| Project InitiationThis Section must be Completed Prior to Project Dataset(s) Creation |
| --- |
| **Project Title:** | The Incidence and Burden of *Clostridium difficile* in Ontario |
| **Project TRIM number:** | 2017 0970 071 000 |
| **Research Program:** | DAS |
| **Site:** | ICES Central |
| **Project Objectives:** | *Insert Project Objectives as listed in the approved ICES Project PIA* |
| 1. Measure the annual incidence in Ontario of *Clostridium difficile* infection (CDI) requiring hospitalization, overall and in acute care hospitals (ACHs), long-term care facilities (LTCFs) and community-dwelling populations
2. Determine the medical burden associated with CDI in these populations, compared to patients with similar demographics and medical history without CDI
3. Estimate the cost of health care utilization associated with hospitalized CDI in Ontario
 |
| **ICES Project PIA Initial Approval Date:** | *The ICES Employee or agent who is responsible for creating the Project Dataset(s) is responsible for ensuring there is an approved ICES Project PIA and verifying the date of approval prior to creating the Project Dataset(s)* |
| yyyy-mon-dd |
| **Principal Investigator (PI):** | Jennifer Pereirajennifer.pereira@jrlresearch.com |
| **Check the applicable box if the PI is an ICES Student/Trainee** | [ ]  ICES Student [ ]  ICES Fellow [ ]  ICES Post-Doctoral Trainee [ ]  Visiting Scholar |
| **Responsible ICES Scientist:** | *Name the Responsible ICES Scientist if the PI is not a Full Status ICES Scientist* |
| Refik Saskinrefik.saskin@ices.on.ca |
| **Project Team Member(s) Responsible for Project Dataset Creation and/or Statistical Analysis and date joined (list all):** | *All person(s) (ICES Analyst, Appointed Analyst, Analytic Epidemiologist, PI, and/or Student) responsible for creating the Project Dataset(s) and/or statistical analysis on the Research Analytics Environment (RAE) and the date they joined the project must be recorded* |
| Analytic Epidemiologist: Ryan Ngryan.ng@ices.on.caAnalyst: Shudong LiShudong.li@ices.on.ca | 2017-MAR-132017-AUG-09 |
| **Other ICES Project Team Members and date joined (list all):** | *All other Research Project Team Members (e.g., Research Administrative Assistants, Research Assistants, Project Managers, Epidemiologists) and the date they joined the project must be recorded* |
| Project Manager: Lisa Ishigurolisa.ishiguro@ices.on.ca | 2017-MAR-13 |
| **Confirmation that DCP is consistent with Project Objectives:** | *The following individuals must confirm that the ICES Data provided for in this DCP is relevant (e.g., with respect to cohort, timeframe, and variables) and required to achieve the Project Objectives stated in the ICES Project PIA prior to initial Project Dataset creation: 1) PI; 2) Responsible ICES Scientist if the PI is not a Full Status ICES Scientist, or a second ICES Scientist or the Scientific Program Lead if the PI is creating both the DCP and the Project Dataset[s]; 3) ICES Research and Analysis Staff creating the DCP; and 4) ICES Analytic Staff (ICES Employee or agent responsible for creating the Project Dataset[s]). This may be delegated either verbally or via e-mail.* |
| ***Principal Investigator*** | [ ]  | yyyy-mon-dd |
| ***Responsible ICES Scientist or Second ICES Scientist/Lead*** | [ ]  | yyyy-mon-dd |
| ***ICES Research and Analysis Staff Creating the DCP*** | [ ]  | yyyy-mon-dd |
| ***ICES Analytic Staff*** | [ ]  | yyyy-mon-dd |
| **Designated ICES Research and Analysis Staff accountable for Project Documentation:** | *The person named (ICES staff) is accountable for ensuring that the approved ICES Project PIA, ICES Project PIA Amendments, and DCP are saved on the T Drive, ensuring ICES Project PIA Amendments are submitted as required, ensuring DCP Amendments are documented, and sharing the final DCP with the PI/Responsible ICES Scientist at project completion* |
|  |
| **DCP Creation Date and Author:** | *Date DCP was finalized prior to Project Dataset(s) creation* | *Name of person who created the DCP* |
| ***Date*** | ***Name*** |
| yyyy-mon-dd |  |

| ICES DataThis Section must be Completed Prior to Project Dataset(s) Creation |
| --- |
| *The ICES Employee or agent who is responsible for creating the Project Dataset(s) must ensure that this list includes only data listed in the ICES Project PIA**Changes to this list after initial ICES Project PIA approval require an ICES Project PIA Amendment* | *Mandatory for all datasets that are available by individual year* |
| ***General Use Datasets – Health Services*** | ***Years (where applicable)*** |
| CIHI DAD | 2000 to 2016 |
| CIHI SDS | 2000 to 2016 |
| NACRS | 2000 to 2016 |
| OHIP | 2000 to 2016 |
| ODB | 2005 to 2016 |
| ***General Use Datasets – Care Providers*** |  |
| See list |  |
| See list |  |
| ***General Use Datasets – Population*** |  |
| RPDB | 2005 to 2016 |
| POP | 2005 to 2016 |
| ***General Use Datasets – Coding/Geography*** |  |
| LHIN | 2005 to 2016 |
| See list |  |
| ***General Use Datasets – Facilities*** |  |
| INST | 2005 to 2016 |
| ***General Use Datasets – Other*** |  |
| CHF | 2005 to 2016 |
| COPD | 2005 to 2016 |
|  |  |
| Diabetes | 2005 to 2016 |
| ***Controlled Use Datasets*** |  |
|  |  |
| OCR | 2000 to 2016 |
| See list |  |
| ***Other Datasets*** |  |
|  |  |

| Project Amendments and Reconciliation |
| --- |
| **ICES Project PIA Amendment History (add additional rows as needed):** | *Privacy approval date* | *Person who submitted amendment* | *Note that any changes to the list of ICES Data or Project Objectives require an ICES Project PIA Amendment* |
| ***Date*** | ***Name*** | ***Amendment*** |
| yyyy-mon-dd |  |  |
| **DCP Amendment History (add additional rows as needed):** | *Date DCP amended* | *Person who made the DCP amendment* | *Note that any DCP amendments involving changes to the list of ICES Data or Project Objectives require an ICES Project PIA Amendment* |
| ***Date*** | ***Name*** | ***Amendment*** |
| yyyy-mon-dd |  |  |
| **Date Programs/DCP reconciled** | *The person(s) creating the dataset and/or analyzing the data are responsible for ensuring that the final DCP reflects the final program(s) when the project is completed* |
| yyyy-mon-dd |

| Project Cohort I |
| --- |
| **Study Design** | [ ]  Cohort study [x]  Matched cohort study [ ]  Case-control study[ ]  Cross-sectional study [ ]  Other (specify):  |
| **Index Event / Inclusion Criteria** | **I. For incidence rates:** All individuals within the target population that meet the study’s case definition of CDI between Apr 1/2005 – Mar 31/2015 (stratified by CDI association and onset, **Table 1**): 1. Index date is admission date.
2. ICD-10-CM diagnosis code for CDI (A04.7) during an in-patient hospital stay, diagnosis type is M, 1 and 2.
3. at least 18 years at time of diagnosis.
4. no diagnosis code for CDI (any dxtype) in the previous 180 days (to identify only new incident cases of CDI; if a patient has a second CDI diagnosis after 180 days post-discharge, this will be counted as a separate incidence, or a recurrence).

**II. Clinical impact of ACH-associated CDI:** Individuals within the base population that meet the three criteria above will be categorized into three cohorts, and each cohort will be matched to a control group. (\***Note**: a person can be counted in the incidence numerator more than once i.e. they can be eligible multiple times)1. **ACH-acquired Cohort(Groups I and II in Table I):** ICD-10-CM diagnosis code for CDI (A04.7) during an in-patient hospital stay, coded as a post-admit comorbidity of clinical significance (Diagnosis Type 2)

**ACH-acquired Control:** All DAD records with valid ikn and without CDI diagnosis.Ontario residents at hospital admission.No missing value for all matching variables Alive at hospital admission.Aged 18-105 at hospital admissionOHIP eligible at hospital admission.Keep last record for same patient. **Match Criteria:***Hard-matched:* age (plus or minus 2 yrs), sex, hospitalization admission date (plus or minus 90 days), most responsible diagnosis (Diagnosis Type M, match first 3 digits)*Propensity-score matched*: urban/rural score (*rio2008*), LHIN, Elixhauser score1. **LTCF-acquired Cohort (Group III in Table I):** ICD-10-CM diagnosis code for CDI (A04.7) during an in-patient hospital stay, coded as the most responsible diagnosis (Diagnosis Type M) or a pre-admit comorbidity (Diagnosis Type 1) in LTCF residents with no history of hospitalization (excluding ED visits) in the 12 prior weeks prior to CDI onset.

**LTCF-acquired Control:** Randomly assign a date between Apr 1/2005 and Mar 31/2015 as index date for each person in RPDB database.Alive at index date.Without diagnosis of ICD-10 code A04.7 between Apr 1/2005 – Mar 31/2015.Ontario residents at index date.No missing value for all matching variables. Aged 18-105 at index date.OHIP eligible at index date.Without history of hospitalization 12 weeks prior to index date.LTCF resident in the 12 wks prior to Index date.NOT in the matched controls for group 1).**Match Criteria:***Hard-matched:* age (plus or minus 2 yrs), sex, LTCF resident in the 12 wks prior to the matched cohort’s date of hospitalization (plus or minus 90 days)*Propensity-score matched:* urban/rural score (*rio2008*), LHIN, Elixhauser score1. **Community-acquired Cohort(Group V in Table I):** ICD-10-CM diagnosis code for CDI (A04.7) during an in-patient hospital stay, coded as the most responsible diagnosis (Diagnosis Type M) or a pre-admit comorbidity (Diagnosis Type 1) in those who have not resided in a LTCF or had a history of hospitalization in the 12 weeks prior to CDI onset

**Community-acquired Control:** Randomly assign a date between Apr 1/2005 and Mar 31/2015 as index date for each person in RPDB database.Alive at index date.Without diagnosis of ICD-10 code A04.7 between Apr 1/2005 – Mar 31/2015.Ontario residents at index date.No missing value for all matching variables. Aged 18-105 at index date.OHIP eligible at index date.Without history of hospitalization 12 weeks prior to index date.Not a LTCF resident in the 12 wks prior to index date.NOT in the matched controls for group 1) and 2).**Match Criteria:***Hard-matched:* age (plus or minus 2 yrs), sex, not a LTCF resident in the 12 wks prior to the matched cohort’s date of hospitalization (plus or minus 90 days)*Propensity-score matched:* urban/rural score (*rio2008*), LHIN, Elixhauser score*Note:* Individuals in this control group have not necessarily been hospitalized at index date**4) ACH-acquired, community-onset Cohort (Group VI in Table I):** ICD-10-CM diagnosis code for CDI (A04.7) during an in-patient hospital stay, coded as the most responsible diagnosis (Diagnosis Type M) or a pre-admit comorbidity (Diagnosis Type 1) in those who have had a history of hospitalization in the 12 weeks prior to CDI onset (date of hospital admission) but did not reside in a LTCF in the 12 weeks prior to CDI onset **ACH-acquired, community-onset Control:**All DAD records with valid ikn and without CDI diagnosis.Ontario residents at hospital admission.No missing value for all matching variables. Alive at hospital admission.Aged 18-105 at hospital admission.OHIP eligible at hospital admission.Keep last record for same patient.Not a LTCF resident in the 12 wks prior to index date. Hospitalized in the 12 weeks prior to index date.Not in the matched controls for groups 1), 2) and 3). **Match Criteria:***Hard-matched:* age (plus or minus 2 yrs), sex, community-dwelling but hospitalized in the 12 wks prior to the matched cohort’s index date of hospitalization (plus or minus 90 days) for same Most Responsible Diagnosis (match first 3 digits)*Propensity-score matched:* urban/rural score (*rio2008*), LHIN, Elixhauser score**III. Costing study:** Costing data for the cohorts and control groups identified in Section II will be calculated for the 180 and 365 days post-onset date (the hospital admission dates for cases) and post-index date (for controls).**Index date**: 1. date of hospital admission(for both cases and controls from DAD). 2. Randomly assigned date for controls from RPDB. |
| **Estimated Size of Cohort** **(if known)** | Unknown |
| **Exclusions (in order)** | *Step* | Description |
| 1 | Invalid IKN |
| 2 | Non-Ontario resident (pstlcode ^= K,L,M,N,P ) |
| 3 | Missing variables used for hard-matching or propensity score matching |
| 4 | RPDB age at hospital admission < 18 years |
| 5 | Date of death <= date of hospital admission |
| 6 | RPDB age > 105 at index date |
| 7 | Not eligible for OHIP |
| 8 | CDI less than 180 days from index hospitalization discharge (so considered part of index case), as indicated by ICD-10 code for CDI (A04.7) during 2nd hospitalization or ED visit, or a code for diarrhea (009) at a physician visit: (1). Excluding the cases having a CDI hospitalization less than 180 days prior to index admission date or less than 180 days after index discharge date (DAD). (2). Excluding the cases having CDI ED visit or diarrhea (009) physician visit less than 180 days after index discharge date (NACRS and OHIP).  |
|  | 9. | For episodes with multiple hospitalizations, keep the first CDI hospitalization |

