell adenocarcinoma of Cervix uteri | ICDO3 |
| 44499568 | 8801/3-C53.9 | Spindle cell sarcoma of Cervix uteri | ICDO3 |
| 44499509 | 8380/3-C53.0 | Endometrioid adenocarcinoma of Endocervix | ICDO3 |
| 44499507 | 8260/3-C53.0 | Papillary adenocarcinoma of Endocervix | ICDO3 |
| 44499485 | 8070/2-C53.1 | Squamous cell carcinoma in situ of Exocervix | ICDO3 |
| 44499458 | 8890/3-C53.9 | Leiomyosarcoma of Cervix uteri | ICDO3 |
| 44499445 | 8481/3-C53.0 | Mucin-producing adenocarcinoma of Endocervix | ICDO3 |
| 44499013 | 8071/3-C53.9 | Squamous cell carcinoma, keratinizing of Cervix uteri | ICDO3 |
| 44498939 | 8042/3-C53.9 | Oat cell carcinoma of Cervix uteri | ICDO3 |
| 42689509 | 1.0647E+15 | CGIN - cervical glandular intraepithelial neoplasia | SNOMED |
| 40493012 | 449059000 | Follicular non-Hodgkin's lymphoma of uterine cervix | SNOMED |
| 40491512 | 448774004 | Non-Hodgkin's lymphoma of uterine cervix | SNOMED |
| 40490518 | 448607004 | Diffuse non-Hodgkin's lymphoma of uterine cervix | SNOMED |
| 40486538 | 447760009 | Endocervical adenocarcinoma in situ | SNOMED |
| 37116830 | 733834006 | Invasive carcinoma of uterine cervix co-occurrent with human immunodeficiency virus infection | SNOMED |
| 37103694 | 10029109 | Cervix neoplasms | MedDRA |
| 37016242 | 2.0804E+14 | Primary adenocarcinoma of endocervix | SNOMED |
| 37016238 | 1.8478E+14 | Primary adenocarcinoma of cervix uteri | SNOMED |
| 36716617 | 722683006 | Primary neuroendocrine carcinoma of cervix uteri | SNOMED |
| 36672714 | 10029103 | Neoplasm uterine cervix | MedDRA |
| 36672713 | 10028986 | Neoplasm cervix | MedDRA |
| 36672711 | 10008290 | Cervical neoplasm NOS | MedDRA |
| 36672591 | 10065355 | Lymphoepithelioma-like carcinoma of cervix stage IV | MedDRA |
| 36672590 | 10028991 | Neoplasm cervix stage IV | MedDRA |
| 36672589 | 10026271 | Malignant neoplasm of other specified sites of cervix stage IV | MedDRA |
| 36672588 | 10025908 | Malignant neoplasm of exocervix stage IV | MedDRA |
| 36672587 | 10025896 | Malignant neoplasm of endocervix stage IV | MedDRA |
| 36672586 | 10025836 | Malignant neoplasm of cervix uteri stage IV | MedDRA |
| 36672585 | 10008367 | Cervix uteri cancer stage IV | MedDRA |
| 36672584 | 10008359 | Cervix neoplasm stage IV | MedDRA |
| 36672582 | 10008249 | Cervical carcinoma stage IVB | MedDRA |
| 36672581 | 10008248 | Cervical carcinoma stage IVA | MedDRA |
| 36672580 | 10008247 | Cervical carcinoma stage IV | MedDRA |
| 36672579 | 10008236 | Cervical cancer stage IV | MedDRA |
| 36672578 | 10007499 | Carcinoma uterine cervix stage IV | MedDRA |
| 36672576 | 10007329 | Carcinoma cervix stage IV | MedDRA |
| 36672574 | 10065354 | Lymphoepithelioma-like carcinoma of cervix stage III | MedDRA |
| 36672573 | 10028990 | Neoplasm cervix stage III | MedDRA |
| 36672572 | 10026270 | Malignant neoplasm of other specified sites of cervix stage III | MedDRA |
| 36672571 | 10025907 | Malignant neoplasm of exocervix stage III | MedDRA |
| 36672570 | 10025895 | Malignant neoplasm of endocervix stage III | MedDRA |
| 36672569 | 10025835 | Malignant neoplasm of cervix uteri stage III | MedDRA |
| 36672568 | 10008366 | Cervix uteri cancer stage III | MedDRA |
| 36672567 | 10008358 | Cervix neoplasm stage III | MedDRA |
