| Project InitiationThis Section must be Completed Prior to Project Dataset(s) Creation | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Project Title:** | Examining Systemic Scleroderma with Interstitial Lung Disease (SSc-ILD) in Canada's Largest Province: An Estimate of the Prevalence and Incidence of SSc-ILD in Ontario (Phase 2, a Community Approach) | | | | |
| **Project TRIM number:** | 2020 0970 147 001 | | | | |
| **Research Program:** | DAS | | | | |
| **Site:** | ICES Central | | | | |
| **Project Objectives:** | *Insert Project Objectives as listed in the approved ICES Project PIA* | | | | |
| This study will allow us to get a better understanding of the market for OFEV® (nintedanib). This research will be conducted in anticipation of the Canadian approval of a subsequent indication for the treatment of systemic scleroderma (SSc) in the presence of interstitial lung disease (ILD) in late 2019. The Canadian Patient Access team would like to conduct a real-world evidence study to determine the prevalence and incidence (if possible) of SSc-ILD in Ontario, Canada.  Systemic sclerosis (SSc) is an autoimmune disease that is characterised by skin thickening and fibroblast dysfunction that leads to excessive collagen accumulation in extra-cellular matrix and internal organ damage. SSc is associated with conditions such as renal failure, pulmonary fibrosis/interstitial lung disease, and gastrointestinal disorders, with the highest rates of mortality among patients with SSc-associated interstitial lung disease (SSc-ILD).  To date, no published study has generated population based estimates of prevalence and incidence SSc-ILD in Canada. This primary objective of the current study, which will be described further below, is to develop prevalence and incidence estimates of SSc-ILD in Ontario.  This study is intended to be used to fulfil a requirement of health technology assessments submissions in Canada to CADTH and INESSS. It is also likely to be used to develop public payer budget impact models (BIAs) for the SSc-ILD indication of OFEV®. It could be used in pan- Canadian Pharmaceutical Alliance (pCPA) and/or individual public payer negotiations for listing. This is critical a step to allow the payers to have a better sense of the patient characteristics and potential size of the patient population that could be eligible for OFEV® treatment for SSc-ILD.  •Estimate the prevalence of SSc and SSc-ILD in Ontario  •Estimate the incidence rate of SSc and SSc-ILD in Ontario  •Estimate the prevalence and incidence of SSc and SSc-ILD by age, gender and region within Ontario  •Describe the demographic profile of patients with SSc and SSc-ILD diagnoses in Ontario  PHASE 2: There may be a proportion of patients with SSc and SSc-ILD who are diagnosed and treated in a community setting, and may not be captured in the data sources in Phase 1. To ensure our cohort reflects this missing population, we will be using a combination of OHIP billing codes based on clinical input. These codes will include a specific physician billing code, pulmonary function test (PFT) codes, echocardiography (ECG) codes, and high resolution computed topography (HRCT) codes. These are specified in the inclusion criteria for phase 2 below.  Brief Summary (Purpose)  The purpose of this study is to estimate the prevalence of SSc and SSc-ILD. This will allow payers to have an idea of the number of patients that could be eligible for treatment when a drug for this disease becomes available. It may also let them know how many new patients there will each year. | | | | |
| **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):** |  | | | | |
| **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 Saskin | | | | |
| **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* | | | | |
| Kobina Quansah  Refik Saskin | | | yyyy-mon-dd | |