| Project Time Frame Definitions |
| --- |
| Look-back WindowObservation Window(in which to look for outcomes)**Index Event Date**Accrual WindowMax Follow-up Date |
| **Accrual Start/End Dates** | **I. Incidence rates:** Apr 1/2005 – Mar 31/ 2015, with incidence calculated:a) overall b) per fiscal yearc) from Apr 1/2005 – Dec 31/2008, and Jan 1/2009 – Mar 31/2015**II. Clinical impact of ACH-associated CDI:** Apr 1/2005 – Mar 31/2015**III. Costing study:** Apr 1/2005 – Mar 31/ 2015, based on a) all cases, b) cases per fiscal year, and c) cases from Apr 1/2005 – Dec 31/2008, and Jan 1/2009 – Mar 31/2015 |
| **Max Follow-up Date** | **I. Incidence rates:** N/A**II. Clinical impact of ACH-associated CDI:** Up to one year from CDI hospitalization discharge. The last possible follow-up date is Mar 31/2016.**III. Costing study:** Up to one year from CDI onset date, defined as the date of the first recorded indication of CDI by diagnosis code in-hospital. The last possible follow-up date is Mar 31/2016. |
| **When does observation window terminate?** | **I. Incidence rates:** Incidence is calculated from Apr 1/2005 to Mar 31/2015, per fiscal year; and from Apr 1/2005 – Dec 31/2008, and Jan 1/2009 – Mar 31/2015**II. Clinical impact of ACH-associated CDI:** Whichever of the following occurs first: one year after CDI hospitalization discharge; individual dies; individual moves out of province**III. Costing study:** Whichever of the following occurs first: one year after CDI hospital admission date; individual dies; individual moves into assisted-living facility and/or out of province |
| **Lookback Window(s)** | **I. Incidence rates:** No lookback**II. Clinical impact of ACH-associated CDI:** 5 years prior to CDI hospital admission to assess physician claims data and hospitalization discharge data in order to calculate Elixhauser Score**III. Costing study:** No lookback. |

| Variable Definitions (add additional rows as needed) |
| --- |
| **Main Exposure or Risk Factor** | N/A |
| **Primary Outcome Definition** | **I. Incidence rates:** In-hospital CDI diagnosis**II. Clinical impact of CDI:** 30-day all-cause mortality **III. Costing study:** Costs in 180 and 365 days post-CDI onset (hospital admission) |
| **Secondary Outcome Definition(s)** | **I. Incidence rates:** N/A**II. Clinical impact of CDI:*** Index hospitalization LOS
* ICU admission
* ICU LOS
* Colectomy rates in 365 days after index date (partial, total or radical resection of the large intestine or rectum [procedure codes (*incode:*): 1NM87XX (except 1NM87BA), 1NM89XX, 1NM91XX, 1NQ87XX (except 1NQ87BA), 1NQ89XX, 1NQ90XX
* CDI recurrence rates (occurring between 180-365 days post-discharge)
* All-cause re-hospitalization (30/90/180 days post-discharge)
* Mortality rates (30/90/180 days post-CDI admission)

**III. Costing study:** Costs from admission date (for cohort) through to180 days, and 365 days of follow-up for the following categories (standardized to 2015):* In-patient hospitalizations,
* Same-day surgery procedures,
* ED visits,
* Outpatient medications (for those aged ≥65 years or on social assistance),
* Physician services,
* Outpatient laboratory tests,
* Complex continuing care admissions, and
* Home-care services
 |
| **Baseline Characteristics** | Age Sex Admission source (*instftyp*) Healthcare exposure (hospitalization; DAD) in 90 and 365 days prior to admission **Comorbidities:** * CVD – in OHIP, NACRS or DAD in 5 years prior to admission date
	+ ICD-9: 401.0, 401.1, 401.9, 402.00, 402.01, 402.10, 402.11, 402.90, 402.91, 410.0, 410.1x, 410.91, 412, 413.9, 414.0, 414.01, 414.4, 414.9, 427.31, 428.0, 429.20, 433.10, 433.11, 434.91, 437.0, 437.1, 433.9, 433.10 (NACRS, DAD)

ICD-9: 410, 412, 413, 428 (OHIP)* + ICD-10: I20.9, I21.09, I21.3, I25.10, I25.2, I25.84, I25.9, I10, I11.9, I11.0, I21.09, I25.2, I20.9, I48.91, I50.9, I25.10, I65.29, I63.239, I63.9, I67.2, I67.9, I73.9, I65.23, I65.29 (NACRS, DAD)
* COPD – ICES database
* CHF – ICES database
* Diabetes – ICES database
* Renal disease –in OHIP, NACRS or DAD in 5 years prior to admission date
	+ ICD-9: 403.01, 403.11, 403.91, 404.02, 404.03, 404.12, 404.13, 404.92, 404.93, 582.x, 583.0-583.7, 585.x, 586.x, 588.0, V42.0, V45.1, V56.x (NACRS, DAD)

ICD-9: 403, 404, 582, 583, 585, 586, 588, V56 (OHIP)* + ICD-10: N18.9 (NACRS, DAD)
* Liver disease –in OHIP, NACRS or DAD in 5 years prior to admission date
	+ ICD-9: 070.22, 070.23, 070.32, 070.33, 070.44, 070.54, 456.0, 456.1, 456.20, 456.21, 571.0, 571.2, 571.3, 571.40-571.49, 571.5, 571.6, 571.8, 571.9, 572.3, 572.8, V42.7 (NACRS, DAD)
	+ ICD-9: 070, 571, 572 (OHIP)
	+ ICD-10: K70-K77 (NACRS, DAD)
* Cancer – Diagnosis of cancer in OCR database
* Pulmonary circulatory disorder –in OHIP, NACRS or DAD in 5 years prior to admission date
	+ ICD-9: 416.0-416.9, 417.9 (NACRS, DAD)
	+ ICD-9: 416, 417 (OHIP)
	+ ICD-10: I26-I28 (NACRS, DAD)
* Valvular disease in OHIP, NACRS or DAD in 5 years prior to admission date
	+ ICD-9: 093.20-093.24, 394.0-397.1, 424.0-424.91, 746.3-746.6, V42.2, V43.3 (NACRS, DAD)
	+ ICD-9: 394 (OHIP)
	+ ICD-10: I05-I08, I34-137, Q22-Q23 (NACRS, DAD)
* Inflammatory bowel disease in OHIP, NACRS or DAD in 5 years prior to admission date
	+ ICD-9: 555.0, 555.1, 555.2, 555.9, 556.0, 556.1,556.2, 556.3, 556.4, 556.5, 556.6, 556.8, 556.9 (NACRS, DAD)
	+ ICD-9: 555. 556 (OHIP)
	+ ICD-10: K50, K51 (NACRS, DAD)

Antibiotic use in 30 days prior to onset – ODB, OHIP, NACRS, DAD (see antibiotic DIN list and list of conditions for which antibiotics are usually prescribed in Tables II and III in the Appendix) \***Note**: search ODB for <65 years also, but also include OHIP/NACRS/DAD as a proxy for for antibiotic useHospital location (urban or rural) - TBD – attempt based on hospital postal code.Number of medical beds in hospital (<100, 100-299, 300-499, ≥500) (*INST.ACUTE\_BEDS* database, *total*. Link by year and inst. For missing values, use closest year data.) Place of discharge (*disrchdisp*) |
| **Other Variables** | Elixhauser (see Table IV in Appendix) LTCF status (12 weeks prior to index date):* Post 2010: use CCRS
* Pre 2010: ltc=1 in ODB, or OHIP claim with W feecode and insttype = NH, HF (Nursing Home, Home for the Aged)
 |