| 36672565 | 10008246 | Cervical carcinoma stage III | MedDRA |
| 36672564 | 10008235 | Cervical cancer stage III | MedDRA |
| 36672563 | 10007498 | Carcinoma uterine cervix stage III | MedDRA |
| 36672561 | 10007328 | Carcinoma cervix stage III | MedDRA |
| 36672559 | 10065353 | Lymphoepithelioma-like carcinoma of cervix stage II | MedDRA |
| 36672558 | 10028989 | Neoplasm cervix stage II | MedDRA |
| 36672557 | 10026269 | Malignant neoplasm of other specified sites of cervix stage II | MedDRA |
| 36672556 | 10025906 | Malignant neoplasm of exocervix stage II | MedDRA |
| 36672555 | 10025894 | Malignant neoplasm of endocervix stage II | MedDRA |
| 36672554 | 10025834 | Malignant neoplasm of cervix uteri stage II | MedDRA |
| 36672553 | 10008365 | Cervix uteri cancer stage II | MedDRA |
| 36672552 | 10008357 | Cervix neoplasm stage II | MedDRA |
| 36672550 | 10008245 | Cervical carcinoma stage IIB | MedDRA |
| 36672549 | 10008244 | Cervical carcinoma stage IIA | MedDRA |
| 36672548 | 10008243 | Cervical carcinoma stage II | MedDRA |
| 36672547 | 10008234 | Cervical cancer stage II | MedDRA |
| 36672546 | 10007497 | Carcinoma uterine cervix stage II | MedDRA |
| 36672544 | 10007327 | Carcinoma cervix stage II | MedDRA |
| 36672542 | 10067069 | Microinvasive cervix cancer | MedDRA |
| 36672541 | 10065352 | Lymphoepithelioma-like carcinoma of cervix stage I | MedDRA |
| 36672540 | 10028988 | Neoplasm cervix stage I | MedDRA |
| 36672539 | 10026268 | Malignant neoplasm of other specified sites of cervix stage I | MedDRA |
| 36672538 | 10025905 | Malignant neoplasm of exocervix stage I | MedDRA |
| 36672537 | 10025893 | Malignant neoplasm of endocervix stage I | MedDRA |
| 36672536 | 10025833 | Malignant neoplasm of cervix uteri stage I | MedDRA |
| 36672535 | 10008364 | Cervix uteri cancer stage I | MedDRA |
| 36672534 | 10008356 | Cervix neoplasm stage I | MedDRA |
| 36672532 | 10008242 | Cervical carcinoma stage IB | MedDRA |
| 36672531 | 10008241 | Cervical carcinoma stage IA | MedDRA |
| 36672530 | 10008240 | Cervical carcinoma stage I | MedDRA |
| 36672529 | 10008233 | Cervical cancer stage I | MedDRA |
| 36672528 | 10007496 | Carcinoma uterine cervix stage I | MedDRA |
| 36672526 | 10007326 | Carcinoma cervix stage I | MedDRA |
| 36672524 | 10065697 | Papanicolaou smear abnormal, class IV b | MedDRA |
| 36672523 | 10065696 | Papanicolaou smear abnormal, class IV a | MedDRA |
| 36672522 | 10065351 | Lymphoepithelioma-like carcinoma of cervix stage 0 | MedDRA |
| 36672520 | 10059383 | Cervical carcinoma stage 0 | MedDRA |
| 36672519 | 10046771 | Uterine cervix carcinoma stage 0 | MedDRA |
| 36672518 | 10021571 | In situ cancer of cervix | MedDRA |
| 36672517 | 10009215 | CIS of cervix | MedDRA |
| 36672516 | 10008343 | Cervix carcinoma in situ | MedDRA |
| 36672515 | 10008237 | Cervical carcinoma in situ | MedDRA |
| 36672514 | 10008232 | Cervical cancer stage 0 | MedDRA |
| 36672513 | 10007494 | Carcinoma uterine cervix in situ | MedDRA |
| 36672512 | 10007364 | Carcinoma in situ of cervix uteri | MedDRA |
| 36672511 | 10007363 | Carcinoma in situ of cervix | MedDRA |
| 36672510 | 10007324 | Carcinoma cervix in situ | MedDRA |
| 36672509 | 10065592 | Lymphoepithelioma-like carcinoma of cervix recurrent | MedDRA |
