*Epidemiology and Infection*

Article title: Comorbid conditions as risk factors for West Nile neuroinvasive disease in Ontario, Canada: a population-based cohort study

Authors: Jessica Sutinen, Deshayne B. Fell, Beate Sander, Manisha A. Kulkarni

Supplementary Material

Supplementary Table S1: ICES data holdings and data used in this study.

|  |  |  |
| --- | --- | --- |
| Data Holding | Description | Data Provided |
| Registered Persons Database (RPDB) | Information on individuals registered under the Ontario Health Insurance Plan (OHIP) and those eligible for the Ontario Drug Programme | Date of birth, date of death, sex |
| Discharge Abstract Database (DAD) | Clinical and administrative information on hospital discharges from all provincial and territorial acute care hospitals | Ascertainment of outcomes: WNND  Ascertainment of: CRD, MS, Alzheimer’s disease/dementia, stroke |
| National Ambulatory Care Reporting System (NACRS) | Information on all hospital-based and community-based ambulatory care (day surgeries, outpatient and community-based clinics, emergency departments) | Ascertainment of outcomes: WNND  Ascertainment of: CRD, MS, Alzheimer’s disease/dementia, stroke |
| Ontario Health Insurance Plain (OHIP) Claims Database | Information on OHIP billing claims | Ascertainment of outcomes: WNND  Ascertainment of: CRD, MS, Alzheimer’s disease/dementia, stroke |
| Ontario Drug Benefits Programme (ODB) | Information on drug claims history of ODB recipients (for this study period, ≥65 years) | Ascertainment of: Alzheimer’s disease/dementia |
| ICES special registries – Ontario Cancer Registry | Information on all Ontario residents diagnosed with cancer (exception: basal cell and squamous cell skin cancers), or who have died from cancer | Ascertainment of: cancer |
| ICES derived cohorts | Information on chronic conditions in Ontario in cohorts developed at ICES using linked data algorithms | Ascertainment of: asthma, CHF, COPD, HIV, hypertension, diabetes, rheumatoid arthritis |
| ICES health services – Canadian Organ Replacement Registry | Information on groups of individuals in Canada who have had similar health services experiences | Ascertainment of: organ transplant |

Abbreviations: CHF – congestive heart failure; COPD – chronic obstructive pulmonary disease; CRD – chronic renal disease; HIV – human immunodeficiency virus; MS – multiple sclerosis; WNND – West Nile neuroinvasive disease.

Supplementary Table S2. ICD-10-CA and OHIP codes used to identify cases of WNND in the WNV cohort.

|  |  |  |
| --- | --- | --- |
| ICD-10-CA | | |
| Manifestation | Code | Description |
| WNM | A878 | Other viral meningitis |
|  | A879 | Meningitis, viral |
|  | G020 | Meningitis in viral diseases classified elsewhere |
|  | G028 | Meningitis in other specified infectious and parasitic diseases  classified elsewhere |
|  | G030 | Nonpyogenic meningitis |
|  | G031 | Chronic meningitis |
|  | G038 | Meningitis due to other specified causes |
|  | G039 | Meningitis, unspecified |
| WNP | A801 | Acute paralytic poliomyelitis, wild virus, imported |
|  | A802 | Acute paralytic poliomyelitis, wild virus, indigenous |
|  | A803 | Acute paralytic poliomyelitis, other and unspecified |
|  | A804 | Acute nonparalytic poliomyelitis |
|  | A809 | Acute poliomyelitis, unspecified |
|  | A818 | Other atypical virus infections of central nervous system |
|  | A819 | Atypical virus infection of central nervous system, unspecified |
|  | B91 | Sequelae of poliomyelitis |
|  | G373 | Acute transverse myelitis in demyelinating disease of  central nervous system |
|  | G378 | Other specified demyelinating diseases of central nervous system |
|  | G379 | Demyelinating disease of central nervous system, unspecified |
|  | G610 | Guillain-Barré syndrome |
|  | G8100 | Flaccid hemiplegia of dominant side |
|  | G8101 | Flaccid hemiplegia of non-dominant side |
|  | G8109 | Flaccid hemiplegia of unspecified [unilateral] side |
|  | G8110 | Spastic hemiplegia of dominant side |
|  | G8111 | Spastic hemiplegia of non-dominant side |
|  | G8119 | Spastic hemiplegia of unspecified [unilateral] side |
|  | G8190 | Hemiplegia of unspecified type of dominant side |
|  | G8191 | Hemiplegia of unspecified type of non-dominant side |
|  | G8199 | Hemiplegia of unspecified type of unspecified [unilateral] side |
|  | G830 | Diplegia of upper limbs |
|  | G831 | Monoplegia of lower limb |
|  | G8320 | Monoplegia of upper limb on dominant side |
|  | G8321 | Monoplegia of upper limb on non-dominant side |
|  | G8322 | Monoplegia of upper limb on unspecified [unilateral] side |
|  | G833 | Monoplegia, unspecified |
| WNE | A838 | Other mosquito-borne viral encephalitis |
|  | A839 | Mosquito-borne viral encephalitis, unspecified |
|  | A852 | Arthropod-borne viral encephalitis, unspecified |
|  | A858 | Other specified viral encephalitis |
|  | A86 | Unspecified viral encephalitis |
|  | B941 | Sequelae of viral encephalitis |
|  | G040 | Acute disseminated encephalitis |
|  | G048 | Other encephalitis, myelitis and encephalomyelitis |
|  | G049 | Encephalitis, myelitis and encephalomyelitis, unspecified |
|  | G051 | Encephalitis, myelitis and encephalomyelitis in viral diseases  classified elsewhere |
|  | G052 | Encephalitis, myelitis and encephalomyelitis in other infectious  and parasitic diseases classified elsewhere |
|  | G058 | Encephalitis, myelitis and encephalomyelitis in other diseases  classified elsewhere |
|  | G934 | Encephalopathy, unspecified |
| OHIP | | |
| Manifestation | Code | Description |
| WNM | 036 | Meningococcal infection or meningitis |
|  | 321 | Meningitis due to other organisms |
| WNP | 045 | Acute poliomyelitis |
|  | 356 | Idiopathic peripheral neuritis |
|  | 358 | Myoneural disorders |
|  | 359 | Muscular dystrophies |
| WNE | 062 | Mosquito-borne viral encephalitis |
|  | 323 | Encephalitis, encephalomyelitis |