| Analysis Plan and Dummy Tables (expand/modify as needed) |
| --- |
| **Descriptive Tables (insert or append dummy tables):** |
|  **Table I: Cohort definitions** |
|  **Table II: Diagnoses for which an antibiotic is prescribed**  |
|  **Table III: Antibiotic DINs** |
|  **Table IV: Elixhauser Comorbidity Burden – ICD-9 and 10 codes** |
|  **Table V. Baseline characteristics of CDI cases** |
|  **Table VI. Incidence of CDI** |
|  **Table VII. CDI by Year, Overall Number, Location of Onset, and Attribution** |
|  **Table VIII: Baseline characteristics for CDI cohort/control groups****\*Note:** separate tables for each cohort |
|  **Table IX: Impact of CDI on patient outcomes (unadjusted) for CDI cohort/control groups1** |
|  **Table X: Outcomes by CDI risk factors** **\*Note:** separate tables for each outcome |
|  **Table XI: Adjusted outcomes of hospitalized patients with and without CDI~****\*Note:** separate tables for each outcome |
|  **Table XII: Exclusion Table - CDI less than 180 days from index hospitalization discharge**  |
|  |
| **Statistical Model(s)** |
|  **Type of model** | **Model 1 (incidence rate calculation):** To calculate the number of cases overall, per person-years from Apr 1/2005 to Mar 31/2015, as well as pre- and post-Dec 31/2008, the number of cases will be divided by the denominator (number of base population that is ≥18 years but < 105 years, based on the RPDB). **Person-years will be calculated based on Ontario postal code, OHIP eligibility, date of death, date of last contact with healthcare system (considered to have moved if have not been seen in healthcare system for > 7 years, postal code**, and that those with CDI are considered infected for 180 days. For those who have recurring CDI diagnoses within a 180-day period, only the first event will be considered **(Appendix - Table VI)**.\***Note**: this 180-day period is a moving window based on the last CDI date. It shifts if there is another infection within the 180-day window.Specific incidence rates will also be measured depending on whether onset occurred in an ACH, a LTCF or in the community **(Appendix - Table VII)**. ACH onset will be calculated using patient-days at hospital as the denominator. The denominator of LTCF-onset will be number of person-years living in LTC for LTCF residents. The denominator for community-onset CDI will be number of person-years living in the community. **Model 2 (propensity scoring): Clinical Impact of CDI:** There are 4 cohorts, each with matched control groups. Each CDI cohort member will be matched to 3 non-CDI controls based on a combination of hard-matching and propensity scores, as described above in the Project Cohort section. ACH-acquired cohort and controls are matched on the propensity to acquire CDI in-hospital. LTCF-aquired cohort and controls are matched on the propensity to acquire CDI in LTCF. The controls will all have resided in an LTCF in the 12 weeks prior to their match’s CDI onset date (plus or minus 30 days). Community-acquired cohort and controls are matched on the propensity to acquire CDI in the community. The controls will all have resided in the community in the 12 weeks prior to their match’s CDI onset date (plus or minus 30 days). ACH-acquired, community-onset cohort and controls are matched on the propensity to acquire CDI in-hospital. They controls will all be community-dwelling individuals but will have been hospitalized in the previous 12 weeks for the same Most Responsible Diagnosis as the cohort.For all 4 sets of matches, calipers of width equal to 0.2 of the standard deviation of the propensity score will be used. To assess balance, the standardized differences between the cohort and controls will be calculated for each variable included in the propensity score, with standardized differences less than 0.1 indicating good balance. |
|  | Summary statistics will be calculated and compared for each cohort/control matched group (Tables VIII and IX). Categorical variables will be compared using McNemar test, and continuous variables will be evaluated using paired t-test. Unadjusted models will be developed for the primary and secondary outcomes. Categorical outcomes will be modeled using conditional logistic regression, and continuous variables will be modeled using generalized linear models (Table X). Using the 4 groups of matched samples, the relative risk of the various outcomes listed below (excluding LOS, ICU LOS and cost) will be determined through negative binomial generalized linear modeling (Table XI).When applying exclusion criteria, we will calculate the number of individuals who were coded again for CDI less than 180 days from index hospitalization discharge (Table XII). |
|  **Primary independent variable** | CDI-infection (Case / control assignment). |
|  **Dependent variable** | * LOS (continuous) (for controls, only calculate for individuals who are hospitalized within 90 days of index date of paired case)
* ICU LOS (continuous)(for controls, only calculate for individuals who are hospitalized within 90 days of index date of paired case)
* ICU admission
* Colectomy rates in 365 days after hospital admission (partial, total or radical resection of the large intestine or rectum [procedure codes: 1NM87XX, 1NM89XX, 1NM91XX, 1NQ87XX, 1NQ89XX, 1NQ90XX excluding 1NM87BA and 1NQ87BA]). The index hospitalization is eligible for this calculation.
* CDI recurrence rates (occurring > 180 days after discharge but before 180/365 days post-discharge) as defined by ICD-10 code for CDI at physician visit, ED visit or hospitalization
* All-cause re-hospitalization (30/90/180 days post-discharge, for a control, within 90 days of the index date of paired case, link the control to DAD database. For multiple linked records, use the closest one and treat the admission/discharge date as the ones for this control. For non-linked controls, treat index date as both admission date and discharge date. ) (binary)
* Mortality rates (30/90/180 days post-admission)
* Cost (standardized to 2015)
 |
|  **Covariates** | Refer to tables X and XI |
| **Sensitivity Analyses** |  |
|  **Type of model** | 1.Excluding those with lowest and biggest comorbidity burden, based on Elixhauser Scale (using point system from Table 1 of **attached van Walraven paper**), from clinical impact and costing study components (defined as the highest and lowest 5% of scores)2. Excluding those with a previous hospital admission (all-cause) in last 90 days  |
|  |

| Project Cohort 2 |
| --- |
| **Study Design** | [x]  Cohort study [ ]  Matched cohort study [ ]  Case-control study[ ]  Cross-sectional study [ ]  Other (specify):  |
| **Index Event / Inclusion Criteria** | All individuals who met the previously described definition for CDI (Project Cohort 1) between Apr 1/2005 – Mar 31/ 2015, stratified into the 6 groups based on onset/association (Appendix - Table 1) and at least 65 years at time of hospital admission for CDI.From this group, we will identify:1. Proportion seen in ED with an ICD-10-CM diagnosis code for CDI (A04.7) or diarrhea (R19.7) in the 12 weeks prior to admission
2. Proportion seen in ED with an ICD-10-CM diagnosis code for CDI (A04.7) or diarrhea (R19.7) in the 12 weeks prior to admission, that were prescribed oral metronidazole (DINs: 00545066, 02248562) or vancomycin (02430193, 02430185) without a concomitant prescription (meaning that there is any overlap in prescription length with metronidazole or vancomycin) for a second antibiotic (including carbapenems, cephalosporins, penicillins, aminoglycosides, tetracyclines, macrolides, fluoroquinolones, and b-lactams on the formulary), indicative of a non-CDI condition (please see Table II and III for DINs and for codes for conditions for which antibiotics are prescribed)
 |
| **Estimated Size of Cohort** **(if known)** | Unknown |
| **Exclusions (in order)** | *Step* | Description |
| (0) | Use the CDI cases from Project Cohort 1  |
| 1 | < 65 years of age at 12 weeks prior to the index date (i.e. index date – 12 weeks) |

| Project Time Frame Definitions 2 |
| --- |
| Look-back WindowObservation Window(in which to look for outcomes)**Index Event Date**Accrual WindowMax Follow-up Date |
| **Accrual Start/End Dates** | **I. Incidence rates:** Apr 1/2005 – Mar 31/ 2015, with incidence calculated:a) overall b) per fiscal yearc) from Apr 1/2005 – Dec 31/2008, and Jan 1/2009 – Mar 31/2015 |
| **Max Follow-up Date** | Mar 31, 2016 |
| **When does observation window terminate?** | One year after index date. |
| **Lookback Window(s)** | ED visit - 12 weeks prior to hospital admission for CDI5 years prior to CDI hospital admission to assess physician claims data and hospitalization in order to find comorbidities |

| Variable Definitions (add additional rows as needed) 2 |
| --- |
| **Main Exposure or Risk Factor** | N/A |
| **Primary Outcome Definition** | Presented to ED in 12 weeks prior to hospital admission for CDIPrescribed oral metronidazole (DINs: 00545066, 02248562) or vancomycin (02430193, 02430185) without a concomitant prescription (meaning that there is any overlap in prescription length with metronidazole or vancomycin) for a second antibiotic (including carbapenems, cephalosporins, penicillins, aminoglycosides, tetracyclines, macrolides, fluoroquinolones, and b-lactams on the formulary), indicative of a non-CDI condition (please see Appendix Tables II and III for DINs and list of conditions for which antibiotics are commonly prescribed) |
|  |  |
| **Baseline Characteristics** | Age Sex Admission source (*instftyp*) Healthcare exposure (hospitalization; DAD) in 90 and 365 days prior to admission **Comorbidities:** * CVD in OHIP, NACRS or DAD in 5 years prior to admission date
	+ ICD-9: 401.0, 401.1, 401.9, 402.00, 402.01, 402.10, 402.11, 402.90, 402.91, 410.0, 410.1x, 410.91, 412, 413.9, 414.0, 414.01, 414.4, 414.9, 427.31, 428.0, 429.20, 433.10, 433.11, 434.91, 437.0, 437.1, 433.9, 433.10 (NACRS, DAD)

ICD-9: 410, 412, 413, 428 (OHIP)* + ICD-10: I20.9, I21.09, I21.3, I25.10, I25.2, I25.84, I25.9, I10, I11.9, I11.0, I21.09, I25.2, I20.9, I48.91, I50.9, I25.10, I65.29, I63.239, I63.9, I67.2, I67.9, I73.9, I65.23, I65.29 (NACRS, DAD)
* COPD – ICES database
* CHF – ICES database
* Diabetes – ICES database
* Renal disease –in OHIP, NACRS or DAD in 5 years prior to admission date
	+ ICD-9: 403.01, 403.11, 403.91, 404.02, 404.03, 404.12, 404.13, 404.92, 404.93, 582.x, 583.0-583.7, 585.x, 586.x, 588.0, V42.0, V45.1, V56.x (NACRS, DAD)

ICD-9: 403, 404, 582, 583, 585, 586, 588, V56 (OHIP)* + ICD-10: N18.9 (NACRS, DAD)
* Liver disease –in OHIP, NACRS or DAD in 5 years prior to admission date
	+ ICD-9: 070.22, 070.23, 070.32, 070.33, 070.44, 070.54, 456.0, 456.1, 456.20, 456.21, 571.0, 571.2, 571.3, 571.40-571.49, 571.5, 571.6, 571.8, 571.9, 572.3, 572.8, V42.7 (NACRS, DAD)
	+ ICD-9: 070, 571, 572 (OHIP)
	+ ICD-10: K70-K77 (NACRS, DAD)
* Cancer – Diagnosis of cancer in OCR database
* Pulmonary circulatory disorder –in OHIP, NACRS or DAD in 5 years prior to admission date
	+ ICD-9: 416.0-416.9, 417.9 (NACRS, DAD)
	+ ICD-9: 416, 417 (OHIP)
	+ ICD-10: I26-I28 (NACRS, DAD)
* Valvular disease in OHIP, NACRS or DAD in 5 years prior to admission date
	+ ICD-9: 093.20-093.24, 394.0-397.1, 424.0-424.91, 746.3-746.6, V42.2, V43.3 (NACRS, DAD)
	+ ICD-9: 394 (OHIP)
	+ ICD-10: I05-I08, I34-137, Q22-Q23 (NACRS, DAD)
* Inflammatory bowel disease in OHIP, NACRS or DAD in 5 years prior to admission date
	+ ICD-9: 555.0, 555.1, 555.2, 555.9, 556.0, 556.1,556.2, 556.3, 556.4, 556.5, 556.6, 556.8, 556.9 (NACRS, DAD)
	+ ICD-9: 555. 556 (OHIP)
	+ ICD-10: K50, K51 (NACRS, DAD)

Antibiotic use in 30 days prior to onset – ODB, OHIP, NACRS, DAD (see antibiotic DIN list and list of conditions for which antibiotics are usually prescribed in Tables II and III in the Appendix) \***Note**: search ODB for <65 years also, but also include OHIP/NACRS/DAD as a proxy for for antibiotic useHospital location (urban or rural) - TBD – attempt based on hospital postal code.Number of medical beds in hospital (<100, 100-299, 300-499, ≥500) (*INST.ACUTE\_BEDS* database, *total*) Place of discharge (*disrchdisp*) |
|  |  |

| Analysis Plan and Dummy Tables (expand/modify as needed) 2 |
| --- |
| **Descriptive Tables (insert or append dummy tables):** |
|  **Table XIII: Comparison of CDI cases in individuals over 65 years, based on prior ED visits for diarrhea/CDI and antibiotic use** |
|  |
|  |
| **Descriptive table** | Proportion of hospitalized CDI cases (based on Project Cohort 1) that previously presented to the ED with ICD-10 codes for CDI and/or diarrhea (Table XII)Proportion of hospitalized CDI cases (based on Project Cohort 1) that previously presented to the ED with ICD-10 codes for CDI and/or diarrhea who are given a prescription for metronidazole or vancomycin without a concomitant antibiotic prescription that would indicate a non-CDI condition (Table XIII). |
|  |

| Quality Assurance Activities  |
| --- |
| **RAE Directory of SAS Programs** |  |
| **RAE Directory of Final Dataset(s)** | *The* *final analytic dataset for each cohort includes all the data required to create the baseline tables and run all the models. It should include all covariates for all models such as patient risk factors, hospital characteristics, physician characteristics, exposure measures (continuous, categorical) and outcomes. It should include covariates that were considered but didn’t make the final cut. This would permit an analyst to easily re-run the models in the future.* |
|  |
| **RAE README file available:** [ ] Yes [ ] No |
| **Date results of quality assurance tools for final dataset shared with project team (where applicable):** |  |
|  | **%assign** | yyyy-mon-dd |
|  | **%evolution** | yyyy-mon-dd |
|  | **%dinexplore** | yyyy-mon-dd |
|  | **%track / %exclude** | yyyy-mon-dd |
|  | **%codebook** | yyyy-mon-dd |
| **Additional comments:** |  |