| 36672508 | 10028987 | Neoplasm cervix recurrent | MedDRA |
| 36672507 | 10026267 | Malignant neoplasm of other specified sites of cervix recurrent | MedDRA |
| 36672506 | 10025904 | Malignant neoplasm of exocervix recurrent | MedDRA |
| 36672505 | 10025892 | Malignant neoplasm of endocervix recurrent | MedDRA |
| 36672504 | 10025832 | Malignant neoplasm of cervix uteri recurrent | MedDRA |
| 36672503 | 10008363 | Cervix uteri cancer recurrent | MedDRA |
| 36672502 | 10008355 | Cervix neoplasm recurrent | MedDRA |
| 36672500 | 10008239 | Cervical carcinoma recurrent | MedDRA |
| 36672499 | 10008231 | Cervical cancer recurrent | MedDRA |
| 36672498 | 10007495 | Carcinoma uterine cervix recurrent | MedDRA |
| 36672496 | 10007325 | Carcinoma cervix recurrent | MedDRA |
| 36672494 | 10065698 | Papanicolaou smear abnormal, class V | MedDRA |
| 36672493 | 10065350 | Lymphoepithelioma-like carcinoma of cervix | MedDRA |
| 36672492 | 10064444 | Invasive cervix cancer | MedDRA |
| 36672490 | 10025903 | Malignant neoplasm of exocervix | MedDRA |
| 36672489 | 10025891 | Malignant neoplasm of endocervix | MedDRA |
| 36672488 | 10025837 | Malignant neoplasm of cervix uteri, unspecified | MedDRA |
| 36672487 | 10025831 | Malignant neoplasm of cervix uteri | MedDRA |
| 36672486 | 10008362 | Cervix uteri cancer | MedDRA |
| 36672484 | 10008238 | Cervical carcinoma NOS | MedDRA |
| 36672483 | 10008229 | Cervical cancer | MedDRA |
| 36672482 | 10007493 | Carcinoma uterine cervix | MedDRA |
| 36672480 | 10007323 | Carcinoma cervix | MedDRA |
| 36672478 | 10065593 | Lymphoepithelioma-like carcinoma of cervix metastatic | MedDRA |
| 36672476 | 10008226 | Cervical adenosquamous carcinoma | MedDRA |
| 36672474 | 10008224 | Cervical adenocarcinoma | MedDRA |
| 36672354 | 10028673 | Nabothian cyst | MedDRA |
| 36617601 | 10008354 | Cervix neoplasm | MedDRA |
| 36617573 | 10041848 | Squamous cell carcinoma of the cervix | MedDRA |
| 36617572 | 10041057 | Small cell carcinoma of the cervix | MedDRA |
| 36617571 | 10008348 | Cervix carcinoma stage IV | MedDRA |
| 36617570 | 10008347 | Cervix carcinoma stage III | MedDRA |
| 36617569 | 10008346 | Cervix carcinoma stage II | MedDRA |
| 36617568 | 10008345 | Cervix carcinoma stage I | MedDRA |
| 36617567 | 10061809 | Cervix carcinoma stage 0 | MedDRA |
| 36617566 | 10008344 | Cervix carcinoma recurrent | MedDRA |
| 36617565 | 10008342 | Cervix carcinoma | MedDRA |
| 36617564 | 10055094 | Cervix cancer metastatic | SNOMED |
| 36617563 | 10001244 | Adenosquamous carcinoma of the cervix | SNOMED |
| 36617562 | 10001197 | Adenocarcinoma of the cervix | SNOMED |
| 36617531 | 10008254 | Cervical cyst | SNOMED |
| 4319273 | 22288000 | Tumor of cervix affecting pregnancy | SNOMED |
| 4314644 | 94819002 | Neoplasm of uncertain behavior of endocervix | SNOMED |
| 4314638 | 94792004 | Neoplasm of uncertain behavior of uterine cervix | SNOMED |
| 4313498 | 94829009 | Neoplasm of uncertain behavior of exocervix | SNOMED |
| 4311881 | 94290006 | Secondary malignant neoplasm of exocervix | SNOMED |
| 4310575 | 423973006 | Carcinoma of uterine cervix, invasive | SNOMED |
| 4294181 | 385478001 | Adenoma malignum | SNOMED |
| 4289673 | 369497003 | Malignant tumor involving uterine cervix by direct extension from fallopian tube | SNOMED |
