Administrative data validation, incidence, prevalence, & mortality of Giant Cell Arteritis (GCA) in Ontario, Canada

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Outline

- Validation study to accurately identify GCA using Ontario health administrative data

- Application of validated case definitions to estimate:
  - incidence
  - prevalence
  - all-cause mortality

What do we know about GCA incidence?

- Giant cell arteritis (GCA) is the most common chronic systemic vasculitis.
- Primarily affects older adults (average 70-80 years) of Northern European descent
  - highest rates from UK, USA, & Scandinavian countries (20 - 33 cases per 100,000 population older than 50 years) compared to other regions in the world.[1-7]
- There is a paucity of data on the incidence of GCA in Canada
- Previous Ontario study[8] estimated incidence from **biopsy-proven** cases:
  - 5 cases per 100 000 persons ≥50 years

[1] Chandran AK, et al. The incidence of giant cell arteritis in Olmsted County, Minnesota, over a 60-year period 1950-2009. Scand J Rheumatol. 2015;44(3):215-8.
[2] Lee JL, et al. The geo-epidemiology of temporal (giant cell) arteritis. Clin Rev Allergy Immunol. 2008;35(1-2):88-95.
[3] Elling P, et al. Synchronous variations of the incidence of temporal arteritis and polymyalgia rheumatica in different regions of Denmark. J Rheumatol. 1996;23(1):112-9.
[4] Franzen P, et al . Giant cell arteritis and polymyalgia rheumatica in a region of Finland. J Rheumatol. 1992;19(2):273-6.
[5] Baldursson O, et al. Giant cell arteritis in Iceland. An epidemiologic and histopathologic analysis. Arthritis Rheum. 1994;37(7):1007-12.
[6] Gonzalez-Gay MA, et al. Giant cell arteritis in northwestern Spain: a 25-year epidemiologic study. Medicine (Baltimore). 2007;86(2):61-8.
[7] Salvarani C, et al. Epidemiologic and immunogenetic aspects of polymyalgia rheumatica and giant cell arteritis in northern Italy. Arthritis Rheum. 1991;34(3):351-6.
[8] Ing EB, et al. The incidence of giant cell arteritis in Ontario, Canada. Can J Ophthalmol. 2019;54(1):119-24.

What do we know about GCA prevalence?

- Prevalence of GCA is infrequently reported in the literature & often estimated from incidence rates.
- USA[1]:
  - 2015 → 204 cases per 100,000 population aged ≥50 yrs.
    - Women → 304 cases per 100,000 pop
    - Men → 91 cases per 100,000 pop
- Germany[2]:
  - Rates doubled over a 12-year period (1994 to 2006)

[1] Crowson CS, Matteson EL. Contemporary prevalence estimates for giant cell arteritis and polymyalgia rheumatica, 2015. Semin Arthritis Rheum. 2017;47(2):253-256.
[2] Herlyn K, et al. Doubled prevalence rates of ANCA-associated vasculitides and giant cell arteritis between 1994 and 2006 in northern Germany. Rheumatology (Oxford). 2014;53(5):882-

What do we know about GCA mortality?

- Risk of mortality among individuals with GCA have produced conflicting reports[1]
- Individuals with GCA are at increased risk of serious morbidity including cardiovascular disease & stroke
  - Would expect mortality to be increased relative to the general pop

[1] Hill CL, et al. Risk of mortality in patients with giant cell arteritis: a systematic review and meta-analysis. Semin Arthritis Rheum. 2017;46(4):513-9.

Research AIM

- To estimate trends in the incidence, prevalence of GCA over time
- To estimate excess mortality among individuals with GCA (relative to the general population).

Uncertainty how to define GCA in health administrative data

How do we identify GCA in health administrative data?

- 1 prior Canadian validation study on VASCULITIS; did not assess GCA alone[1] → dx code (446)
  - sensitivity: 94% specificity: 95% (reference standard: n=92 clinical diagnoses made by 8 rheumatologists)

- In BC: Amiri et al (BC)[2] have defined GCA patients:
  - > 40 years of age
  - 1 ICD-9 446.5 by a rheumatologist
    - OR
  - 1 ICD-9 446.5 OR ICD-10 M31.5 code from hospital
    - OR
  - 2 ICD-9 446.5 at least 2 months apart, 2-years by a non-rheumatologist;
    - AND
  - 1 prescription for oral glucocorticoids between 1 month before and 6 months after the index date.
  - Excluding those with 2 dx codes for with other inflammatory disease diagnoses (e.g. RA, SpA, SLE) ≥2 months apart subsequent to a GCA code

[1] Bernatsky S, Linehan T, Hanly JG. The accuracy of administrative data diagnoses of systemic autoimmune rheumatic diseases. J Rheumatol. 2011; 38:1612-6
[2] Amiri/Avina-Zubieta. Increased risk of cardiovascular disease in giant cell arteritis: a general population based study. Rheumatology 2016;55:3340

How do we identify GCA in health administrative data?