**Appendix**

**Table I: Cohort definitions**

|  |  |
| --- | --- |
| 1. ***ACH-onset,***

***ACH-associated CDI\**** | CDI was coded as a post-admit comorbidity of clinical significance (Diagnosis Type 2) **AND**patient did not reside in a LTCF in the 12 weeks prior to admission |
| 1. ***ACH-onset,***

***ACH/LTCF-associated CDI*** | CDI was coded as a post-admit comorbidity of clinical significance (Diagnosis Type 2) **AND**patient resided in a LTCF in the 12 weeks prior to admission  |
| 1. ***LTCF-onset LTCF-associated CDI\*\****
 | CDI was coded as the most responsible diagnosis (Diagnosis Type M) or a pre-admit comorbidity (Diagnosis Type 1) **AND**patient resided in a LTCF with no history of hospitalization in the 12 weeks prior to admission |
| 1. ***LTCF-onset,***

***LTCF/ACH-associated CDI\*\**** | CDI was coded as the most responsible diagnosis (Diagnosis Type M) or a pre-admit comorbidity (Diagnosis Type 1) **AND**patient resided in a LTCF in the 12 weeks prior to admission AND had  a history of hospitalization during this time |
| 1. ***Community-onset, Community-associated CDI\*\****
 | CDI was coded as the most responsible diagnosis (Diagnosis Type M) or a pre-admit comorbidity (Diagnosis Type 1) **AND**patient neither resided in a LTCF nor was hospitalized in the 12 weeks prior to admission |
| 1. ***Community-onset,***

***ACH-associated CDI\*\**** | CDI was coded as the most responsible diagnosis (Diagnosis Type M) or a pre-admit comorbidity (Diagnosis Type 1) **AND**patient did not reside in a LTCF but was hospitalized in the 12 weeks prior to admission |

\*ACH-onset/community-associated CDI and community-onset/LTCF-associated CDI cases were excluded due to difficult to define as well as very rare

\*\*We calculate the date of onset as the date of the hospital admission (index date), since it is not possible to identify when onset truly occurred for community-onset and LTCF-onset cases

**Table II: ICD-10-CA and Ontario Health Insurance Plan codes of infectious syndromes that could have led to a prescription for an antibiotic**

| **Syndrome** | **OHIP code** | **ICD-10-CA code** |
| --- | --- | --- |
| **Acute Bronchitis** | 466 | J200-J209J22 |
| **Bacterial Meningitis** |  | G000-G003G008G009G01 |
| **Bronchiolitis** |  | J210J218J219 |
| **Cellulitis** | 682 | L0300L0301L0310L0311L032L0330-L0336L0339L038L039L089 |
| **Cervicitis** | 616 | N72 |
| **Endocarditis** |  | I330I339I38I398 |
| **Necrotizing Fasciitis** |  | M7260-M7269 |
| **Orchitis/Epididymitis** | 604 | N511N4500-N4502N4590-N4592 |
| **Otitis Media** | 381382 | H650-H654H659-H664H669-H671H678 |
| **Pelvic Inflammatory Disease** | 614615 | N700N701N709-N711N719N741-N744N748 |
| **Pharyngitis** | 460 | J020J028-J030J038J039 |
| **Pneumonia** | 486 | J100J110J120-J122J128J129J13J14J150-J160J168J170-J173J178J180-J182J188J189 |
| **Septic Arthritis** | 711 | M0000-M0029M0080-M0139M0180-M0189 |
| **Septicaemia** |  | A021A227A267A327A392-A394A400-A403A408-A414A4150-A4152A4158A4180A4188A419A427B377 |
| **Upper Respiratory Tract Infection** | 460464 | J00J040-J042J050J051J060J068J069 |
| **Urethritis** | 597 | N340-N342N370 |
| **Urinary Tract Infections** | 590595601 | N10N12N151N300N308N309N410N412N413N510N390 |
| **Osteomyelitis** | 730 | M4620M4625M4628M4629M8600-M8669M8680-M8699 |

ICD-10- CA – International Statistical Classification of Diseases and Related Health Problems, 10th Revision, Canada; OHIP – Ontario Health Insurance Plan.

**Table III: Antibiotic DINs**

Co-Azithromycin 02256088

PMS-Azithromycin 02261642

Biaxin BID 02126710

Apo-Clarithromycin 02274752

Mylan-Clarithromycin 02248857

PMS-Clarithromycin 02247574

Ran-Clarithromycin 02361434

Ratio-Clarithromycin 02247819

Sandoz Clarithromycin 02266547

Teva-Clarithromycin 02248805

Amoxil Chewable 02041685

Novamoxin Chewable 02036347

Amoxil Chewable 02041286

Novamoxin Chewable 02036355

Tazocin 02170817

Piperacillin & Tazobactam for Injection 02308444

Piperacillin & Tazobactam for Injection 02362619

Tazocin 02170795

Piperacillin & Tazobactam for Injection 02308452

Piperacillin & Tazobactam for Injection 02391538

Piperacillin & Tazobactam for Injection 02362627

Piperacillin/Tazobactam Powder for Inj. 02370166

Tazocin 02170809

Piperacillin & Tazobactam 02308460

Injection Piperacillin & Tazobactam for injection 02362635

Injection Piperacillin/Tazobactam Powder for Injection 02370174

Vibra-Tabs 00578452

Apo-Doxy-Tabs 00874256

Novo-Doxylin Tablets 02158574

Minocin 02173514

Apo-Minocycline 02084090

Mylan-Minocycline 02230735

Novo-Minocycline 02108143

PMS-Minocycline 02294419

Ratio-Minocycline 01914138

Sandoz Minocycline 02237313

Minocin 02173506

Apo-Minocycline 02084104

Mylan-Minocycline 02230736

Novo-Minocycline 02108151

PMS-Minocycline 02294427

Ratio-Minocycline 01914146

Sandoz Minocycline 02237314

Tygacil 02285401

Tigecycline 02409356

Cefazolin for Injection 02297205

Cefazolin for Injection 02108127

Cefazolin for Injection 02297213

Cefazolin for Injection 02108135

Mefoxin 00663697

Cefoxitin for Injection 02291711

Cefoxitin for Injection USP 02128187

Mefoxin 00663700

Cefoxitin for Injection 02291738

Cefoxitin for Injection USP 02128195

Rocephin 00851957

Ceftriaxone for 02292904

Ceftriaxone Sodium 02325632

Vancocin 00800430

Jamp-Vancomycin 02407744

Vancocin 00788716

Jamp-Vancomycin 02407752

Mylan Imipenem and cilastatin 02441225

Imipenem and cilastatin 02441223

Imipenem and cilastatin 02439840

Imipenem and cilastatin 02439859

Imipenem and cilastatin 02357429

Meropenem 02430495

Meropenem 02430509

Meropenem 02413787

Meropenem 02436493

Meropenem 02421518

Meropenem 02421526

Clindamycin 02245232/02245232

Ciprofloxacin 02237514/02155958/02155966/02155974

Gemifloxacin 02248968

Levofloxacin 02248262/02248263/02285649

Moxifloxacin 02246414/02252260/02432242

Norfloxacin 02237682/02246956

Ofloxacin 02231529/02231531/02231532/02248398

**Table IV: Elixhauser Comorbidity Burden – ICD-9 and 10 codes**

|  |  |  |  |
| --- | --- | --- | --- |
| **Comorbidities** | **ICD-9 (DAD, NACRS)** | **ICD-9 (OHIP)** | **ICD-10 codes (DAD, NACRS)** |
| **Congestive heart failure****(ICES Database)** | 398.91, 402.01, 402.11, 402.91, 404.01, 404.11, 404.91, 428.0-428.9 | 428 | I09.9, I11.0, I13.0, I13.2, I25.5, I42.0, 142.5-I42.9, I43.x, I50.x, P29.0 |
| **Cardiac arrhythmias**  | 427.x | 427 | I44.1-I44.3, I45.6, I45.9, I47.x-I49.x, R00.0, R00.1, R00.8, T82.1, Z45.0, Z95.0 |
| **Valvular disease**  | 093.20-093.24, 394.0-397.1, 424.0-424.91, 746.3-746.6, V42.2, V43.3 | 394 | A52.0, I05.x-I08.x, I09.1, I09.8, I34.x-I39.x, Q23.O, Q23.3, Z95.2, Z95.4 |
| **Pulmonary circulation****Disorders** | 416.0-416.9, 417.9 | 416, 417 | I26.x, I27.x, I28.0, I28.8, I28.9 |
| **Peripheral vascular disorders**  | 440.0-440.9, 441.00-441.9, 442.0-442.9, 443.1-443.9, 447.1, 557.1, 557.9, V43.4 | 440, 441.442, 443, 557 | I70.x, I71.x, I73.1, I73.8, I73.9, I77.1, I79.0, I79.2, K55.1, K55.8, K55.9, Z95.8, Z95.9 |
| **Hypertension, uncomplicated**  | 401.1, 401.9, 642.00-642.04 | 401 | I10.x |
| **Hypertension, complicated**  | 401.0, 402.00, 402.10, 402.90, 403.00, 403.10, 403.90, 404.00, 404.10, 404.90, 405.01, 405.09, 405.11, 405.19, 405.91, 405.99, 642.10- 642.24, 642.70-642.94 | 402, 403, 404, 405, 642 | I11.x-I13.x, I15.x  |
| **Paralysis**  | 342.0-342.12, 342.9-344.9, 438.20-438.53 | 342 | G04.1, G80.1, G80.2, G81.x, G82.x, G83.0-G83.4, G83.9 |
| **Other neurological disorders**  | 330.0-331.9, 332.0, 333.4, 333.5, 334.0-335.9, 340, 341.1- 341.9, 345.00-345.11, 345.2-345.3, 345.40-345.91, 348.1, 348.3-348.39, 780.3, 780.39, 784.3 | 330, 331, 332, 333, 334, 335, 340, 341, 345, 348 | G10.x-G 13.x, G20.xG22.x, G25.4, G25.5, G31.2, G31.8, G31.9, G32.x, G35.x-G37.x, G40.x, G41.x, G93.1, G93.4, R47.0, R56.x |
| **Chronic pulmonary disease**  | 490-492.8, 493.00-493.92, 494-494.1, 495.0-505, 506.4 | 490, 491, 492, 493, 495-505 | I27.8, 127.9, J40.x-J47.x, J60.x-J67.x, J68.4, J70.1, J70.3 |
| **Diabetes, uncomplicated** **(ICES Database)** | 250.00-250.33 | 250 | E10.0, E10.1, E10.9, E11.0, E11.1, E11.9, E12.0, E12.1, E12.9,E13.0, E13.1, E13.9, E14.0, E14.1, E14.9 |
| **Diabetes, complicated** **(ICES Database)** | 250.40-250.93 | N/A | E10.2-E10.8, E11.2-E11.8, E12.2-E12.8, E13.2-E13.8,E14.2-E14.8 |
| **Hypothyroidism**  | 243-244.2, 244.8, 244.9 | 243, 244 | E00.x-E03.x, E89.0 |
| **Renal failure**  | 403.01, 403.11, 403.91, 404.02, 404.03, 404.12, 404.13, 404.92, 404.93, 585, 586, V42.0, V45.1, V56.0-V56.2, V56.8 | 403, 404, 582, 583, 585, 586, 588, V56 | I12.0, I13.1, N18.x, NI9.x, N25.0, Z49.0-Z49.2, Z94.0, Z199.2 |
| **Liver disease**  | 070.22, 070.23, 070.32, 070.33, 070.44, 070.54, 456.0, 456.1, 456.20, 456.21, 571.0, 571.2, 571.3, 571.40-571.49, 571.5, 571.6, 571.8, 571.9, 572.3, 572.8, V42.7 | 070, 571, 572 | B18.x, I85.x, I86.4, I98.2, K70.x, K71.1, K71.3-K71.5, K71.7, K72.xK74.x, K76.0, K76.2-K76.9. Z94.4 |
| **Peptic ulcer disease** **excluding bleeding** | 531.41, 531.51, 531.61, 531.70, 531.71, 531.90, 531.91, 532.41, 532.51, 532.61, 532.70, 532.71, 532.90, 532.91, 533.41, 533.51, 533.61, 533.70, 533.71, 533.90, 533.91, 534.41, 534.51, 534.61, 534.70, 534.71, 534.90, V12.71 | 531, 532, 533, 534 | K25.7, K25.9, K26.7, K26.9, K27.7, K27.9, K28.7, K28.9 |
| **AIDS/HIV**  | 042-044.9 | 042,043, 044 | B20.x-B22.x, B24.x |
| **Lymphoma** **(OCR Database)** | 200.00-202.38, 202.50-203.01, 203.8-203.81, 238.6, 273.3, V10.71, V10.72, V10.79 | 200, 201. 202, 203 | C81.x-C85.x, C88.x, C96.x, C90.0, C90.2 |
| **Metastatic cancer** **(OCR Database)** | 196.0-199.1 | 196, 197, 198 | C77.x-C80.x |
| **Solid tumor without** **Metastasis** | 140.0-172.9, 174.0-175.9, 179-195.8, V10.00-V10.59, V10.81- V10.9 | 140-172, 174, 175, 179-195 | C00.x-C26.x, C30.x-C34.x, C37.x-C41.x, C43.x, C45.x-C58.x, C60.x-C76.x, C97.x |
| **Rheumatoid arthritis/** **collagen vascular diseases** | 701.0, 710.0-710.9, 714.0-714.9, 720.0-720.9, 725  | 710, 714, 720, 725 | L94.0, L94.1, L94.3, M05.x, M06.x, M08.x, M12.0, M12.3, M30.x, M31.0-M31.3, M32.x-M35.x, M45.x, M46.1, M46.8, M46.9 |
| **Coagulopathy**  | 286.0-286.9, 287.1, 287.3-287.5, 289.81-289.82 | 286, 287, 289 | D65-D68.x, D69.1,D69.3-D69.6 |
| **Obesity**  | 278.0, 278.00, 278.01 | N/A | E66.x |
| **Weight loss**  | 260-263.9 | 260, 261, 262, 263 | E40.x-E46.x, R63.4, R64 |
| **Fluid and electrolyte** **Disorders** | 276.0-276.9 | 276 | E22.2, E86.x, E87.x  |
| **Blood loss anemia**  | 280.0, 648.20-648.24 | N/A | D50.0 |
| **Deficiency anemia**  | 280.1-281.9, 285.21-285.29, 285.9 | 280, 281, 285 | D50.8, D50.9, D51.x-D53.x |
| **Alcohol abuse**  | 291.0-291.3, 291.5, 291.8, 291.81, 291.89, 291.9, 303.00- 303.93, 305.00-305.03, V113 | 291, 303, V113 | F10, E52, G62.1, I42.6, K29.2, K70.0, K70.3, K70.9, T51.x, Z50.2, Z71.4, Z72.1 |
| **Drug abuse**  | 292.0, 292.82-292.89, 292.9, 304.00-304.93, 305.20-305.93, 648.30-648.34 | 292, 304 | F11.x-F16.x, F18.x, F19.x, Z71.5. Z72.2 |
| **Psychoses**  | 295.00-298.9, 299.10, 299.11 | 295, 296, 297, 298 | F20.x, F22.x-F25.x, F28.x, F29.x, F30.2, F31.2, F31.5 |
| **Depression**  | 300.4, 301.12, 309.0, 309.1, 311 | 311 | F31.3-F31.4, F32.x, F33.x, F34.1, F41.2, F43.2 |