| **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* | | | | |
| TBD | | | yyyy-mon-dd | |
| **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*** | | | |
| 2018-Dec-14 | RS | | | |

| 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 | 2008-2018 |
| CIHI SDS | 2008-2018 |
| NACRS | 2008-2018 |
| OHIP | 2008-2018 |
| ***General Use Datasets – Care Providers*** |  |
| See list |  |
| ***General Use Datasets – Population*** |  |
| RPDB |  |
| See list |  |
| ***General Use Datasets – Coding/Geography*** |  |
| LHIN |  |
| See list |  |
| ***General Use Datasets – Facilities*** |  |
| See list |  |
| ***General Use Datasets – Other*** |  |
| See list |  |
| ***Controlled Use Datasets*** |  |
| 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 | | |
| --- | --- | --- |
| **Study Design** | Cohort study  Matched cohort study  Case-control study  Cross-sectional study  Other (specify): | |
| Index Event / Inclusion Criteria | SSc and SSc-ILD patients will be identified via the following inclusion and exclusion criteria  Inclusion Criteria- Ontario:  Age greater than 18 years of age  with a valid health card on the first day of the fiscal year (s) of interest (April 1)  Date of last contact with the health care system within 7 years prior to the first day of the fiscal year of interest (April 1)  Eligible for the provincial insurance plan on the first day of the fiscal year (s) of interest (April 1)  Patient identified with a diagnosis (defined below) between April 1, 2008 to March 31, 2018:  **COHORT 1: USING SSc DATE AS DATE OF DIAGNOSIS**  **SSc definition and index date:**  OHIP Schedule of Benefits Physician:  710: Diagnosis of Lupus Erythaematosus, Generalized Scleroderma, Dermatomyositis, MCTD, undifferentiated CTD  (CODE APPEARS AT LEAST TWO TIMES IN THE STUDY TIME FRAME)  SSc index date will be based on the date the 710 code first appears.  OHIP Schedule of Benefits Pulmonary Function Tests:  J301: Volume versus Time Study - must include Vital capacity, FEV1, FEV1 /FVC  J304: Volume versus Flow Study - from which an expiratory limb, and inspiratory limb if indicated, are generated  J310: Carbon monoxide diffusing capacity by single breath method  (ANY OF THE CODES ABOVE APPEARS AT LEAST TWO TIMES IN THE STUDY TIME FRAME)  OHIP Schedule of Benefits Echocardiography Tests:  G570 AND G571: Complete study, 1 and 2 dimensions  G582/G583: Stress study  G574/G575: Focused study  (ANY OF THE CODES ABOVE APPEARS AT LEAST TWO TIMES IN THE STUDY TIME FRAME)  ILD DIAGNOSIS MUST OCCUR AFTER SSC DIAGNOSIS  **SSc-ILD definition:**  OHIP Schedule of Benefits Physician  710: Diagnosis of Disseminated Lupus Erythaematosus, Generalized Scleroderma, Dermatomyositis  (CODE APPEARS AT LEAST TWO TIMES IN THE STUDY TIME FRAME)  OHIP Schedule of Benefits Pulmonary Function Tests:  J301: Volume versus Time Study - must include Vital capacity, FEV1, FEV1 /FVC  J304: Volume versus Flow Study - from which an expiratory limb, and inspiratory limb if indicated, are generated  J310: Carbon monoxide diffusing capacity by single breath method  (ANY OF THE CODES ABOVE APPEARS AT LEAST TWO TIMES IN THE STUDY TIME FRAME)  OHIP Schedule of Benefits Echocardiography Tests:  G570/G571: Complete study, 1 and 2 dimensions  G582/G583: Stress study  G574/G575: Focused study  (ANY OF THE CODES ABOVE APPEARS AT LEAST TWO TIMES IN THE STUDY TIME FRAME)  OHIP Schedule of Benefits High Resolution Computed Tomography (HRCT) thorax Scans:  X417: Three dimensional CT acquisition sequencing, including post-processing (minimum of 60 slices; maximum 1 scan per patient per day) Specific to lung area  WITH ONE of the following codes billed WITHIN SEVEN DAYS:  X406: Thorax, without IV contrast OR  X407: Thorax, with IV contrast OR  X125: Thorax, with and without IV contrast OR   1. (X417 MUST APPEAR AT LEAST ONCE WITH ONE OF THE CODES ABOVE, WHICH APPEARS AT LEAST ONCE IN THE STUDY