- In Ontario, GCA is difficult to discriminate from other forms of vasculitis in administrative data due to non-specific OHIP diagnosis codes
  - **OHIP**
    - 446: “Polyarteritis nodosa, temporal arteritis”
    - 447: “Vasculitis, Other disorders of arteries”
  - **ICD9**
    - 446.5: “Giant Cell Arteritis”
  - **ICD10**
    - M31.5: “Giant cell arteritis with polymyalgia rheumatica”
    - M31.6: “Other giant cell arteritis”
  - **Procedure codes**
    - Z815: “temporal artery biopsy”

Validation study of administrative data case definitions

- To validate case definitions to ascertain GCA patients from health administrative data, the validation cohort was derived from primary care EMRs from 381 family physicians and 563,181 patients distributed throughout Ontario

- We used a rule-based approach of GCA-related terms (e.g. Giant Cell Arteritis, Giant Cell Aortitides, Giant Cell Aortic Arteritis, Temporal arteritis, Large vessel vasculitis) to identify patients with GCA in the EMR database.

Validation of administrative data case definitions

- Using our systematic search strategy, we identified 143 patients with GCA (prevalence: 0.2% among 50y +)
  - 78% were female
  - mean (SD) age of 79 (9) years
  - 41% had documentation of a temporal artery biopsy report within their EMR

Validation of administrative data case definitions

- Patients not identified as GCA cases (& including those being tested for GCA who were deemed not to have it) were classified as non-cases.

- We then obtained a random sample of 15% of non-cases from a total of 50,292 eligible patients (n=7,524) in order to compute specificity and negative predictive value (NPV).

Health administrative data case definitions

- Case definitions were derived from different data sources:
  - **OHIP claims database** identified physician billing diagnosis codes for vasculitis (OHIP codes 446, 447) and procedure fee codes (Z815) for temporal artery biopsy procedures
    - Exclusions: procedure codes for lung, renal, skin or sinonasal biopsies (Z113, Z116, Z309, Z310, Z333, Z336, Z338, Z340, Z601) - an indication these individuals had another form of vasculitis
  - **ICES Physician Database** identified physician specialty for billing claims (rheumatologist, general internist, ophthalmologist)
  - **CIHI Discharge Abstract Database** identified GCA hospitalizations (ICD9 446.5, ICD10 M31.5, M31.6)
  - **Ontario Drug Benefit** Pharmacy claims for glucocorticoids dispensations

Accuracy of "Simple" Case Definitions

Case Definition	Sensitivity	Specificity	PPV	NPV
≥1 H	22.1 (15.0-29.2)	100.0 (100.0-100.0)	96.7 (90.2-100.0)	98.7 (98.4-98.9)
≥1 P	71.0 (63.2-78.8)	95.5 (95.0-95.9)	21.4 (17.5-25.2)	99.5 (99.3-99.6)
≥1 P by a specialist	64.1 (55.9-72.3)	99.3 (99.1-99.5)	61.3 (53.2-69.5)	99.4 (99.2-99.6)

H = hospitalization diagnosis code (in any primary or secondary position);
P = physician diagnosis code;
Specialist refers to rheumatologist, internal medicine, or ophthalmologist;

Top Performing Case Definitions with highest sensitivity & PPV

Case Definition	Sensitivity	Specificity	PPV	NPV
Definition 1: ≥1 H or [≥ 2 P with ≥ 1 P by a specialist and (≥ 1 Rx or TAB) in 3 yrs]*	60%	100%	81%	99%
Definition 2: ≥1 H or [≥ 2 P with ≥ 1 P by a specialist and (≥ 1 Rx or TAB) in 1 yr]	56%	100%	81%	99%
Definition 3: ≥1 H or [≥ 2 P with ≥ 1 P by a specialist and (≥ 1 Rx or TAB) in 2 yrs]	57%	100%	81%	99%
Definition 4: ≥1 H or [≥ 2 P with ≥ 1 P by a specialist and ≥ 1 Rx in 3 yrs] ***NO TAB ***	60%	100%	80%	99%
Definition 5: ≥1 H or [≥ 3 P and (≥ 1 Rx or TAB) in 1 yr] ***NO specialist****	55%	100%	82%	99%

- The top performing case definition (Definition 1) defined GCA patients who had at least 1 hospitalization, OR at least 2 diagnosis claims with at least 1 by a specialist AND at least 1 glucocorticoid prescription or at least 1 temporal artery biopsy in 3 years and excluded those with kidney, lung, skin, and nasal biopsies in the 1 year period of a diagnosis claim (81% PPV, 60% sensitivity)

Incidence

To compare results, we applied the top performing case definitions to estimate population rates.

Disease onset (to identify new cases) was defined as the first GCA diagnosis code OR temporal artery biopsy code, whichever came first.

