Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.
**eTable 1. List and Description of Datasets Available to ICES**

| Dataset | Related Variable | Description |
|---------|------------------|-------------|
| **Owner: Cancer Care Ontario** | | |
| Cancer Activity Level Reporting (ALR) 2005 | - Systemic therapy - Supportive drugs - Radiation therapy | Contains patient level activity within the cancer system focused on radiation and systemic therapy services and outpatient oncology clinic visits. |
| **Owner: Ontario Ministry of Health and Long term Care** | | |
| Client Agency Program Enrolment (CAPE) 1999 | - Capitation costs | Registry of patients enrolled in a primary care model. Data elements include program type (family health team, family health organization, family health network, etc.) and patient enrolment status. |
| Home Care Database (HCD), Ontario Home Care Administrative System (OHCAS) 1990 | - Home care services | Captures information on all services provided or coordinated by Ontario Community Care Access Centres, including client data, intake and assessment information, admission and discharge, etc. |
| New Drug Funding Program (NDFP) 1995 | - Medication use including systemic therapy | Administered by Cancer Care Ontario, the NDFP funds new, and often very expensive, cancer drugs. |
| Ontario Cancer Registry (OCR) 1964 | - Cancer diagnosis - Tumour characteristics (molecular) | Contains the diagnosis code for invasive cancer (International Classification of Diseases version 10) and the date of diagnosis for all residents of Ontario. |
| Ontario Drug Benefit (ODB) claims 1990 | - Medication use including systemic therapy | Contains claims for oral prescription drugs covered under the ODB program. Primarily includes drug claims for individuals 65 years of age and older, but also coverage under special ODB programs. |
| Ontario Health Insurance Plan (OHIP) claims database 1991 | - Outpatient physician visits - Laboratory services - Non-physician services - Physician services (including costs related to breast reconstruction) | Contains claims paid by OHIP, the universal, single-payer provincial health insurance plan, for services provided by all eligible health care providers, including physicians (primary and specialist), groups, and laboratories. |
| Registered Persons Database (RPDB) 1991 | - Health service subscriber data | Contains birth and death dates, age, sex, and date of last contact with health care services in Ontario. |
| **Owner: Canadian Institute for Health Information** | | |
| Continuing Care Reporting System (CCRS) 1996 | - Complex continuing care (CCC) - Long-term care (LTC) | Contains information about residents receiving facility-based continuing care services. Range of services includes CCC, extended or chronic care, and residential care providing nursing services (that is, long-term care). |
| Discharge Abstract Database (DAD) 1988 | - Inpatient hospitalizations | Contains demographic, clinical, and administrative data for inpatient hospital admissions (patient separations). |
| National Ambulatory Care Reporting System (NACRS) 2000/2003 | - Ambulatory emergency department visit, dialysis clinic visits, and cancer clinic visits | Contains data from hospital- and community-based ambulatory care services, including same day surgery, outpatient clinics, and emergency departments. |
| Dataset                                      | Related Variable   | Description                                                                                                                                 |
|----------------------------------------------|--------------------|---------------------------------------------------------------------------------------------------------------------------------------------|
| National Rehabilitation Reporting System (NRS) 2000 | - Rehabilitation admissions | Contains client data from adult inpatient rehabilitation facilities, such as administrative data (referral, admission, and discharge) and health and functional characteristics. |
| Ontario Mental Health Reporting System (OMHRS) 2005 | - Mental health admissions | Contains data on patients in adult designated inpatient mental health beds in acute and psychiatric facilities. Data elements include admission and discharge dates, diagnoses, service utilization, etc. |

Reference: ICES Data Dictionary [Internet]. 2019. Available from: [https://datadictionary.ices.on.ca/Applications/DataDictionary/Default.aspx](https://datadictionary.ices.on.ca/Applications/DataDictionary/Default.aspx)
eTable 2. Inclusion and Exclusion Criteria

| Exclusions                                                                 | Patients excluded | Patients remaining |
|---------------------------------------------------------------------------|-------------------|--------------------|
| Cohort of Ontario women diagnosed with breast cancer between 01/01/2009 and 31/12/2018 | 100,747           |                    |
| Previous cancer cases                                                     | 13,332            | 87,415             |
| Subsequent non-breast cancer cases                                        | 4,623             | 82,792             |
| Age <18                                                                   | 583               | 82,209             |
| Death before or on index date                                             | 448               | 81,761             |
| Non-Ontario residents at index date                                       | 43                | 81,718             |
| Ineligible for OHIP at index date                                         | 483               | 81,235             |
| Patients with Stage 1-3 disease or unknown stage                          | 77,319            | 3,916              |
**eTable 3.** Baseline Characteristics of Patients With Metastatic Breast Cancer Who Did vs Did Not Develop Brain Metastases