**Table V: Baseline characteristics of CDI cases\***

**\*Note:** Individuals can enter this cohort more than once. For individuals who enter the cohort more than once, calculate and report their baseline characteristics as of each separate index date.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **CDI****(all)** | **ACH-onset,****ACH-assoc.**  | **ACH-onset, ACH/LTCF-assoc.** | **LTCF-onset, LTCF-assoc.** | **LTCF-onset, LTCF/ACH-assoc.** | **Com-onset,****Com-assoc.** | **Com-onset,****ACH-assoc.** |
| **All patients (total)** | N | N | N | N | N | N | N |
| **Patient days (mean, SD median, IQR, range)** | N | N | N | N | N | N | N |
| **Age group (years) (mean, SD, median, IQR range)** |  |  |  |  |  |  |  |
| 18-44 | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| 45-64 | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| 65-74 | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| 75-84 | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| 85+ | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| **Sex, female** | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| **Sex, male** | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| **LTCF resident** | n (%) | n (%) | n (%) | 100 (%) | 100 (%) | n (%) | n (%) |
| **Admission source** |  |  |  |  |  |  |  |
| ER | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| Home | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| Transfer | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| Nursing home | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| Other | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| **Healthcare exposure in year prior to onset\*\*** | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| **Healthcare exposure in 90 days prior to onset**  | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| **Antibiotic use in 30 days prior to onset** | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| **Comorbidities** |  |  |  |  |  |  |  |
| CVD | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| COPD | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| CHF | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| Diabetes | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| Renal/liver disease | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| Renal/liver failure | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| Cancer | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| Pulmonary circulatory disorder | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| Valvular disease | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| Inflammatory bowel disease | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| **Hospital characteristic:** |  |  |  |  |  |  |  |
| Urban |  | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| Rural |  | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| **Hospital characteristics:** **# of beds** |  |  |  |  |  |  |  |
| < 100 |  | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| 100 – 299 |  | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| 300 – 499 |  | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| ≥ 500 |  | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| **Outcomes:** |  |  |  |  |  |  |  |
| **Discharge status** |  |  |  |  |  |  |  |
| Home | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| Transfer |  | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| Nursing home | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| Hospice care |  | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| Death | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| Other | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
|  |  |  |  |  |  |  |  |
| LOS |  |  |  |  |  |  |  |
| ICU admission | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| ICU LOS |  |  |  |  |  |  |  |
| 30-day all-cause mortality post-CDI onset~  | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| 90-day all-cause mortality post-CDI onset~ | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| 180-day all-cause mortality post-CDI onset~ | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| 180-365 days post-discharge CDI recurrence | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| 30-day post-discharge all-cause re-hospitalization  | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| 90-day post-discharge all-cause re-hospitalization | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| 180-day post-discharge all-cause re-hospitalization | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| 365-day colectomy post-CDI onset | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| Cost of In-patient hospitalizations in the 180 days post-admission |  |  |  |  |  |  |  |
| Costs of same-day surgery procedures in the 180 days post-admission |  |  |  |  |  |  |  |
| Costs of ED visits in the 180 days post-admission |  |  |  |  |  |  |  |
| Costs of Outpatient medications in the 180 days post-admission |  |  |  |  |  |  |  |
| Costs of physician services in the 180 days post-admission |  |  |  |  |  |  |  |
| Costs of outpatient laboratory tests in the 180 days post-admission |  |  |  |  |  |  |  |
| Costs of complex continuing care admissions in the 180 days post-admission |  |  |  |  |  |  |  |
| Costs of Home-care services in the 180 days post-admission |  |  |  |  |  |  |  |
| Total costs in the 180 days post-admission | Mean, SD, range | Mean, SD, range | Mean, SD, range | Mean, SD, range | Mean, SD, range | Mean, SD, range | Mean, SD, range |
| Costs of inpatient hospitalizations in the 365 days post-admission |  |  |  |  |  |  |  |
| Costs of same-day surgery procedures in the 365 days post-admission |  |  |  |  |  |  |  |
| Costs of ED visits in the 365 days post-admission |  |  |  |  |  |  |  |
| Costs of outpatient medications in the 365 days post-admission |  |  |  |  |  |  |  |
| Costs of physician services in the 365 days post-admission |  |  |  |  |  |  |  |
| Costs of outpatient laboratory tests in the 365 days post-admission |  |  |  |  |  |  |  |
| Costs of complex continuing care admissions in the 365 days post-admission |  |  |  |  |  |  |  |
| Costs of home-care services |  |  |  |  |  |  |  |
| Total costs in the 365 days post-admission | Mean, SD, range | Mean, SD, range | Mean, SD, range | Mean, SD, range | Mean, SD, range | Mean, SD, range | Mean, SD, range |

 \*Com = community

 \*\*ACH-stay or LTCF-stay

 ~Hospital admission

**Table VI: Incidence of CDI**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Characteristic | 2014 | 2013 | 2012 | 2011 | 2010 | 2009 | 2008 | 2007 | 2006 | 2005 |
| # of hospitalized CDI cases |  |  |  |  |  |  |  |  |  |  |
| CDI cases/ 100,000 person-years (CI) |  |  |  |  |  |  |  |  |  |  |
| CDIs/1000 hospital-days (CI) |  |  |  |  |  |  |  |  |  |  |

* \*Only index visit will be included (per 180 days)

\* For a given fiscal year, person-years is calculated using RPDB database. Please have a look at the following criteria for fical year 2009:

Alive persons from RPDB on 01APR2009.

Aged 18-105 on 01APR2009.

Ontario residents on 01APR2009 based on postal code

OHIP eligible on 01APR2009 .

Date of last contact with healthcare system is after 31MAR2002

(1) If a person had no CDI and alive at 31MAR2010, then person year=1.

(2) If a person had CDI within fiscal year 2009, then person year=(CDI date-01APR2009 )/365.

(3) if a person died within fiscal year 2009 and had no CDI, then person year=(death date - 01APR2009 )/365.

\*For a given fiscal year, hospital-days is calculated via all the patients from DAD database using following inclusion criteria:

1. Valid IKN.
2. Ontario resident (pstlcode = K,L,M,N,P ).
3. Available age and sex.
4. Aged 18-105 at hospital admission.
5. Consistent data: date of death >date of hospital admission.

6. OHIP eligible at admission date.

**Table VII: CDI by Year, Overall Number, Location of Onset, and Attribution**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Characteristic | 2014 | 2013 | 2012 | 2011 | 2010 | 2009 | 2008 | 2007 | 2006 | 2005 |
| **Total CDI cases** |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |
| **ACH-onset** |  |  |  |  |  |  |  |  |  |  |
| ACH-associated  | n(%) | n(%) | n(%) | n(%) | n(%) | n(%) | n(%) | n(%) | n(%) | n(%) |
| ACH/LTCF-associated | n(%) | n(%) | n(%) | n(%) | n(%) | n(%) | n(%) | n(%) | n(%) | n(%) |
|  |  |  |  |  |  |  |  |  |  |  |
| **LTCF-onset** |  |  |  |  |  |  |  |  |  |  |
| LTCF-associated | n(%) | n(%) | n(%) | n(%) | n(%) | n(%) | n(%) | n(%) | n(%) | n(%) |
| LTCF/ACH-associated | n(%) | n(%) | n(%) | n(%) | n(%) | n(%) | n(%) | n(%) | n(%) | n(%) |
|  |  |  |  |  |  |  |  |  |  |  |
| **Community-onset** |  |  |  |  |  |  |  |  |  |  |
| Community-associated | n(%) | n(%) | n(%) | n(%) | n(%) | n(%) | n(%) | n(%) | n(%) | n(%) |
| ACH-associated | n(%) | n(%) | n(%) | n(%) | n(%) | n(%) | n(%) | n(%) | n(%) | n(%) |
|  |  |  |  |  |  |  |  |  |  |  |
| ACH-associated CDIs per 100,000 population (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) |
| Age-adjusted ACH-associated CDIs per 100,000 population (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) |
| LTCF-associated CDIs per 100,000 population (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) |
| Age-adjusted LTCF-associated CDIs per 100,000 population (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) |
| ACH/LTCF-associated CDIs per 100,000 population (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) |
| Age-adjusted ACH/LTCF-associated CDIs per 100,000 population (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) |
| Community-associated CDIs per 100,000 population (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) |
| Age-adjusted Community-associated CDIs per 100,000 population (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) | n (CI) |

\*% = percent of total CDI in given year

**\*Note**: Age-adjustments are made to the 2010 Ontario population. General population is generated from RPDB : Ontario residents with valid age and sex, aged 18-105 at 01APR for a given year. OHIP eligible at 01APR.