Crude incidence of GCA

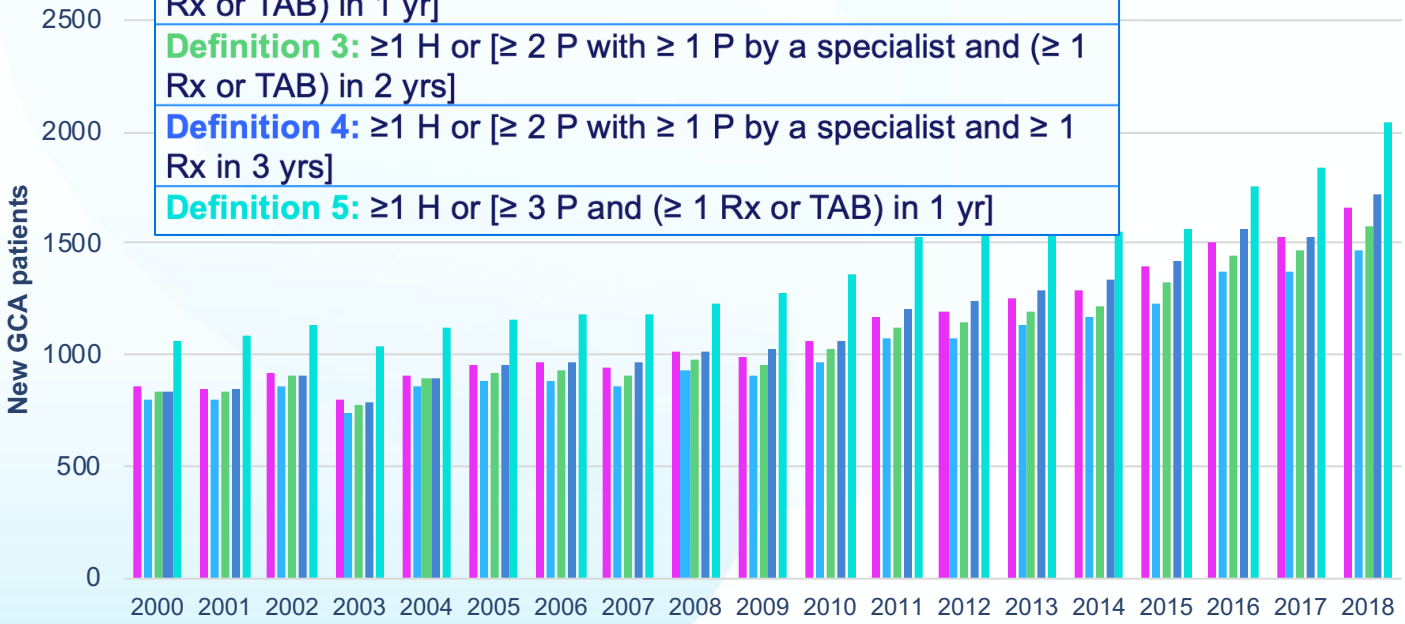
Definition 1: ≥1 H or [≥ 2 P with ≥ 1 P by a specialist and (≥ 1 Rx or TAB) in 3 yrs]*

Definition 2: ≥1 H or [≥ 2 P with ≥ 1 P by a specialist and (≥ 1 Rx or TAB) in 1 yr]

Definition 3: ≥1 H or [≥ 2 P with ≥ 1 P by a specialist and (≥ 1 Rx or TAB) in 2 yrs]

Definition 4: ≥1 H or [≥ 2 P with ≥ 1 P by a specialist and ≥ 1 Rx in 3 yrs]

Definition 5: ≥1 H or [≥ 3 P and (≥ 1 Rx or TAB) in 1 yr]



- 4/5 Case definitions produced comparable findings
- Case definition 5 (which did not require a specialist) identified the most cases
  - ?? identifying additional patients who were never referred to a specialist, or more false positives??
  - BUT highest PPV but lower sensitivity

Age/sex-standardized incidence rates

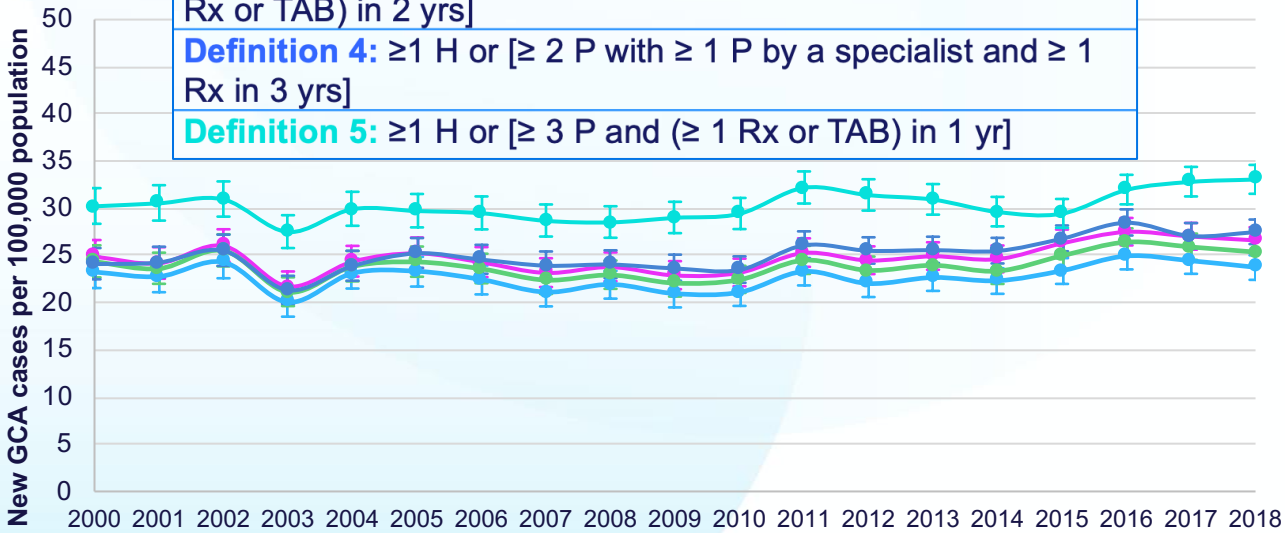
Definition 1: ≥1 H or [≥ 2 P with ≥ 1 P by a specialist and (≥ 1 Rx or TAB) in 3 yrs]*