(n=3,916)

| Variable                              | No BRM (N=3,367) | BRM (N=549) | All (N=3,916) | p-value |
|---------------------------------------|------------------|-------------|---------------|---------|
| **Breast Cancer Subtype, n (%)**      |                  |             |               |         |
| TNBC                                  | 204 (79.1)       | 54 (20.9)   | 258 (6.6)     | <.001   |
| ERBB2+/HR+                            | 246 (79.4)       | 64 (20.6)   | 310 (7.9)     |         |
| ERBB2+/HR-                            | 146 (73.0)       | 54 (27.0)   | 200 (5.1)     |         |
| HR+/ERBB2-                            | 1,092 (89.9)     | 123 (10.1)  | 1,215 (31.0)  |         |
| Unknown                               | 1,679 (86.9)     | 254 (13.1)  | 1,933 (49.4)  |         |
| **Age at Treatment**                  |                  |             |               |         |
| Median (IQR)                          | 64 (53-77)       | 56 (48-65)  | 63 (52-75)    | <.001   |
| ≤60, n (%)                            | 1,369 (40.7)     | 345 (62.8)  | 1,714 (43.8)  | <.001   |
| >60, n (%)                            | 1,998 (59.3)     | 204 (37.2)  | 2,202 (56.2)  |         |
| **Location, n (%)**                   |                  |             |               | 0.11    |
| Urban                                 | 3,015 (89.5)     | 479 (87.2)  | 3,494 (89.2)  |         |
| Rural                                 | 352 (10.5)       | 70 (12.8)   | 422 (10.8)    |         |
| **Income quintile, n (%)**            |                  |             |               | 0.38    |
| 1                                     | 733 (21.8)       | 100 (18.2)  | 833 (21.3)    |         |
| 2                                     | 771 (22.9)       | 127 (23.1)  | 898 (22.9)    |         |
| 3                                     | 653 (19.4)       | 115 (20.9)  | 768 (19.6)    |         |
| 4                                     | 624 (18.5)       | 102 (18.6)  | 726 (18.5)    |         |
| 5                                     | 586 (17.4)       | 105 (19.1)  | 691 (17.6)    |         |
| **Elixhauser co-morbidity index, n (%)** |              |             |               | <.001   |
| Score < 0                             | 461 (13.7)       | 83 (15.1)   | 544 (13.9)    |         |
| Score = 0                             | 1,311 (38.9)     | 231 (42.1)  | 1,542 (39.4)  |         |
| Score = 1-4                           | 856 (25.4)       | 156 (28.4)  | 1,012 (25.8)  |         |
| Score ≥ 5                             | 739 (21.9)       | 79 (14.4)   | 818 (20.9)    |         |
| **Index year at diagnosis, n (%)**    |                  |             |               | <.001   |
| 2009-2010                             | 614 (18.2)       | 138 (25.1)  | 752 (19.2)    |         |
| 2011-2012                             | 619 (18.4)       | 133 (24.2)  | 752 (19.2)    |         |
| 2013-2014                             | 662 (19.7)       | 125 (22.8)  | 787 (20.1)    |         |
| 2015-2016                             | 713 (21.2)       | 102 (18.6)  | 815 (20.8)    |         |
| 2017-2018                             | 759 (22.5)       | 51 (9.3)    | 810 (20.7)    |         |