**Table VIII: Baseline characteristics for CDI cohort/control groups**

**\*Note:** separate tables for each of the four cohort/control pairs

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **CDI cohort** | **Non-CDI cohort** | **Standardized differences** | **p-value** |
| **All patients (total)**  | N | N |  |  |
| **Patient days (mean, SD, median, IQR, range)** | N | N |  |  |
| **Age group (years)** |  |  |  |  |
| 18-44 | n (%) | n (%) |  |  |
| 45-64 | n (%) | n (%) |  |  |
| 65-74 | n (%) | n (%) |  |  |
| 75-84 | n (%) | n (%) |  |  |
| 85+ | n (%) | n (%) |  |  |
| **Sex, female** | n (%) | n (%) |  |  |
| **Sex, male** | n (%) | n (%) |  |  |
| **LTCF resident** | n (%) | n (%) |  |  |
| **Number of individuals hospitalized** | n (%) | n (%) |  |  |
| **Admission source** |  |  |  |  |
| ER | n (%) | n (%) |  |  |
| Home | n (%) | n (%) |  |  |
| Transfer | n (%) | n (%) |  |  |
| Nursing home | n (%) | n (%) |  |  |
| Other | n (%) | n (%) |  |  |
| **Healthcare exposure in previous 90 days \*\***  | n (%) | n (%) |  |  |
| **Healthcare exposure in previous year\*\*** | n (%) | n (%) |  |  |
| **Acute infection in previous 30 days**  | n (%) | n (%) |  |  |
| **Comorbidities** |  |  |  |  |
| CVD | n (%) | n (%) |  |  |
| COPD | n (%) | n (%) |  |  |
| CHF | n (%) | n (%) |  |  |
| Diabetes | n (%) | n (%) |  |  |
| Renal/liver disease | n (%) | n (%) |  |  |
| Renal/liver failure | n (%) | n (%) |  |  |
| Cancer | n (%) | n (%) |  |  |
| Pulmonary circulatory disorder | n (%) | n (%) |  |  |
| Valvular disease | n (%) | n (%) |  |  |
| Inflammatory bowel disease | n (%) | n (%) |  |  |
| **Antibiotic use in previous 30 days** | n (%) | n (%) |  |  |
| **Hospital characteristic:** |  |  |  |  |
| Urban | n (%) | n (%) |  |  |
| Rural | n (%) | n (%) |  |  |
| **Hospital characteristics:** **# of beds** | n (%) | n (%) |  |  |
| < 100 | n (%) | n (%) |  |  |
| 100 – 299 | n (%) | n (%) |  |  |
| 300 – 499 | n (%) | n (%) |  |  |
| ≥ 500 | n (%) | n (%) |  |  |
|  |  |  |  |  |

* \*\*ACH-stay or LTCF-stay

**Table IX: Impact of CDI on patient outcomes (unadjusted) for CDI cohort/control groups1**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **CDI cohort** | **Non-CDI cohort** | **Standardized differences** | **p-value** |
| Number of individuals hospitalized~ |  |  |  |  |
| LOS | Mean ± SD, median, IQR, range | Mean ± SD, median, IQR, range |  |  |
| ICU LOS | Mean ± SD, median, IQR, range | Mean ± SD, median, IQR, range |  |  |
| Mortality rate 30-days post-admission date | n (%) | n (%) |  |  |
| Mortality rate 90-days post-admission date | n (%) | n (%) |  |  |
| Mortality rate 180-days post-admission date | n (%) | n (%) |  |  |
| Mortality rate 30-days post-discharge date | n (%) | n (%) |  |  |
| Mortality rate 90-days post-discharge date | n (%) | n (%) |  |  |
| Mortality rate 180-days post-discharge date | n (%) | n (%) |  |  |
| CDI recurrence 180 days post-discharge | n (%) | n (%) |  |  |
| CDI recurrence 365 days post-discharge | n (%) | n (%) |  |  |
| All-cause re-hospitalization (30 days) | n (%) | n (%) |  |  |
| All-cause re-hospitalization (90 days) | n (%) | n (%) |  |  |
| All-cause re-hospitalization (180 days) | n (%) | n (%) |  |  |
| Colectomy 365 days post-diagnosis | n (%) | n (%) |  |  |
| Cost (8 groups and total for both 180-day and 365-day post-admission) | Mean ± SD, median, IQR, range | Mean ± SD, median, IQR, range |  |  |

1 Separate tables for each of the 4 cohort/control groups

\*\*ACH-stay or LTCF-stay

~Not all individuals in the control groups will have been hospitalized

**Table X: Outcomes by CDI risk factors**

|  |  |
| --- | --- |
| **OUTCOME: e.g. LENGTH OF STAY\* (see below for the other outcomes)** |  |
|  | **CDI cohort** | **Non-CDI cohort+** | **P-value for mean difference** | **Attributable outcome (CI)** |
| **Age group (years)** |  |  |  |  |
| 18-44 | Mean ± SD, median, IQR, range | Mean ± SD, median, IQR, range |  | Difference in mean (95% CI) |
| 45-64 | Mean ± SD, median, IQR, range | Mean ± SD, median, IQR, range |  | Difference in mean (95% CI) |
| 65-74 | Mean ± SD, median, IQR, range | Mean ± SD, median, IQR, range |  | Difference in mean (95% CI) |
| 75-84 | Mean ± SD, median, IQR, range | Mean ± SD, median, IQR, range |  | Difference in mean (95% CI) |
| 85+ | Mean ± SD, median, IQR, range | Mean ± SD, median, IQR, range |  | Difference in mean (95% CI) |
| **Sex, female** | Mean ± SD, median, IQR, range | Mean ± SD, median, IQR, range |  | Difference in mean (95% CI) |
| **Sex, male** | Mean ± SD, median, IQR, range | Mean ± SD, median, IQR, range |  | Difference in mean (95% CI) |
| **LTCF resident** | Mean ± SD, median, IQR, range | Mean ± SD, median, IQR, range |  | Difference in mean (95% CI) |
| **Healthcare exposure in 90 days prior to onset\*\***  | Mean ± SD, median, IQR, range | Mean ± SD, median, IQR, range |  | Difference in mean (95% CI) |
| **Healthcare exposure in 365 days prior to onset \*\*** | Mean ± SD, median, IQR, range | Mean ± SD, median, IQR, range |  | Difference in mean (95% CI) |
| **Antibiotic use in 30 days prior to onset**  | Mean ± SD, median, IQR, range | Mean ± SD, median, IQR, range |  | Difference in mean (95% CI) |
| **Comorbidities** | Mean ± SD, median, IQR, range | Mean ± SD, median, IQR, range |  | Difference in mean (95% CI) |
| CVD | Mean ± SD, median, IQR, range | Mean ± SD, median, IQR, range |  | Difference in mean (95% CI) |
| COPD | Mean ± SD, median, IQR, range | Mean ± SD, median, IQR, range |  | Difference in mean (95% CI) |
| CHF | Mean ± SD, median, IQR, range | Mean ± SD, median, IQR, range |  | Difference in mean (95% CI) |
| Diabetes | Mean ± SD, median, IQR, range | Mean ± SD, median, IQR, range |  | Difference in mean (95% CI) |
| Renal/liver disease | Mean ± SD, median, IQR, range | Mean ± SD, median, IQR, range |  | Difference in mean (95% CI) |
| Renal/liver failure | Mean ± SD, median, IQR, range | Mean ± SD, median, IQR, range |  | Difference in mean (95% CI) |
| Cancer | Mean ± SD, median, IQR, range | Mean ± SD, median, IQR, range |  | Difference in mean (95% CI) |
| Pulmonary circulatory disorder | Mean ± SD, median, IQR, range | Mean ± SD, median, IQR, range |  | Difference in mean (95% CI) |
| Valvular disease | Mean ± SD, median, IQR, range | Mean ± SD, median, IQR, range |  | Difference in mean (95% CI) |
| Inflammatory bowel disease | Mean ± SD, median, IQR, range | Mean ± SD, median, IQR, range |  | Difference in mean (95% CI) |

\*Similar tables to be drafted for each of the 4 cohort/control matched groups, for each of the following outcomes:

* Index hospitalization LOS (data entered as mean [days] ± SD)
* ICU admission (data entered as n [%])
* ICU LOS (data entered as mean [days] ± SD)
* colectomy in 365 days after onset (partial, total or radical resection of the large intestine or rectum [procedure codes: 1NM87XX, INM89XX, INM91XX, 1NQ87XX, 1NQ89XX, 1NQ90XX excluding INM87BA and 1NQ87BA]) (data entered as n [%])
* CDI recurrence (occurring between 180 and 365 days post-discharge) as defined by hospitalization for CDI (data entered as n [%])
* all-cause re-hospitalization (30/90/180 days post-discharge) (data entered as n [%])
* mortality (30/90/180 days post-CDI admission) (data entered as n [%])
* costs for 180 days and 365 post-CDI onset (hospital admission) (data entered as mean ± SD)

\*\*ACH-stay or LTCF-stay

For Table X, can we par down to the following outcomes:

* CDI recurrence  (occurring between 180 and 365 days post-discharge) as defined by hospitalization for CDI (n [%])
* All-cause re-hospitalization (30/90/180 days post-discharge) (n [%])
* Mortality (30/90/180 days post-CDI admission) ( n [%])
* Costs for 180 days and 365 post-CDI onset (hospital admission) (mean  ± SD)

+Not all individuals in the LTCF and Community control groups will be hospitalized, so this table will only include the subset who are.