| 4289386 | 369501008 | Malignant tumor involving uterine cervix by separate metastasis from ovary | SNOMED |
| 4283743 | 369500009 | Malignant tumor involving uterine cervix by separate metastasis from fallopian tube | SNOMED |
| 4283742 | 369499000 | Malignant tumor involving uterine cervix by direct extension from vagina | SNOMED |
| 4281162 | 369574004 | Malignant tumor involving uterine cervix by separate metastasis from vagina | SNOMED |
| 4281020 | 369498008 | Malignant tumor involving uterine cervix by direct extension from ovary | SNOMED |
| 4247949 | 94279001 | Secondary malignant neoplasm of endocervix | SNOMED |
| 4247367 | 406103009 | Squamous cell carcinoma in situ of uterine cervix | SNOMED |
| 4219339 | 81956008 | Cyst of cervix | SNOMED |
| 4216500 | 80914001 | Anaplasia of cervix | SNOMED |
| 4201484 | 314970000 | Local recurrence of malignant tumor of cervix | SNOMED |
| 4162134 | 372098004 | Carcinoma of endocervix | SNOMED |
| 4157450 | 372100004 | Carcinoma of exocervix | SNOMED |
| 4131759 | 126913006 | Neoplasm of exocervix | SNOMED |
| 4131009 | 126912001 | Neoplasm of endocervix | SNOMED |
| 4116082 | 254889004 | Carcinoma of cervix stage 0 | SNOMED |
| 4116081 | 254888007 | Adenosquamous carcinoma of cervix | SNOMED |
| 4116080 | 254886006 | Squamous cell carcinoma of cervix | SNOMED |
| 4112875 | 254890008 | Adenocarcinoma in situ of cervix | SNOMED |
| 4112314 | 285432005 | Carcinoma of cervix | SNOMED |
| 4110872 | 254887002 | Adenocarcinoma of cervix | SNOMED |
| 4108901 | 253833001 | Embryonic cyst of cervix | SNOMED |
| 4098948 | 252991009 | Cervical intraepithelial neoplasia grade III with severe dysplasia | SNOMED |
| 4095746 | 188183000 | Malignant neoplasm of cervical stump | SNOMED |
| 4095158 | 188184006 | Malignant neoplasm of squamocolumnar junction of cervix | SNOMED |
| 4095156 | 188176007 | Malignant neoplasm of endocervical canal | SNOMED |
| 4092514 | 188177003 | Malignant neoplasm of endocervical gland | Vocabulary |
| 4091766 | 188469005 | Secondary malignant neoplasm of cervix uteri | SNOMED |
| 4077230 | 24565001 | Nabothian follicles on cervix | SNOMED |
| 4061209 | 198203009 | Cervicitis with Nabothian cyst | SNOMED |
| 4061049 | 198206001 | Endocervicitis with Nabothian cyst | SNOMED |
| 4047649 | 123842006 | Endocervical adenocarcinoma | SNOMED |
| 4047648 | 123841004 | Neoplasm of uterine cervix | SNOMED |
| 4023453 | 19372002 | Chronic cystic cervicitis | SNOMED |
| 4003682 | 109880006 | Overlapping malignant neoplasm of uterine cervix | SNOMED |
| 506725 | 1.054E+15 | Invasive carcinoma of uterine cervix co-occurrent with human immunodeficiency virus infection | SNOMED |
| 441805 | 93779009 | Primary malignant neoplasm of endocervix | MedDRA |
| 436358 | 93789008 | Primary malignant neoplasm of exocervix | ICDO3 |
| 198572 | 285636001 | Cervical intraepithelial neoplasia | ICDO3 |

Malignancy Diagnosis

Descendants of “Malignant neoplastic disease” (Concept ID 443392, Concept Code 363346000) were included. Descendants of “Basal cell carcinoma of skin” (Concept ID 4112752, Concept Code 254701007) and “Squamous cell carcinoma of skin” (Concept ID 4111921, Concept Code 234651007) were excluded.