Legend: BRM = brain metastases; HR= hormone receptor; MBC = metastatic breast cancer; TNBC= triple negative breast cancer.
ETable 4. Cumulative Incidence of Brain Metastases and Cumulative Incidence of Death in the Overall Patient Population

| Follow-up Time | Cumulative incidence of brain metastases (%; 95% CI) | Cumulative incidence of death (%; 95% CI) |
|----------------|-----------------------------------------------------|------------------------------------------|
| 3 months       | 3.1 (2.6–3.7)                                       | 14.4 (13.3–15.5)                        |
| 6 months       | 4.0 (3.4–4.6)                                       | 21.0 (19.7–22.3)                        |
| 9 months       | 4.9 (4.3–5.6)                                       | 25.8 (24.4–27.2)                        |
| 1 year         | 6.2 (5.4–6.9)                                       | 29.6 (28.2–31.1)                        |
| 2 years        | 10.1 (9.2–11.1)                                     | 42.3 (40.7–43.9)                        |
| 3 years        | 12.6 (11.5–13.7)                                    | 52.4 (50.7–54.0)                        |
| 4 years        | 14.5 (13.3–15.7)                                    | 59.0 (57.3–60.7)                        |
| 5 years        | 15.5 (14.3–16.8)                                    | 64.4 (62.7–66.1)                        |
| 6 years        | 16.4 (15.1–17.7)                                    | 68.8 (67.1–70.5)                        |
| 7 years        | 16.6 (15.3–18.0)                                    | 71.6 (69.8–73.2)                        |
| 8 years        | 16.7 (15.4–18.0)                                    | 73.7 (71.9–75.4)                        |
| 9 years        | 16.9 (15.5–18.2)                                    | 75.9 (74.1–77.7)                        |
| 10 years       | N.R                                                 | 76.3 (74.3–78.1)                        |

Note: N.R, not reportable due to small sample size.
**eTable 5.** Baseline Characteristics of Patients with Breast Cancer Brain Metastases Undergoing Radiation Therapy (n=549)

| Variable                                   | SRS (N=94) | WBRT (N=455) | All (N=549) | a p-value |
|---------------------------------------------|------------|--------------|-------------|-----------|
| **Breast Cancer Subtype, n (%)**            |            |              |             |           |
| TNBC                                        | 8 (8.5)    | 46 (10.1)    | 54 (9.8)    | <.001     |
| ERBB2+/HR+                                  | 23 (24.5)  | 41 (9.0)     | 64 (11.7)   |           |
| ERBB2+/HR-                                  | 14 (14.9)  | 40 (8.8)     | 54 (9.8)    |           |
| HR+/ERBB2-                                 | 16 (17.0)  | 107 (23.5)   | 123 (22.4)  |           |
| Unknown                                     | 33 (35.1)  | 221 (48.6)   | 254 (46.3)  |           |
| **Age at Treatment**                        |            |              |             |           |
| Median (IQR)                                | 51 (42-60) | 58 (48-65)   | 56 (48-65)  | <.001     |
| ≤60, n (%)                                  | 71 (75.5)  | 274 (60.2)   | 345 (62.8)  | 0.01      |
| >61, n (%)                                  | 23 (24.5)  | 181 (39.8)   | 204 (37.2)  |           |
| **Location, n (%)**                         |            |              |             | 0.18      |
| Urban                                       | 86 (91.5)  | 393 (86.4)   | 479 (87.2)  |           |
| Rural                                       | 8 (8.5)    | 62 (13.6)    | 70 (12.8%)  |           |
| **Income quintile, n (%)**                  |            |              |             | 0.22      |
| 1                                           | 11 (11.7)  | 89 (19.6)    | 100 (18.2)  |           |
| 2                                           | 26 (27.7)  | 101 (22.2)   | 127 (23.1)  |           |
| 3                                           | 16 (17.0)  | 99 (21.8)    | 115 (20.9)  |           |
| 4                                           | 19 (20.2)  | 83 (18.2)    | 102 (18.6)  |           |
| 5                                           | 22 (23.4)  | 83 (18.2)    | 105 (19.1)  |           |
| **Time from MBC diagnosis to BRM treatment (days)** |            |              |             | <.001     |
| Median (IQR)                                | 630 (352-1,153) | 435 (109-842) | 461 (137-900) |           |
| **VW Elixhauser co-morbidity index, n (%)** |            |              |             | 0.37      |
| Score < 0                                   | 18 (19.1)  | 65 (14.3)    | 83 (15.1)   |           |
| Score = 0                                   | 39 (41.5)  | 192 (42.2)   | 231 (42.1)  |           |
| Score = 1-4                                 | 28 (29.8)  | 128 (28.1)   | 156 (28.4)  |           |
| Score ≥ 5                                   | 9 (9.6)    | 70 (15.4)    | 79 (14.4)   |           |
| **Index year at diagnosis, n (%)**          |            |              |             | <.001     |
| 2009-2010                                   | 16 (17.0)  | 122 (26.8)   | 138 (25.1)  |           |
| 2011-2012                                   | 18 (19.1)  | 115 (25.3)   | 133 (24.2)  |           |
| 2013-2014                                   | 22 (23.4)  | 103 (22.6)   | 125 (22.8)  |           |
| 2015-2016                                   | 32 (34.0)  | 70 (15.4)    | 102 (18.6)  |           |

