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Impact of variation in cancer registration practice on observed international cancer survival differences between International Cancer Benchmarking Partnership (ICBP) jurisdictions

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ABSTRACT

Background: International cancer survival comparisons use cancer registration data to report cancer survival, which informs the development of cancer policy and practice. Studies like the International Cancer Benchmarking Partnership (ICBP) have a duty to understand how registration differences impact on survival prior to drawing conclusions.

Methods: Key informants reported differences in registration practice for capturing incidence date, death certificate case handling and registration of multiple primary tumours. Sensitivity analyses estimated their impact on one-year survival using baseline and supplementary cancer registration data from England and Sweden.

Results: Variations in registration practice accounted for up to a 7.3 percentage point difference between unadjusted (estimates from previous ICBP survival data) and adjusted (estimates recalculated accounting for registration differences) one-year survival, depending on tumour site and jurisdiction.

One-year survival estimates for four jurisdictions were affected by adjustment: New South Wales, Norway, Ontario, Sweden. Sweden and Ontario's survival reduced after adjustment, yet they remained the jurisdictions

Abbreviations: DCO, death certificate only; DCI, death certificate initiated; ICBP, International Cancer Benchmarking Partnership; IARC, International Agency for Research on Cancer; ENCR, European Network of Cancer Registries; NCRAS, National Cancer Registration and Analysis Service

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with the highest survival for breast and ovarian cancer respectively. Sweden had the highest unadjusted lung cancer survival of 43.6% which was adjusted to 39.0% leaving Victoria and Manitoba with the highest estimate at 42.7%. For colorectal cancer, Victoria's highest survival of 85.1% remained unchanged after adjustment.
Conclusion: Population-based cancer survival comparisons can be subject to registration biases that may impact the reported 'survival gap' between populations. Efforts should be made to apply consistent registration practices internationally. In the meantime, survival comparison studies should provide acknowledgement of or adjustment for the registration biases that may affect their conclusions.

1. Introduction

Many countries have established population-based cancer registries to collect and record various cancer data. They provide an essential resource to measure the burden of cancer, assess health systems and inform cancer control policies and clinical practices. Therefore, the quality and comparability of data collected is fundamental to meaningful comparisons between populations.

Internationally agreed standards for data collection and classification have been in existence for many years [1–4]. Variation between these standards does exist, for example, the International Agency for Research on Cancer (IARC) and the European Network of Cancer Registries (ENCR) have different rules and hierarchies for defining the incidence date [5,6]. Previous studies have noted differences in the availability, collection, processing and recording of data, which affects both incidence and survival [7].

International cancer survival comparisons, such as the International Cancer Benchmarking Partnership (ICBP), use cancer registration data to report one-year survival, among other outcome metrics [8–10]. One-year survival can be used as a proxy for early or late diagnosis, with higher one-year survival suggesting earlier diagnosis [11]. Estimations of shorter-term survival are much more sensitive to the differences in registration practice as any effect, changing an incidence date by 30 days, for example, produces a greater proportional change in survival time when assessed over one-year than five or ten years.

Differences in definitions and handling of data underlying survival estimates can lead to bias and misleading comparisons. For example, differences in incidence date definition have the potential to introduce lead-time bias and inflate one-year survival estimates by increasing the calculated time survived. This has been recognised by EUROCOURSE (EUROpe against Cancer: Optimisation of the Use of Registries for Scientific Excellence in research); a European network that explores the differences in the quality, usage and output of cancer registries and aims to improve their use through information exchange and sharing of best practice [12].

Death certificate processing also has the potential to influence survival. Processing starts with death certificate initiated (DCI) cases where cancer is mentioned on a death certificate and the registry has no other information on the patient. Where additional information is available, cases are fully registered and would be included in survival analyses. In cases where no additional information is available or where death notifications are not investigated cases are categorized as death certificate only (DCO) registrations – these are routinely excluded from international survival analyses [8–10]. A high proportion of DCO cases in a population will tend to artificially improve one-year survival estimates. Conversely, where efforts have been made by registries to trace data on these cases, their inclusion in analyses will reduce one-year survival as DCI cases often have a very short survival [7,13].

Multiple tumours in a patient can be classified according to the order in which they arise, with the first defined as '1st order', the second as '2nd order' and so on. Rules for how multiple primaries are registered (e.g. the inclusion/exclusion of 2nd order tumours) can also influence survival estimates as 2nd order primaries tend to have worse one-year survival and excluding them from a cancer register would artificially improve one-year survival calculations [14].