IUD Observations (Claims Database)

|  |  |  |  |
| --- | --- | --- | --- |
| Concept Id | Concept Code | Name | Vocabulary |
| 4061405 | 169477005 | Intrauterine contraceptive device fitted | SNOMED |
| 4186930 | 46706006 | Replacement of intrauterine contraceptive device | SNOMED |
| 4275113 | 65200003 | Insertion of intrauterine contraceptive device | SNOMED |
| 2110194 | 58300 | Insertion of intrauterine device (IUD) | CPT4 |
| 43012754 | 1366343 | Levonorgestrel 0.00354 MG/HR Drug Implant | RxNorm |
| 2718682 | J7300 | Intrauterine copper contraceptive | HCPCS |
| 44792289 | 3.41E+14 | Insertion of T shaped 380 millimetres squared copper coated intrauterine contraceptive device | SNOMED |
| 44792288 | 3.41E+14 | Insertion of T shaped 375 millimetres squared copper coated intrauterine contraceptive device | SNOMED |
| 44792287 | 3.41E+14 | Insertion of frameless 330 millimetres squared copper coated intrauterine contraceptive device | SNOMED |
| 44786600 | Q0090 | Levonorgestrel-releasing intrauterine contraceptive system, (skyla), 13.5 mg | HCPCS |
| 44786565 | J7301 | Levonorgestrel-releasing intrauterine contraceptive system (skyla), 13.5 mg | HCPCS |
| 44127810 | OMOP1122441 | Levonorgestrel 19.5 MG Drug Implant [Kyleena] by Bayer | RxNorm Extension |
| 44123197 | OMOP1117828 | Levonorgestrel 13.5 MG Drug Implant | RxNorm Extension |
| 44121637 | OMOP1116268 | Levonorgestrel Drug Implant [Jaydess] | RxNorm Extension |
| 44101836 | OMOP1096467 | Levonorgestrel 13.5 MG Drug Implant [Jaydess] by Bayer | RxNorm Extension |
| 44101834 | OMOP1096465 | Levonorgestrel 36 MG Drug Implant [Norplant] by Wyeth | RxNorm Extension |
| 44097167 | OMOP1091798 | Levonorgestrel 19.5 MG Drug Implant | RxNorm Extension |
| 44086126 | OMOP1080757 | Levonorgestrel 19.5 MG Drug Implant [Kyleena] | RxNorm Extension |
| 44082723 | OMOP1077354 | Levonorgestrel Drug Implant [Kyleena] | RxNorm Extension |
| 44073214 | OMOP1067845 | Levonorgestrel 52 MG Drug Implant [Mirena] | RxNorm Extension |
| 44073213 | OMOP1067844 | Levonorgestrel 36 MG Drug Implant [Norplant] | RxNorm Extension |
| 44060436 | OMOP1055067 | Levonorgestrel 13.5 MG Drug Implant [Jaydess] | RxNorm Extension |
| 44050232 | OMOP1044863 | Levonorgestrel 52 MG Drug Implant [Mirena] by Bayer | RxNorm Extension |
| 44045536 | OMOP1040167 | Levonorgestrel 52 MG Drug Implant | RxNorm Extension |
| 44045535 | OMOP1040166 | Levonorgestrel 36 MG Drug Implant | RxNorm Extension |
| 44025740 | OMOP1020371 | Levonorgestrel Drug Implant [Mirena] | RxNorm Extension |
| 43020952 | 4.73E+08 | Insertion of hormone releasing intrauterine contraceptive device | SNOMED |
| 43012755 | 1366345 | Levonorgestrel 0.00354 MG/HR Drug Implant [Norplant] | RxNorm |
| 40001199 | 370481 | Levonorgestrel Drug Implant [Norplant] | RxNorm |
| 40001198 | 378923 | Levonorgestrel Drug Implant | RxNorm |
| 19123248 | 608565 | Levonorgestrel 75 MG Drug Implant | RxNorm |
| 2721260 | S4981 | Insertion of levonorgestrel-releasing intrauterine system | HCPCS |
| 2718683 | J7302 | Levonorgestrel-releasing intrauterine contraceptive system, 52 mg | HCPCS |
| 937612 | Q9984 | Levonorgestrel-releasing intrauterine contraceptive system (kyleena), 19.5 mg | HCPCS |
| 937575 | J7296 | Levonorgestrel-releasing intrauterine contraceptive system, (kyleena), 19.5 mg | HCPCS |
| 915801 | J7298 | Levonorgestrel-releasing intrauterine contraceptive system (mirena), 52 mg | HCPCS |
| 915800 | J7297 | Levonorgestrel-releasing intrauterine contraceptive system (liletta), 52 mg | HCPCS |
| 2008124 | 97.71 | Removal of intrauterine contraceptive device | ICD9Proc |
| 2110195 | 58301 | Removal of intrauterine device (IUD) | CPT4 |
| 44513458 | Q12.4 | Removal of intrauterine contraceptive device NEC | OPCS4 |
| 44513457 | Q12.3 | Removal of displaced intrauterine contraceptive device NEC | OPCS4 |
| 44512751 | P31.5 | Removal of intrauterine contraceptive device from pouch of Douglas | OPCS4 |
| 43020953 | 4.73E+08 | Removal of hormone releasing intrauterine contraceptive device | SNOMED |
| 4238715 | 68254000 | Removal of intrauterine device | SNOMED |
| 4074284 | 1.77E+08 | Removal of intrauterine contraceptive device from pouch of Douglas | SNOMED |
| 4072712 | 1.77E+08 | Removal of displaced intrauterine contraceptive device | SNOMED |
| 4032736 | 2.37E+08 | Removal of displaced intrauterine device from peritoneal cavity | SNOMED |