Supplementary Table S3. Bivariable analyses for West Nile meningitis, with other characteristics.

|  |  |  |  |
| --- | --- | --- | --- |
| Characteristica | WNM  Yes (%)b,c No (%)b,c  n=145 n=1739 | | Cumulative incidence per 100 (95% CI)b |
| Sex  Female  Male | 76 (52.4)  69 (47.6) | 912 (52.4)  827 (47.6) | 7.7 (6.1-9.5)  7.7 (6.1-9.6) |
| Age at WNM development (mean, SD; years)d | 48.7 (19.7) | 49.3 (18.0) | - |
| Any chronic condition  Yes  No | 78 (53.8)  67 (46.2) | 809 (56.5)  930 (53.5) | 8.8 (7.0-10.9)  6.7 (5.2-8.5) |
| Asthma | 21 (14.5) | 240 (13.8) | 8.0 (5.1-12.0) |
| COPD | 13 (9.7) | 121 (7.0) | 9.7 (5.3-16.0) |
| Diabetes | 18 (12.4) | 203 (11.7) | 8.1 (4.9-12.6) |
| Hypertension | 47 (32.4) | 529 (30.4) | 8.2 (6.1-10.7) |

aImmunocompromised, MS, CHF, stroke, CRD, Alzheimer’s disease/dementia, rheumatoid arthritis, and cancer not shown because cell counts were <6.

bRow percentages

cColumn percentages

dAge categories not shown because most age groups had cell sizes <6.

Abbreviations: CHF – congestive heart failure; COPD – chronic obstructive pulmonary disease; CRD – chronic renal disease; MS – multiple sclerosis; SD – standard deviation; WNM – West Nile meningitis.

Supplementary Table S4. Bivariable analyses for West Nile acute flaccid paralysis, with other characteristics.

|  |  |  |  |
| --- | --- | --- | --- |
| Characteristica | WNP  Yes (%)b,c No (%)b,c  n=66 n=1818 | | Cumulative incidence per 100 (95% CI)b |
| Sex  Female  Male | 29 (43.9)  37 (56.1) | 959 (52.7)  860 (47.3) | 31.7-56.7  43.3-68.3 |
| Age at WNP development (age categories; years)  44 and under  45 and older | 18 (27.3)  48 (72.7) | 693 (38.1)  1 125 (61.9) | 17.0-39.6  60.4-83.0 |
| Age at WNP development (mean, SD; years) | 53.2 (21.5) | 49.1 (18.0) | - |
| Any chronic condition  Yes  No | 37 (56.1)  29 (43.9) | 850 (46.8)  968 (53.2) | 4.2 (3.0-5.7)  2.9 (2.0-4.1) |
| Asthma | 6 (9.1) | 255 (14.0) | 2.3 (0.8-4.9) |
| Diabetes | 12 (18.2) | 209 (11.5) | 5.4 (2.8-9.3) |
| Hypertension | 28 (42.4) | 548 (30.1) | 4.9 (3.3-6.9) |

aImmunocompromised, MS, COPD, CHF, stroke, CRD, Alzheimer’s disease/dementia, rheumatoid arthritis, and cancer were removed from this table because cell counts were <6.

bColumn percentages

cRow percentages

Abbreviations: CHF – congestive heart failure; COPD – chronic obstructive pulmonary disease; CRD – chronic renal disease; MS – multiple sclerosis; SD – standard deviation; WNP – West Nile acute flaccid paralysis.