**Table XI: Adjusted outcomes of hospitalized patients with and without CDI~**

|  |
| --- |
| **OUTCOME (see below for list)\*** |
|  | **Relative Risk**  | **95% CI** |
| **Age group (years)** |  |  |
| 18-44 |  |  |
| 45-64 |  |  |
| 65-74 |  |  |
| 75-84 |  |  |
| 85+ |  |  |
| **Sex, female** |  |  |
| **Sex, male** |  |  |
| **CDI infection status** |  |  |
| **LTCF resident** |  |  |
| **Healthcare exposure in 90 days prior to onset\*\***  |  |  |
| **Healthcare exposure in 365 days prior to onset \*\*** |  |  |
| **Antibiotic use in 30 days prior to onset**  |  |  |
| **Comorbidities** |  |  |
| CVD |  |  |
| COPD |  |  |
| CHF |  |  |
| Diabetes |  |  |
| Renal/liver disease |  |  |
| Renal/liver failure |  |  |
| Cancer |  |  |
| Pulmonary circulatory disorder |  |  |
| Valvular disease |  |  |
| Inflammatory bowel disease |  |  |
| **Concomitant antibiotics** |  |  |

\*Tables to be drafted for each of the four cohorts for the following outcomes:

* ICU admission
* colectomy in 365 days after onset (partial, total or radical resection of the large intestine or rectum [procedure codes: 1NM87XX, INM89XX, INM91XX, 1NQ87XX, 1NQ89XX, 1NQ90XX excluding INM87BA and 1NQ87BA])
* CDI recurrence (occurring between 180-365 days post-discharge) as defined by hospitalization for CDI
* all-cause re-hospitalization (30/90/180 days post-discharge)
* mortality (30/90/180 days post-CDI admission)

\*\*ACH-stay or LTCF-stay

**Table XII: Exclusion Table**

|  |  |
| --- | --- |
| **Reason for exclusion\*** | **Number of exclusions** |
| **CDI less than 180 days from index hospitalization discharge (considered same case)** |  |

\*identified and presented per year

\*\*indicated by post-hospitalization discharge ICD-10 code for CDI (A04.7) during 2nd hospitalization, physician visit or ED visit

**Table XIII: Comparison of CDI cases in individuals over 65 years, based on prior ED visits for diarrhea/CDI and antibiotic use\***

For each of the 6 groups (Table I), we’d like a table with the following:

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **No prior ED visit for diarrhea/CDI****(A)** | **Prior ED visit for diarrhea/CDI****(B)** | **Prior ED visit for diarrhea/CDI + antibiotic (C)** | **p-value****(A and B)** | **p-value** **(A and C)** |
| **All patients (total)** | N (%) | N (%) | N (%) |  |  |
| **Patient days (mean, SD median, IQR, range)** | N | N | N |  |  |
| **Age group (years) (mean, SD, median, IQR range)** |  |  |  |  |  |
| 65-74 | n (%) | n (%) | n (%) |  |  |
| 75-84 | n (%) | n (%) | n (%) |  |  |
| 85+ | n (%) | n (%) | n (%) |  |  |
| **Sex, female** | n (%) | n (%) | n (%) |  |  |
| **Sex, male** | n (%) | n (%) | n (%) |  |  |
| **LTCF resident** | n (%) | n (%) | n (%) |  |  |
| **Admission source** |  |  |  |  |  |
| ER | n (%) | n (%) | n (%) |  |  |
| Home | n (%) | n (%) | n (%) |  |  |
| Transfer | n (%) | n (%) | n (%) |  |  |
| Nursing home | n (%) | n (%) | n (%) |  |  |
| Other | n (%) | n (%) | n (%) |  |  |
| **Healthcare exposure in year prior to onset\*\*** | n (%) | n (%) | n (%) |  |  |
| **Healthcare exposure in 90 days prior to onset**  | n (%) | n (%) | n (%) |  |  |
| **Antibiotic use in 30 days prior to onset** | n (%) | n (%) | n (%) |  |  |
| **Comorbidities** |  |  |  |  |  |
| CVD | n (%) | n (%) | n (%) |  |  |
| COPD | n (%) | n (%) | n (%) |  |  |
| CHF | n (%) | n (%) | n (%) |  |  |
| Diabetes | n (%) | n (%) | n (%) |  |  |
| Renal/liver disease | n (%) | n (%) | n (%) |  |  |
| Renal/liver failure | n (%) | n (%) | n (%) |  |  |
| Cancer | n (%) | n (%) | n (%) |  |  |
| Pulmonary circulatory disorder | n (%) | n (%) | n (%) |  |  |
| Valvular disease | n (%) | n (%) | n (%) |  |  |
| Inflammatory bowel disease | n (%) | n (%) | n (%) |  |  |
| Concomitant antibiotic | n (%) | n (%) | n (%) |  |  |
| **Hospital characteristic:** |  |  |  |  |  |
| Urban | n (%) | n (%) | n (%) |  |  |
| Rural | n (%) | n (%) | n (%) |  |  |
| **Hospital characteristics:** **# of beds** |  |  |  |  |  |
| < 100 | n (%) | n (%) | n (%) |  |  |
| 100 – 299 | n (%) | n (%) | n (%) |  |  |
| 300 – 499 | n (%) | n (%) | n (%) |  |  |
| ≥ 500 | n (%) | n (%) | n (%) |  |  |
| **Discharge status** |  |  |  |  |  |
| Home | n (%) | n (%) | n (%) |  |  |
| Transfer | n (%) | n (%) | n (%) |  |  |
| Nursing home | n (%) | n (%) | n (%) |  |  |
| Hospice care | n (%) | n (%) | n (%) |  |  |
| Death | n (%) | n (%) | n (%) |  |  |
| Other | n (%) | n (%) | n (%) |  |  |
| **OUTCOMES** |  |  |  |  |  |
| LOS | Mean, SD, median, IQR, range | Mean, SD, median, IQR, range | Mean, SD, median, IQR, range |  |  |
| ICU admission | n (%) | n (%) | n (%) |  |  |
| ICU LOS | Mean, SD, median, IQR, range | Mean, SD, median, IQR, range | Mean, SD, median, IQR, range |  |  |
| 30-day all-cause mortality post-CDI onset~  | n (%) | n (%) | n (%) |  |  |
| 90-day all-cause mortality post-CDI onset~ | n (%) | n (%) | n (%) |  |  |
| 180-day all-cause mortality post-CDI onset~ | n (%) | n (%) | n (%) |  |  |
| 180-day post-discharge CDI recurrence | n (%) | n (%) | n (%) |  |  |
| 365-day post-discharge CDI recurrence | n (%) | n (%) | n (%) |  |  |
| 30-day post-discharge all-cause re-hospitalization  | n (%) | n (%) | n (%) |  |  |
| 90-day post-discharge all-cause re-hospitalization | n (%) | n (%) | n (%) |  |  |
| 180-day post-discharge all-cause re-hospitalization | n (%) | n (%) | n (%) |  |  |
| 365-day colectomy post-CDI onset | n (%) | n (%) | n (%) |  |  |
| Costs in the 180 days post-admission | Mean, SD, median, IQR, range | Mean, SD, median, IQR, range | Mean, SD, median, IQR, range |  |  |
| Costs in the 365 days post-admission | Mean, SD, median, IQR, range | Mean, SD, median, IQR, range | Mean, SD, median, IQR, range |  |  |

 \*Com = community

 \*\*ACH-stay or LTCF-stay

 ~Hospital admission

**Additional request (January 17, 2019)**

|  |
| --- |
| **Table 1: Adjusted outcomes of hospitalized patients with ACH-acquired/ACH-onset CDI and their controls** |
| **Mortality within 30 days post-CDI discharge**  |
|   | **Relative Risk** | **Lower 95% CI** | **Upper 95% CI** | **P-Value** |
| ***CDI***  |  |  |  |  |

**Table 2: Adjusted outcomes of hospitalized patients with ACH-acquired/ACH-onset CDI and their controls**

|  |
| --- |
| **Mortality within 90 days post-CDI discharge**  |
|   | **Relative Risk** | **Lower 95% CI** | **Upper 95% CI** | **P-Value** |
| ***CDI***  |  |  |  |  |

**Table 3: Adjusted outcomes of hospitalized patients with ACH-acquired/ACH-onset CDI and their controls**

|  |
| --- |
| **Mortality within 180 days post-CDI discharge**  |
|   | **Relative Risk** | **Lower 95% CI** | **Upper 95% CI** | **P-Value** |
| ***CDI***  |  |  |  |  |

**Table 4: Adjusted outcomes of hospitalized patients with LTCF-acquired/LTCF-onset CDI and their controls**

|  |
| --- |
| **All-cause 30-days re-hospitalization post-discharge**  |
|   | **Relative Risk** | **Lower 95% CL** | **Upper 95% CL** | **P-Value** |
| ***CDI***  |  |  |  |  |

**Table 5: Risk factors for hospitalization and mortality outcomes in patients with ACH-acquired/ACH-onset CDI, using adjusted logistic regression models**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **All-cause 30-day re-hospitalization** | **All-cause 30-day mortality** | **All-cause 180 day mortality** |
|  | **OR**  | **95% CI** | **p-value** | **OR**  | **95% CI** | **p-value** | **OR**  | **95% CI** | **p-value** |
| **Age group (years)** |  |  |  |  |  |  |  |  |  |
| 45-64 | ref | ref | ref | ref | ref | ref | ref | ref | Ref |
| 65-74 |  |  |  |  |  |  |  |  |  |
| 75-84 |  |  |  |  |  |  |  |  |  |
| 85+ |  |  |  |  |  |  |  |  |  |
| **Sex (male: ref)** |  |  |  |  |  |  |  |  |  |
| **LTCF resident** |  |  |  |  |  |  |  |  |  |
| **Healthcare exposure in 90 days prior to onset\*\***  |  |  |  |  |  |  |  |  |  |
| **Healthcare exposure in 365 days prior to onset**  |  |  |  |  |  |  |  |  |  |
| **Antibiotic use in 30 days prior to onset**  |  |  |  |  |  |  |  |  |  |
| **Comorbidities** |  |  |  |  |  |  |  |  |  |
| CVD |  |  |  |  |  |  |  |  |  |
| COPD |  |  |  |  |  |  |  |  |  |
| CHF |  |  |  |  |  |  |  |  |  |
| Diabetes |  |  |  |  |  |  |  |  |  |
| Renal disease |  |  |  |  |  |  |  |  |  |
| Liver disease |  |  |  |  |  |  |  |  |  |
| Cancer |  |  |  |  |  |  |  |  |  |
| Pulmonary circulatory disorder |  |  |  |  |  |  |  |  |  |
| Valvular disease |  |  |  |  |  |  |  |  |  |
| Inflammatory bowel disease |  |  |  |  |  |  |  |  |  |

**Table 6: Risk factors for hospitalization and mortality outcomes in patients with LTCF-acquired/LTCF-onset CDI, using adjusted logistic regression models**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **All-cause 30-day re-hospitalization** | **All-cause 30-day mortality** | **All-cause 180 day mortality** |
|  | **OR**  | **95% CI** | **p-value** | **OR**  | **95% CI** | **p-value** | **OR**  | **95% CI** | **p-value** |
| **Age group (years)** |  |  |  |  |  |  |  |  |  |
| 45-64 | ref | ref | ref | ref | ref | ref | ref | ref | Ref |
| 65-74 |  |  |  |  |  |  |  |  |  |
| 75-84 |  |  |  |  |  |  |  |  |  |
| 85+ |  |  |  |  |  |  |  |  |  |
| **Sex (male: ref)** |  |  |  |  |  |  |  |  |  |
| **Healthcare exposure in 90 days prior to onset\*\***  |  |  |  |  |  |  |  |  |  |
| **Healthcare exposure in 365 days prior to onset**  |  |  |  |  |  |  |  |  |  |
| **Antibiotic use in 30 days prior to onset**  |  |  |  |  |  |  |  |  |  |
| **Comorbidities** |  |  |  |  |  |  |  |  |  |
| CVD |  |  |  |  |  |  |  |  |  |
| COPD |  |  |  |  |  |  |  |  |  |
| CHF |  |  |  |  |  |  |  |  |  |
| Diabetes |  |  |  |  |  |  |  |  |  |
| Renal disease |  |  |  |  |  |  |  |  |  |
| Liver disease |  |  |  |  |  |  |  |  |  |
| Cancer |  |  |  |  |  |  |  |  |  |
| Pulmonary circulatory disorder |  |  |  |  |  |  |  |  |  |
| Valvular disease |  |  |  |  |  |  |  |  |  |
| Inflammatory bowel disease |  |  |  |  |  |  |  |  |  |