Definition 2: ≥1 H or [≥ 2 P with ≥ 1 P by a specialist and (≥ 1 Rx or TAB) in 1 yr]

Definition 3: ≥1 H or [≥ 2 P with ≥ 1 P by a specialist and (≥ 1 Rx or TAB) in 2 yrs]

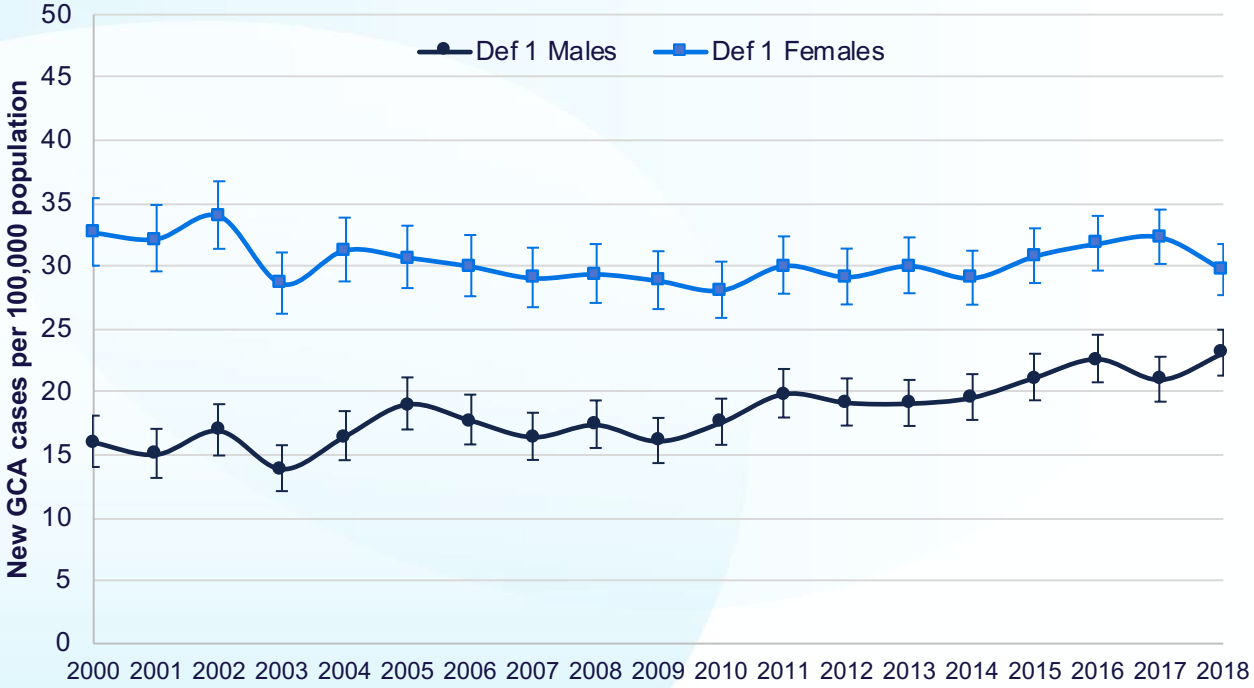
Definition 4: ≥1 H or [≥ 2 P with ≥ 1 P by a specialist and ≥ 1 Rx in 3 yrs]

Definition 5: ≥1 H or [≥ 3 P and (≥ 1 Rx or TAB) in 1 yr]