Supplementary Table S5. Unadjusted and adjusted risk ratios for West Nile meningitis.

|  |  |  |
| --- | --- | --- |
| Characteristic | Unadjusted RR, 95% CI | Adjusted RR, 95% CI |
| Sex  Female  Male | Ref.  1.00 (0.73-1.37) | Ref.  0.99 (0.72-1.36) |
| Age at time of WNM development (continuous variable, years) | 1.00 (0.99-1.01) | 1.00 (0.99-1.01) |
| Alzheimer’s Disease/Dementia | 2.38 (0.43-6.18) | 2.68 (0.47-7.30) |
| Asthma | 1.05 (0.66-1.60) | - |
| Cancer | 1.83 (0.68-3.71) | 1.93 (0.71-3.93) |
| CHF | 0.98 (0.31-2.21) | - |
| COPD | 1.29 (0.71-2.12) | - |
| CRD | 0.33 (0.02-1.40) | - |
| Diabetes | 1.07 (0.64-1.66) | - |
| Immunocompromised | 2.32 (0.61-5.32) | 2.36 (0.62-5.43) |
| Hypertension | 1.09 (0.77-1.51) | - |
| MS | 3.26 (0.21-9.63) | - |
| Rheumatoid Arthritis | 1.08 (0.28-2.68) | - |
| Stroke | 0.50 (0.03-2.07) | - |

-Not included in final model.

Abbreviations: CHF – congestive heart failure; COPD – chronic obstructive pulmonary disease; CRD – chronic renal disease; MS – multiple sclerosis; WNM – West Nile meningitis.

Supplementary Table S6. Unadjusted and adjusted risk ratios for West Nile acute flaccid paralysis.

|  |  |  |
| --- | --- | --- |
| Characteristic | Unadjusted RR, 95% CI | Adjusted RR, 95% CI |
| Sex  Female  Male | Ref.  1.41 (0.87-2.29) | Ref.  1.31 (0.81-2.14) |
| Age at time of WNP development (continuous variable, years) | 1.01 (1.00-1.03) | 1.00 (0.99-1.02) |
| Alzheimer’s Disease/Dementia | 5.32 (0.95-14.14) | 2.93 (0.49-9.61) |
| Asthma | 0.74 (0.31-1.49) | - |
| Cancer | 0.00 (0.00-0.00) | - |
| CHF | 2.23 (0.70-5.15) | 1.21 (0.34-3.29) |
| COPD | 1.07 (0.38-2.36) | - |
| CRD | 0.73 (0.04-3.15) | - |
| Diabetes | 1.67 (0.86-2.96) | 1.22 (0.59-2.34) |
| Immunocompromised | 0.00 (0.00-0.00) | - |
| Hypertension | 1.67 (1.03-2.69) | 1.34 (0.74-2.40) |
| MS | 0.00 (0.00-0.00) | - |
| Rheumatoid Arthritis | 0.00 (0.00-0.00) | - |
| Stroke | 3.40 (0.87-8.39) | 2.09 (0.51-5.71) |

-Not included in final model.

Abbreviations: CHF – congestive heart failure; COPD – chronic obstructive pulmonary disease; CRD – chronic renal disease; MS – multiple sclerosis; WNP - West Nile acute flaccid paralysis.

Supplementary Table S7. Unadjusted and adjusted risk ratios for WNND.

|  |  |  |  |
| --- | --- | --- | --- |
| Characteristic | Unadjusted RR, 95% CI | Adjusted RR, 95% CIa | Adjusted RR, 95% CIb |
| Sex  Female  Male | Ref.  1.29 (1.07-1.56) | Ref.  1.23 (1.02-1.49) | Ref.  1.21 (1.00-1.46) |
| Age at time of WNND development (continuous variable, years) | 1.01 (1.01-1.02) | 1.01 (1.00-1.02) | 1.00 (0.99-1.01) |
| Alzheimer’s disease and/or dementia | 2.00 (0.71-3.63) | - | - |
| Asthma | 0.93 (0.69-1.22) | - | - |
| Cancer | 1.38 (0.70-2.26) | - | - |
| CHF | 2.24 (1.52-3.05) | 1.55 (1.00-2.25) | 1.42 (0.93-2.02) |
| COPD | 1.38 (0.99-1.85) | - | - |
| CRD | 1.56 (0.87-2.43) | 0.75 (0.41-1.25) | 0.66( 0.36-1.08) |
| Diabetes | 1.65 (1.29-2.07) | 1.25 (0.95-1.63) | 1.23 (0.94-1.59) |
| Immunocompromised | 2.27 (1.11-3.61) | 1.95 (0.96-3.19) | 2.26 (1.12-3.68) |
| Hypertension | 1.41 (1.16-1.70) | 1.05 (0.84-1.32) | 0.18 (0.07-0.45) |
| MS | 1.37 (0.09-4.00) | - | - |
| Rheumatoid Arthritis | 1.06 (0.48-1.89) | - | - |
| Stroke | 1.91 (1.01-3.01) | 1.46 (0.78-2.30) | 1.49 (0.80-2.30) |
| Hypertension\*Age | N/A | N/A | 1.03 (1.01-1.04) |

aMultivariable model, no interaction term.  
bMultivariable model, interaction term included.

-Not included in final model.

\*Interaction term.

Abbreviations: CHF – congestive heart failure; COPD – chronic obstructive pulmonary disease; CRD – chronic renal disease; MS – multiple sclerosis.