Legend: SRS = stereotactic radiosurgery, WBRT = whole brain radiotherapy, MBC = metastatic breast cancer, BRM = brain metastases

ap-value compares WBRT and SRS groups.
eTable 6. Univariable and Multivariable Cox Model for Overall Survival Among Women With Breast Cancer Brain Metastases

(n=549)

| Variable | Uni-variable Hazard Ratio (95% CI) | b-p-value | Multi-variable Hazard Ratio (95% CI) | b-p-value |
|----------|-----------------------------------|-----------|-------------------------------------|-----------|
| **Treatment** | | | | |
| SRS vs. WBRT | 0.51 (0.39-0.66) | <.001 | 0.59 (0.45-0.77) | <.001 |
| **Breast cancer subtype** | | | | |
| TNBC vs. ERBB2+/HR- | 2.72 (1.78-4.20) | <.001 | 2.49 (1.62-3.87) | <.001 |
| ERBB2+/HR+ vs. ERBB2+/HR- | 1.12 (0.73-1.74) | 0.60 | 1.20 (0.78-1.88) | 0.41 |
| HR+/ERBB2- vs. ERBB2+/HR- | 1.74 (1.20-2.58) | <.01 | 1.60 (1.10-2.37) | 0.02 |
| Unknown vs. ERBB2+/HR- | 2.03 (1.45-2.93) | <.001 | 1.51 (1.05-2.25) | 0.03 |
| **Age** | | | | |
| ≥61 vs. <60 | 1.37 (1.13-1.65) | <.001 | 1.30 (1.07-1.58) | 0.01 |
| **Rural residence** | | | | |
| Yes vs. no | 0.96 (0.72-1.25) | 0.76 | 0.88 (0.66-1.16) | 0.38 |
| **Income quintile** | | | | |
| 2 vs. 1 | 0.96 (0.73 - 1.27) | 0.75 | 0.95 (0.71-1.26) | 0.71 |
| 3 vs. 1 | 0.81 (0.61-1.09) | 0.16 | 0.76 (0.56-1.01) | 0.06 |
| 4 vs. 1 | 0.71 (0.53-0.97) | 0.03 | 0.70 (0.52-0.95) | 0.02 |
| 5 vs. 1 | 0.74 (0.55-1.00) | 0.05 | 0.72 (0.53-0.98) | 0.04 |
| **Time from initial diagnosis of MBC to BRM treatment** | | | | |
| Per 30-days | 1.00 (1.00-1.01) | 0.82 | 1.00 (1.00-1.01) | 0.47 |
| **VW Elixhauser co-morbidity index** | | | | |
| Score <0 vs. 0 | 0.99 (0.75 - 1.29) | 0.93 | 1.04 (0.79-1.36) | 0.78 |
| Score 1-4 vs. 0 | 1.02 (0.82-1.27) | 0.86 | 1.14 (0.91-1.43) | 0.25 |
| Score >=5 vs. 0 | 0.97 (0.73 -1.28) | 0.83 | 0.98 (0.73-1.29) | 0.87 |
| **Index year at diagnosis** | | | | |
| Continuous from 2009 to 2018 | 0.91 (0.88-0.95) | <.0001 | 0.93 (0.88-0.97) | 0.002 |

Legend: SRS = stereotactic radiosurgery, WBRT = whole brain radiotherapy, MBC = metastatic breast cancer, TNBC= triple negative breast cancer, HR= hormone receptor

aERBB2+/HR- was treated as the reference group, as it had the lowest hazard value, which is different from the reference group for the outcome of time from MBC to BRM

b-p-value compares WBRT and SRS groups.