TIME FRAME) 2. (X417 MUST APPEAR AT LEAST TWO TIMES WITH ONE OF THE CODES ABOVE, WHICH APPEARS AT LEAST TWO TIMES IN THE STUDY TIME FRAME)   **Steps of inclusion of cohort creation are outlined in the table below:**   |  |  |  |  | | --- | --- | --- | --- | | **Step** | **Description** | **# Excluded** | **Total Cohort remaining** | | 1 | All OHIP records with code 710 and valid ikn between 01APR2008 and 31MAR2018 |  |  | | 2 | Keep one record per patient per day |  |  | | 3 | Code 710 appears at least two times between 01APR2008 and 31MAR2018 and second 710 code occurs within up to 3 years of the first 710 code |  |  | | 4 | Had any of following J codes-J301 J304 J310 two times between 01APR2008 and 31MAR2018 and within up to 3 years of the first 710 code |  |  | | 5 | Had any of following G codes - G570 G571 G582 G583 G574 G575 two times between 01APR2008 and 31MAR2018 and within up to 3 years of the first 710 code |  |  | | 6 | Having valid age and sex information |  |  | | 7 | Ontario residents |  |  | | 8 | Alive at index date |  |  | | 9 | Aged 18 and older at index date |  |  | | 10 | Date of last contact within 7 years prior to index date |  |  | | 11 | OHIP eligible at index date |  |  | | 12 | Define the first visit as index ( first code 710) |  |  | | 13 | X417 and any one of X406, X407, X125 appears within 7 days of the X417 code. This combination occur at least two times between 01APR2008 and 31MAR2018 and up to 3 years of the first code 710 |  |  | | 14 | Exclude patients having ILD before SSc index date |  |  | | 15 | Exclude patients having ILD before and on SSc index date |  |  | | 16 | Exclude patients having ILD before and after SSc index date |  |  |   **COHORT 2: USING THE ILD DATE AS DATE OF DIAGNOSIS:**  The same criteria will apply as above, but will use the date the X417 code first appears as the date of diagnosis (ILD diagnosis)  Exclusion Criteria (Ontario):  Under 18 at the start of the study  Stillbirth or cadaveric donations  Non-Ontario residents by postal code  Non-linkable health records:  Invalid health card number  Invalid birth date  Invalid gender | |
| **Estimated Size of Cohort**  **(if known)** | Unknown | |
| **Exclusions (in order)** | *Step* | Description |
| 1 | Invalid ikn, missing age, sex |
| 2 | Non-Ontario resident |
| 3 | Death date before index date |

| Project Time Frame Definitions | | |
| --- | --- | --- |
| Look-back Window  Observation Window  (in which to look for outcomes)  **Index Event Date**  Accrual Window  Max Follow-up Date | |
| **Accrual Start/End Dates** | 2008-2017 |
| **Max Follow-up Date** | 31Mar2018 |
| **When does observation window terminate?** | 31Mar2018 |
| **Lookback Window(s)** | 2 years |

| Variable Definitions (add additional rows as needed) | | |
| --- | --- | --- |
| **Main Exposure or Risk Factor** |  |
| **Primary Outcome Definition** | 1. **Crude rate of prevalence and incidence of SSc-ILD**  * **Overall and annual prevalence of SSc and SSc-ILD**   Annual prevalence rates will be calculated using the following methodology:  For each of the 10 fiscal years of the study, the denominator of eligible patients will be calculated. From this pool of eligible patients, those with the specific diagnosis code(s) of interest in a given fiscal year will be flagged (SSc or SSc-ILD). The number of patients flagged will be divided by the denominator of eligible patients and converted to a prevalence rate out of 100,000 people.  