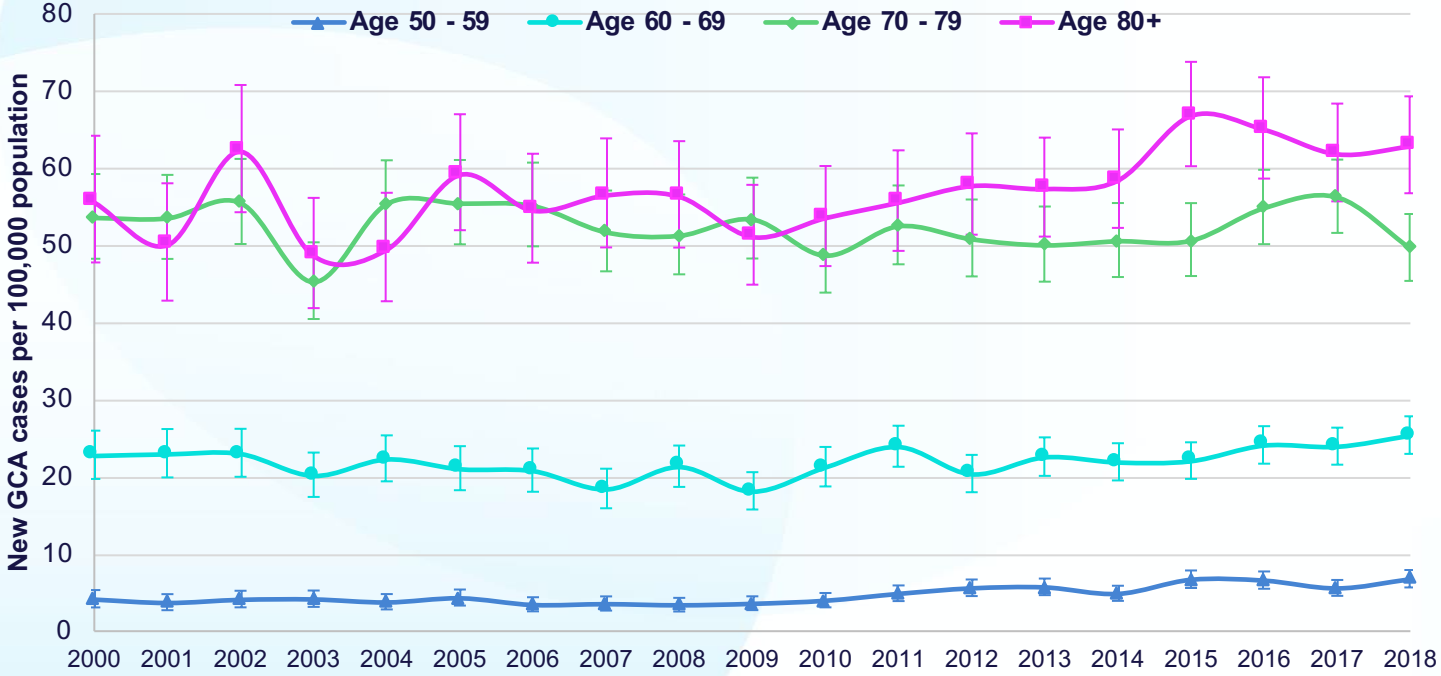
- 25 new cases per 100,000 people annually
- Across all definitions, incidence has **not** changed **much** over an 18-year period
- Incidence temporarily decreased in 2003; (may be an artifact due to changes in conversion between ICD-9 and ICD-10 which occurred in 2002. SARS?

Age-standardized incidence rates of GCA by sex (Definition 1)



- Similar patterns across case definitions
- Incidence higher for females
- Incidence for males increasing over time

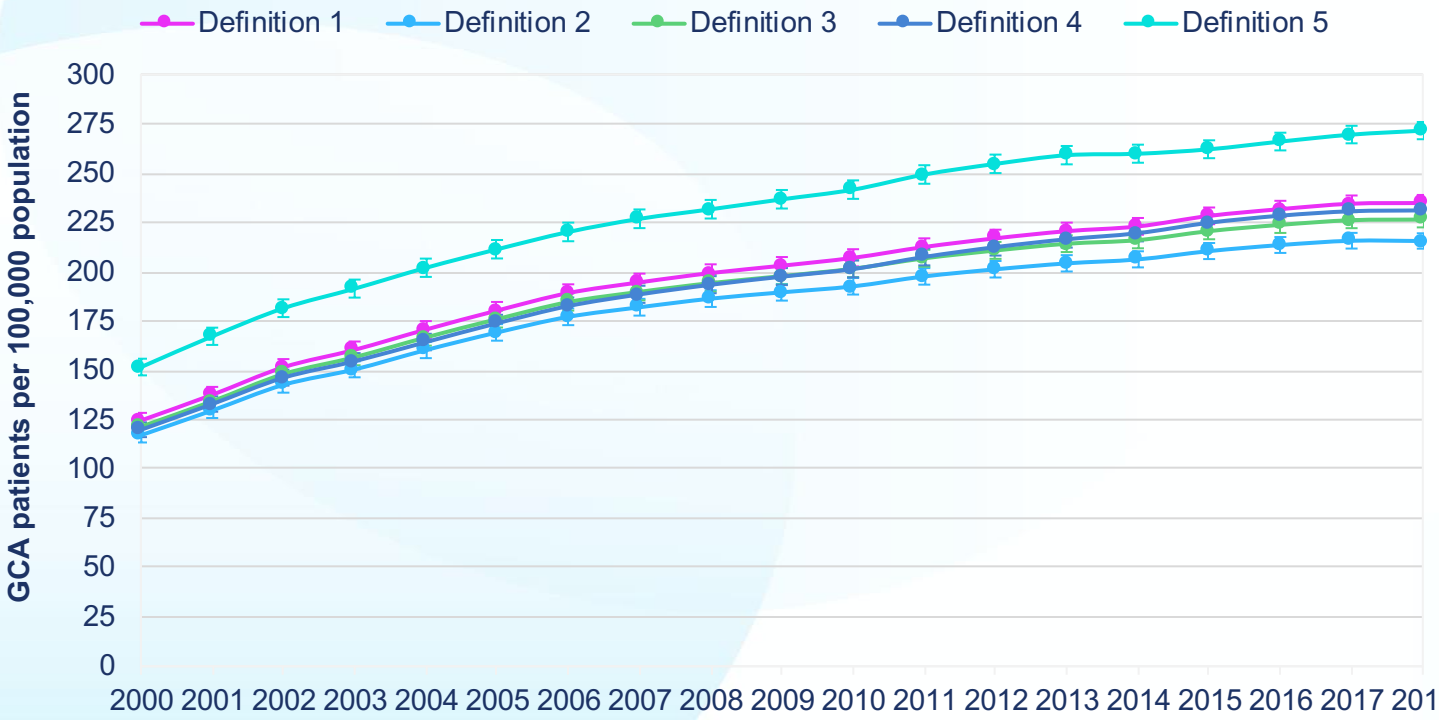
Sex-standardized incidence rates by age group (Definition 1)