**Table 7: Risk factors for hospitalization and mortality outcomes in patients with community-acquired/community-onset CDI, using adjusted logistic regression models**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **All-cause 30-day re-hospitalization** | **All-cause 30-day mortality** | **All-cause 180 day mortality** |
|  | **OR**  | **95% CI** | **p-value** | **OR**  | **95% CI** | **p-value** | **OR**  | **95% CI** | **p-value** |
| **Age group (years)** |
| 45-64 |  |  |  |  |  |  |  |  |  |
| 65-74 |  |  |  |  |  |  |  |  |  |
| 75-84 |  |  |  |  |  |  |  |  |  |
| 85+ | ref | ref | ref | ref | ref | ref | ref | ref | ref |
| **Sex (ref: male)** |  |  |  |  |  |  |  |  |  |
| **Healthcare exposure in 90 days prior to onset\*\***  |  |  |  |  |  |  |  |  |  |
| **Healthcare exposure in 365 days prior to onset \*\*** |  |  |  |  |  |  |  |  |  |
| **Antibiotic use in 30 days prior to onset**  |  |  |  |  |  |  |  |  |  |
| **Comorbidities** |
| CVD |  |  |  |  |  |  |  |  |  |
| COPD |  |  |  |  |  |  |  |  |  |
| CHF |  |  |  |  |  |  |  |  |  |
| Diabetes |  |  |  |  |  |  |  |  |  |
| Renal disease |  |  |  |  |  |  |  |  |  |
| Liver disease |  |  |  |  |  |  |  |  |  |
| Cancer |  |  |  |  |  |  |  |  |  |
| Pulmonary circulatory disorder |  |  |  |  |  |  |  |  |  |
| Valvular disease |  |  |  |  |  |  |  |  |  |
| Inflammatory bowel disease |  |  |  |  |  |  |  |  |  |

**Table 8: Risk factors for hospitalization and mortality outcomes in patients with ACH-acquired/community-onset CDI, using adjusted logistic regression models**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **All-cause 30-day re-hospitalization** | **All-cause 30-day mortality** | **All-cause 180 day mortality** |
|  | **OR**  | **95% CI** | **p-value** | **OR**  | **95% CI** | **p-value** | **OR**  | **95% CI** | **p-value** |
| **Age group (years)** |
| 45-64 |  |  |  |  |  |  |  |  |  |
| 65-74 |  |  |  |  |  |  |  |  |  |
| 75-84 |  |  |  |  |  |  |  |  |  |
| 85+ | ref | ref | ref | ref | ref | ref | ref | ref | ref |
| **Sex (ref: male)** |  |  |  |  |  |  |  |  |  |
| **Antibiotic use in 30 days prior to onset**  |  |  |  |  |  |  |  |  |  |
| **Comorbidities** |
| CVD |  |  |  |  |  |  |  |  |  |
| COPD |  |  |  |  |  |  |  |  |  |
| CHF |  |  |  |  |  |  |  |  |  |
| Diabetes |  |  |  |  |  |  |  |  |  |
| Renal disease |  |  |  |  |  |  |  |  |  |
| Liver disease |  |  |  |  |  |  |  |  |  |
| Cancer |  |  |  |  |  |  |  |  |  |
| Pulmonary circulatory disorder |  |  |  |  |  |  |  |  |  |
| Valvular disease |  |  |  |  |  |  |  |  |  |
| Inflammatory bowel disease |  |  |  |  |  |  |  |  |  |

**Additional request (January 22, 2019)**

|  |
| --- |
| **Table 1: Adjusted outcomes of hospitalized patients with ACH-acquired/ACH-onset CDI and their controls** |
| **Mortality within 30 days post-CDI discharge**  |
|   | **Relative Risk** | **Lower 95% CI** | **Upper 95% CI** | **P-Value** |
| ***CDI***  |  |  |  |  |

**Table 2: Adjusted outcomes of hospitalized patients with ACH-acquired/ACH-onset CDI and their controls**

|  |
| --- |
| **Mortality within 90 days post-CDI discharge**  |
|   | **Relative Risk** | **Lower 95% CI** | **Upper 95% CI** | **P-Value** |
| ***CDI***  |  |  |  |  |

**Table 3: Adjusted outcomes of hospitalized patients with ACH-acquired/ACH-onset CDI and their controls**

|  |
| --- |
| **Mortality within 180 days post-CDI discharge**  |
|   | **Relative Risk** | **Lower 95% CI** | **Upper 95% CI** | **P-Value** |
| ***CDI***  |  |  |  |  |

**Table 4: Adjusted outcomes of hospitalized patients with LTCF-acquired/LTCF-onset CDI and their controls**

|  |
| --- |
| **All-cause 30-days re-hospitalization post-discharge**  |
|   | **Relative Risk** | **Lower 95% CL** | **Upper 95% CL** | **P-Value** |
| ***CDI***  |  |  |  |  |

**Table 5: Risk factors for hospitalization and mortality outcomes in patients with ACH-acquired/ACH-onset CDI, using adjusted logistic regression models**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **All-cause 30-day re-hospitalization** | **All-cause 30-day mortality post-discharge** | **All-cause 180 day mortality post-discharge** |
|  | **OR**  | **95% CI** | **p-value** | **OR**  | **95% CI** | **p-value** | **OR**  | **95% CI** | **p-value** |
| **Age group (years)** |  |  |  |  |  |  |  |  |  |
| 45-64 |  |  |  |  |  |  |  |  |  |
| 65-74 |  |  |  |  |  |  |  |  |  |
| 75-84 |  |  |  |  |  |  |  |  |  |
| 85+ | ref | ref | ref | ref | ref | ref | ref | ref | Ref |
| **Sex (male: ref)** |  |  |  |  |  |  |  |  |  |
| **LTCF resident** |  |  |  |  |  |  |  |  |  |
| **Healthcare exposure in 90 days prior to onset\*\***  |  |  |  |  |  |  |  |  |  |
| **Healthcare exposure in 365 days prior to onset**  |  |  |  |  |  |  |  |  |  |
| **Antibiotic use in 30 days prior to onset**  |  |  |  |  |  |  |  |  |  |
| **Comorbidities** |  |  |  |  |  |  |  |  |  |
| CVD |  |  |  |  |  |  |  |  |  |
| COPD |  |  |  |  |  |  |  |  |  |
| CHF |  |  |  |  |  |  |  |  |  |
| Diabetes |  |  |  |  |  |  |  |  |  |
| Renal disease |  |  |  |  |  |  |  |  |  |
| Liver disease |  |  |  |  |  |  |  |  |  |
| Cancer |  |  |  |  |  |  |  |  |  |
| Pulmonary circulatory disorder |  |  |  |  |  |  |  |  |  |
| Valvular disease |  |  |  |  |  |  |  |  |  |
| Inflammatory bowel disease |  |  |  |  |  |  |  |  |  |

**Table 6: Risk factors for hospitalization and mortality outcomes in patients with LTCF-acquired/LTCF-onset CDI, using adjusted logistic regression models**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **All-cause 30-day re-hospitalization** | **All-cause 30-day mortality post-admission** | **All-cause 180 day mortality post-admission** |
|  | **OR**  | **95% CI** | **p-value** | **OR**  | **95% CI** | **p-value** | **OR**  | **95% CI** | **p-value** |
| **Age group (years)** |  |  |  |  |  |  |  |  |  |
| 45-64 |  |  |  |  |  |  |  |  |  |
| 65-74 |  |  |  |  |  |  |  |  |  |
| 75-84 |  |  |  |  |  |  |  |  |  |
| 85+ | ref | ref | ref | ref | ref | ref | ref | ref | Ref |
| **Sex (male: ref)** |  |  |  |  |  |  |  |  |  |
| **Healthcare exposure in 90 days prior to onset\*\***  |  |  |  |  |  |  |  |  |  |
| **Healthcare exposure in 365 days prior to onset**  |  |  |  |  |  |  |  |  |  |
| **Antibiotic use in 30 days prior to onset**  |  |  |  |  |  |  |  |  |  |
| **Comorbidities** |  |  |  |  |  |  |  |  |  |
| CVD |  |  |  |  |  |  |  |  |  |
| COPD |  |  |  |  |  |  |  |  |  |
| CHF |  |  |  |  |  |  |  |  |  |
| Diabetes |  |  |  |  |  |  |  |  |  |
| Renal disease |  |  |  |  |  |  |  |  |  |
| Liver disease |  |  |  |  |  |  |  |  |  |
| Cancer |  |  |  |  |  |  |  |  |  |
| Pulmonary circulatory disorder |  |  |  |  |  |  |  |  |  |
| Valvular disease |  |  |  |  |  |  |  |  |  |
| Inflammatory bowel disease |  |  |  |  |  |  |  |  |  |

**Table 7: Risk factors for hospitalization and mortality outcomes in patients with community-acquired/community-onset CDI, using adjusted logistic regression models**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **All-cause 30-day re-hospitalization** | **All-cause 30-day mortality post-admission** | **All-cause 180 day mortality post-admission** |
|  | **OR**  | **95% CI** | **p-value** | **OR**  | **95% CI** | **p-value** | **OR**  | **95% CI** | **p-value** |
| **Age group (years)** |
| 45-64 |  |  |  |  |  |  |  |  |  |
| 65-74 |  |  |  |  |  |  |  |  |  |
| 75-84 |  |  |  |  |  |  |  |  |  |
| 85+ | ref | ref | ref | ref | ref | ref | ref | ref | ref |
| **Sex (ref: male)** |  |  |  |  |  |  |  |  |  |
| **Healthcare exposure in 90 days prior to onset\*\***  |  |  |  |  |  |  |  |  |  |
| **Healthcare exposure in 365 days prior to onset \*\*** |  |  |  |  |  |  |  |  |  |
| **Antibiotic use in 30 days prior to onset**  |  |  |  |  |  |  |  |  |  |
| **Comorbidities** |
| CVD |  |  |  |  |  |  |  |  |  |
| COPD |  |  |  |  |  |  |  |  |  |
| CHF |  |  |  |  |  |  |  |  |  |
| Diabetes |  |  |  |  |  |  |  |  |  |
| Renal disease |  |  |  |  |  |  |  |  |  |
| Liver disease |  |  |  |  |  |  |  |  |  |
| Cancer |  |  |  |  |  |  |  |  |  |
| Pulmonary circulatory disorder |  |  |  |  |  |  |  |  |  |
| Valvular disease |  |  |  |  |  |  |  |  |  |
| Inflammatory bowel disease |  |  |  |  |  |  |  |  |  |

**Table 8: Risk factors for hospitalization and mortality outcomes in patients with ACH-acquired/community-onset CDI, using adjusted logistic regression models**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **All-cause 30-day re-hospitalization** | **All-cause 30-day mortality post-admission** | **All-cause 180 day mortality post-admission** |
|  | **OR**  | **95% CI** | **p-value** | **OR**  | **95% CI** | **p-value** | **OR**  | **95% CI** | **p-value** |
| **Age group (years)** |
| 45-64 |  |  |  |  |  |  |  |  |  |
| 65-74 |  |  |  |  |  |  |  |  |  |
| 75-84 |  |  |  |  |  |  |  |  |  |
| 85+ | ref | ref | ref | ref | ref | ref | ref | ref | ref |
| **Sex (ref: male)** |  |  |  |  |  |  |  |  |  |
| **Antibiotic use in 30 days prior to onset**  |  |  |  |  |  |  |  |  |  |
| **Comorbidities** |
| CVD |  |  |  |  |  |  |  |  |  |
| COPD |  |  |  |  |  |  |  |  |  |
| CHF |  |  |  |  |  |  |  |  |  |
| Diabetes |  |  |  |  |  |  |  |  |  |
| Renal disease |  |  |  |  |  |  |  |  |  |
| Liver disease |  |  |  |  |  |  |  |  |  |
| Cancer |  |  |  |  |  |  |  |  |  |
| Pulmonary circulatory disorder |  |  |  |  |  |  |  |  |  |
| Valvular disease |  |  |  |  |  |  |  |  |  |
| Inflammatory bowel disease |  |  |  |  |  |  |  |  |  |