Similarly, a 10-year period prevalence will be calculated using the below methodology:  Patients who have the condition at any time from 2008-2018  All adults who live in the province with a valid health card at any time from 2008-2018   * **Overall and annual incidence of SSc and SSc-ILD**   Annual incidence rate will be defined as no diagnosis of the condition in the previous year based ICD coding in the province of interest and be calculated with the following formula:  Incident patients during the fiscal year  All adults with a valid health card person-time during the fiscal year  Overall incidence rate will be calculated with the following formula:  Incidence rate and prevalence will in addition be presented by:   * Age * Sex * LHIN   Statistical analysis:  Descriptive analyses will be conducted to report the results of this study. Continuous variables (e.g., age) will be presented as mean values, medians, ranges, and standard deviations and categorical variables will be presented as absolute and relative frequencies (e.g., sex). |
| **Secondary Outcome Definition(s)** |  |
| **Baseline Characteristics** | Age  Sex  Income quintile  LHIN  Urban/rural  Year  Charlson score (use 2 year lookback) |
| **Other Variables** |  |

| Analysis Plan and Dummy Tables (expand/modify as needed) | | |
| --- | --- | --- |
| **Descriptive Tables (insert or append dummy tables), e.g.:** | | |
| **Table 1. Baseline characteristics according to primary/secondary exposure** | | |
| **Table 2. Outcomes according to primary/secondary exposure** | | |
| **Table 3. Covariates (baseline characteristics) according to outcomes** | | |
| **Statistical Model(s)** | | |
| **Type of model** |  | |
| **Primary independent variable** |  | |
| **Dependent variable** |  | |
| **Covariates** |  | |
| **Sensitivity Analyses** | 1. OHIP Schedule of Benefits Physician  * 710: Diagnosis of Disseminated Lupus Erythaematosus, Generalized Scleroderma, Dermatomyositis   (CODE APPEARS AT LEAST ONCE IN THE STUDY TIME FRAME)  OHIP Schedule of Benefits Pulmonary Function Tests:   * J301: Volume versus Time Study - must include Vital capacity, FEV1, FEV1 /FVC * J304: Volume versus Flow Study - from which an expiratory limb, and inspiratory limb if indicated, are generated * J310: Carbon monoxide diffusing capacity by single breath method   (ONE OF THE CODES ABOVE APPEARS AT LEAST ONCE IN THE STUDY TIME FRAME)  OHIP Schedule of Benefits Echocardiography Tests:   * G570/G571: Complete study, 1 and 2 dimensions * G582/G583: Stress study * G574/G575: Focused study   (ONE OF THE CODES ABOVE APPEARS AT LEAST ONCE IN THE STUDY TIME FRAME)  OHIP Schedule of Benefits High Resolution Computed Tomography (HRCT) thorax Scans:  Allow a maximum of 2 years follow up following G codes for the following combination to occur  X417: Three dimensional CT acquisition sequencing, including post-processing (minimum of 60 slices; maximum 1 scan per patient per day) Specific to lung area  WITH one of the following codes billed within seven days:  X406: Thorax, without IV contrast  X407: Thorax, with IV contrast  X125: Thorax, with and without IV contrast  (X417 MUST APPEAR AT LEAST ONCE WITH ONE OF THE CODES ABOVE, WHICH APPEARS AT LEAST ONCE IN THE STUDY TIME FRAME)  If the combination of x codes does not occur within the maximum follow-up, count as a SSc patient only   1. For SSc-ILD patients allow a maximum of 3 years follow up following G codes for the following combination   OHIP Schedule of Benefits High Resolution Computed Tomography (HRCT) thorax Scans:  X417: Three dimensional CT acquisition sequencing, including post-processing (minimum of 60 slices; maximum 1 scan per patient per day) Specific to lung area  WITH one of the following codes billed within seven days:  X406: Thorax, without IV contrast  X407: Thorax, with IV contrast  X125: Thorax, with and without IV contrast  (X417 MUST APPEAR AT LEAST ONCE WITH ONE OF THE CODES ABOVE, WHICH APPEARS UP TO TWO YEARS AFTER THE OCCURRENCE OF G CODES)  If the combination of x codes does not occur within the maximum follow-up, count as a SSc patient only | |
| **Type of model** |  | |
| **Primary independent variable** |  | |
| **Dependent variable** |  | |
| **Covariates** |  | |
|  | |

| 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:** | |  | |