- Incidence rates were highest among those aged 70 and older

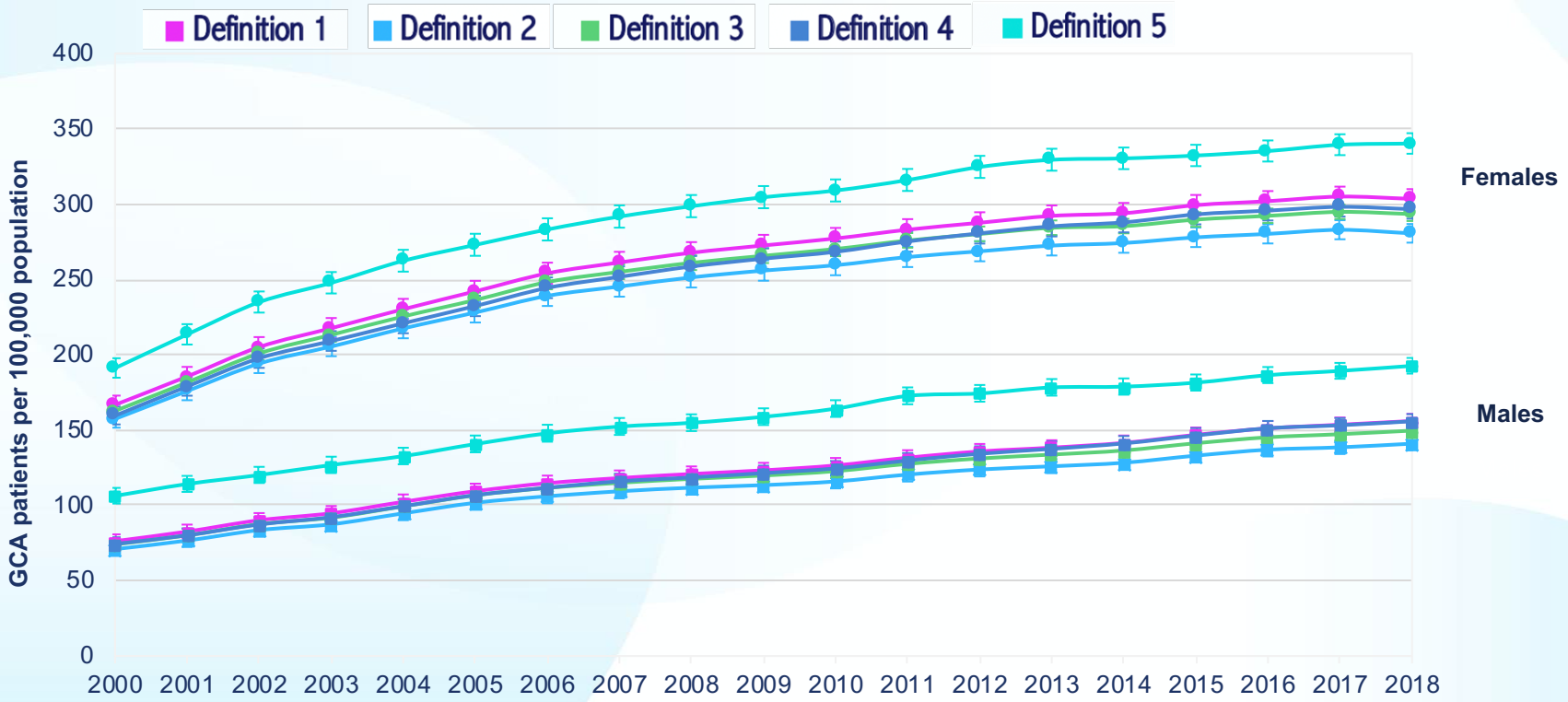
Prevalence

Age/sex-standardized prevalence rates (95% CI) of GCA

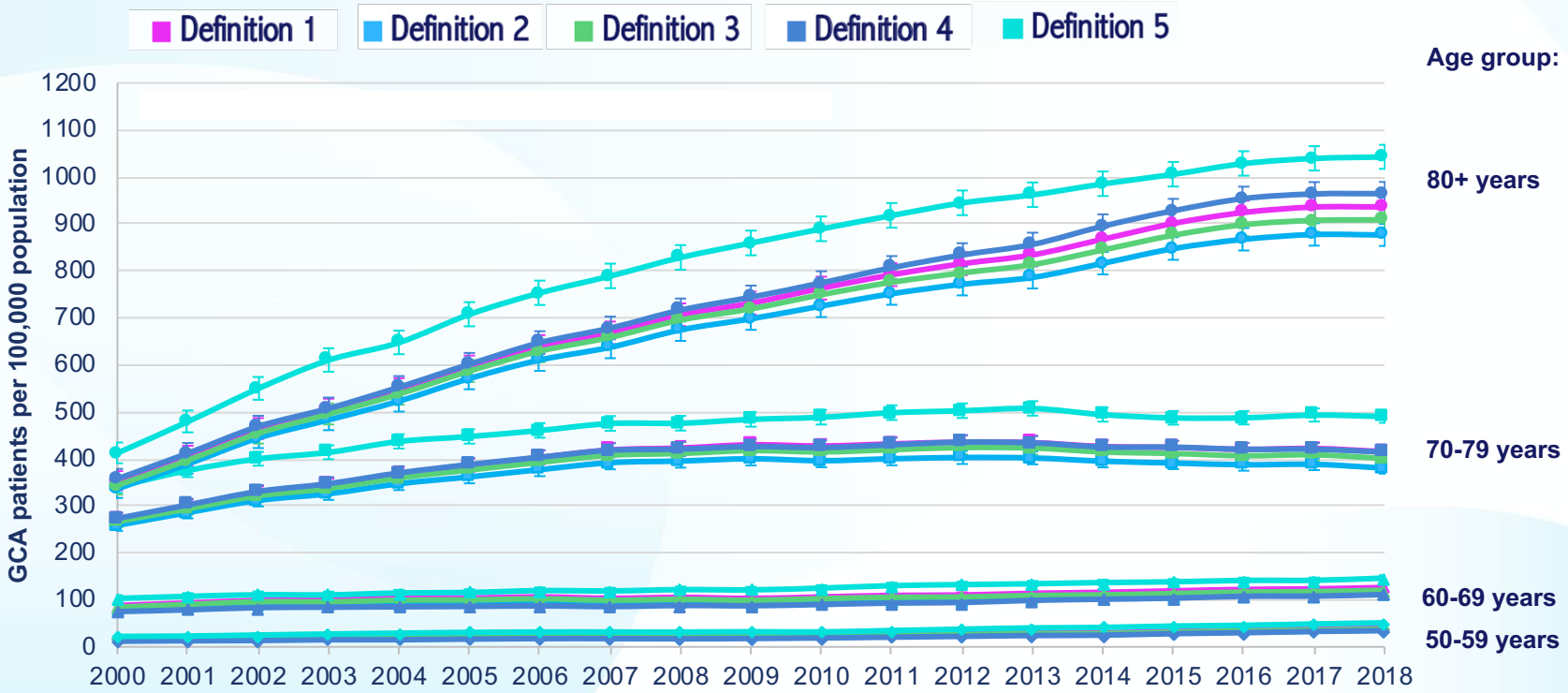


- Prevalence increased over time
- In the absence of increasing incidence, rising prevalence may reflect longer disease duration (i.e. earlier detection), improved survival with GCA, or immigration of cases?

Age-standardized prevalence rates by sex



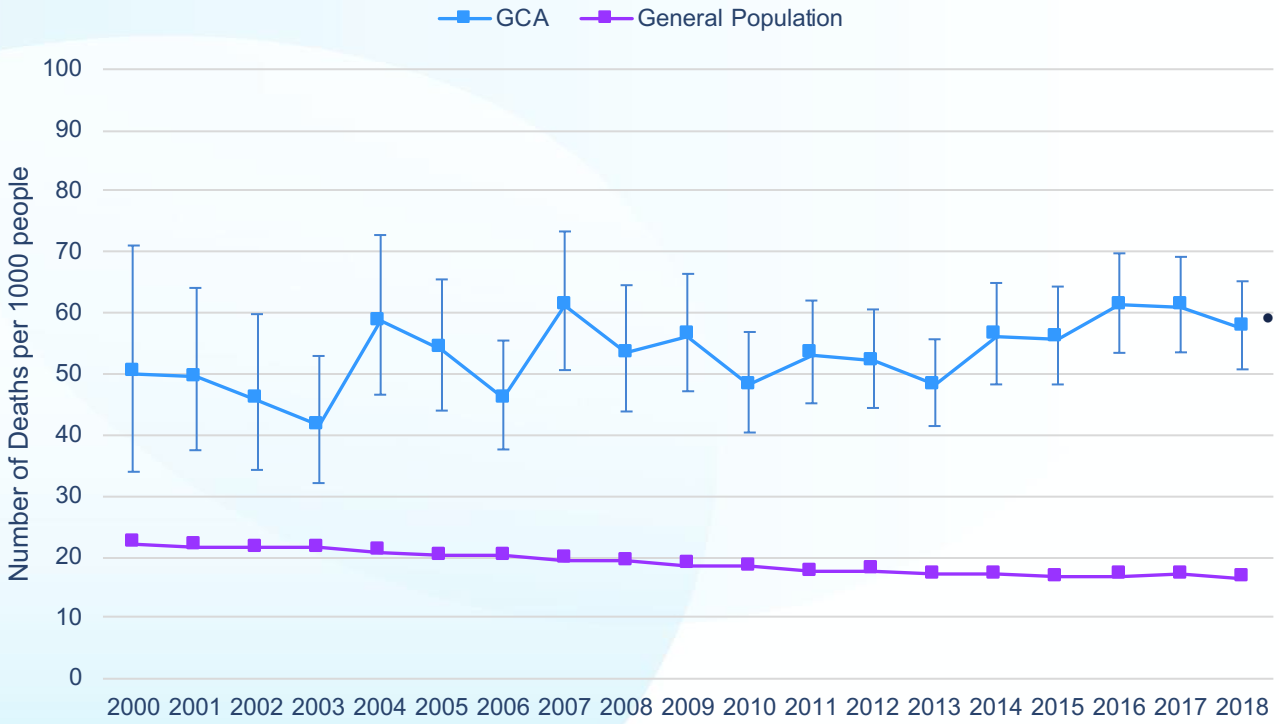
Sex-standardized prevalence rates of GCA by age group



Mortality

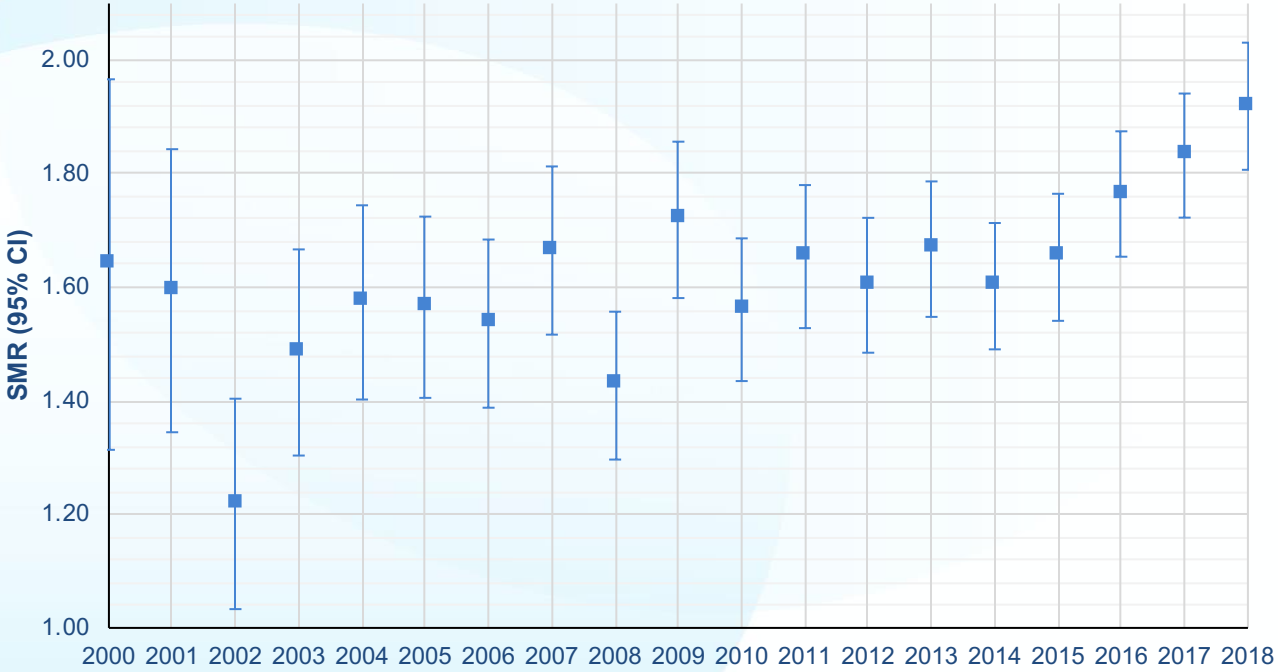
Definition 1 (highest PPV/sensitivity) was used to evaluate mortality

Standardized all-cause mortality rates in GCA vs General Population



- Over a 19-year period, mortality rates remained increased among GCA patients

SMRs among GCA patients



- SMRs for GCA ranged from 1.28 at the lowest in 2002 to 1.96 at the highest in 2018

Limitations

- Validation Study:
  - We defined GCA cases based on **physician-documented diagnoses** as diagnostic criteria may be poorly documented in primary care & classification criteria not always used in establishing a diagnosis.

- Ontario Administrative Data:
  - We were required to construct **more complex case definitions** than that which may be required in other settings (using ICD-9/10 coding systems).
    - OHIP code for GCA also includes polyarteritis nodosa (PAN) or other vasculitides
      - rarer conditions which minimizes the magnitude of potential misclassification.
        - » PAN incidence: 1-3 cases per million people annually.

Conclusions

- By contrasting GCA administrative data case definitions, we were able to describe consistent patterns on the incidence and prevalence of GCA over time.
- Incidence → relatively stable over time (except for males), highest among females & older adults
- Prevalence → increasing over time, highest among females & older adults
- Ontario rates similar to UK/Scandinavian countries, & considerably higher than southern Europe and non-European populations.
- Mortality → increased among GCA patients relative to the general population.
- Improvements to the relative excess mortality for GCA patients over time (mortality gap) did not occur.

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