Previous studies have explored the impact of English cancer registry practice on international survival, including looking at hypothesised cancer registration errors in the UK affecting lung and colorectal cancer survival [15] and the impact on short term survival of death certificates used for case ascertainment in England [16] however, this in-depth assessment of a range of registries' practice and estimation of the combined effects of any differences on one-year survival has not been attempted before on an international scale. This study aimed to address any ongoing criticism of such international comparisons by taking a detailed look at registry practice and its impact on survival calculations.

2. Methods

2.1. Key informant exercise

A key informant exercise involving questionnaires submitted to registries, teleconferences and face to face visits, was undertaken to assess differences in cancer registration practice between ICBP jurisdictions, specifically noting differences in the definitions of incidence date, death certificate case handling and registration of multiple primary tumours. The cancer sites studied were breast, colorectal, lung and ovarian cancer. The jurisdictions included England; Wales; Scotland; Northern Ireland; Sweden; Denmark; Norway; Victoria, Australia; Manitoba and Ontario (Canada). We used a published framework to assess the comparability of registry data [17,18]. A summary of this and relevant findings is available in Supplementary Material 1.

2.2. Modelling impact on registration practice on survival estimates

Modelling assessed the impact of registration differences on one-year survival using information from key informants (Supplementary Material 1), baseline and supplementary cancer registration data from England and Sweden. Analyses focused on the three areas with potential to impact on one-year survival: definition of incidence date, registration of multiple primaries and death certificate case handling. We report the impact of differences in cancer registration practices on one-year survival for each area, and then all three combined.

Baseline data underlying the sensitivity analysis were taken from the East of England region of the English National Cancer Registration and Analysis Service (NCRAS).

NCRAS data was used as a baseline because it provided verifiable data for date of death and multiple time points for incidence date. This enabled the most accurate possible calculations of one-year survival and provided a valid baseline. To investigate the impact of death certificate handling practices in Sweden, data from the Swedish Patient Register and the Swedish Cancer Registry were also used in sensitivity analyses.

NCRAS data included the same tumour sites and used the same protocol as the ICBP survival benchmark [8]. The analysis used tumours[2] diagnosed in 2010 and followed up to May 2014, Analysis of multiple primaries used longer follow-up times and was based on tumours diagnosed in 1996 and followed up to 2012.

[2] Information available on these tumours included incidence date, gender, age, morphology code, topography code, DCO and DCI status, registry integrated stage and where available, clinical, radiological and pathological stage, neo-adjuvant chemotherapy status and date of death.

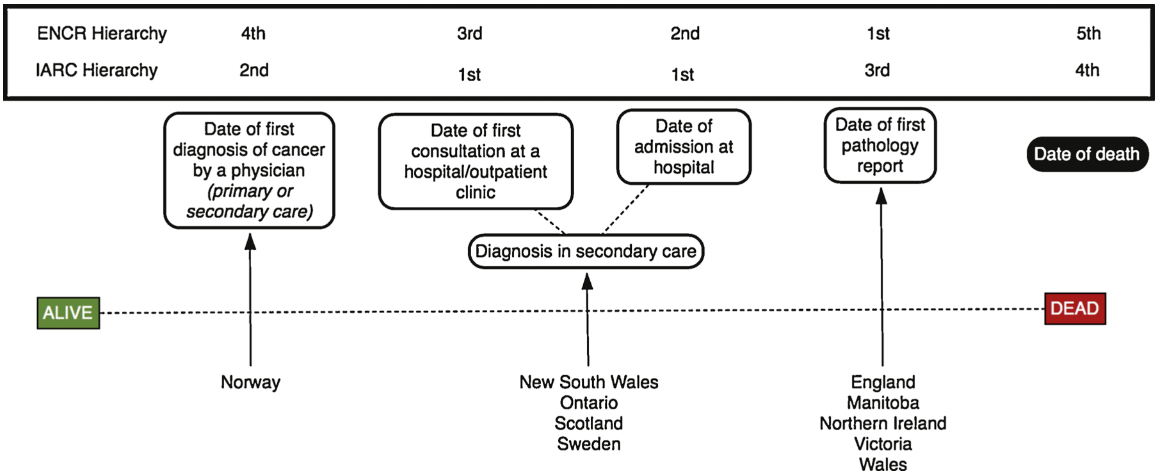

Fig. 1. Illustration of prioritised source of incidence date by jurisdiction. Information collected April 2014.

2.3. Supplementary data

Baseline data from NCRAS were linked to additional information from records in the NHS Hospital Episode Statistics (HES) and Cancer Waiting Times (CWT) datasets. This enriched dataset allowed us to simulate the variation in cancer registration and estimate the differences in survival using 'case-study' modelling for each area of cancer registration practice where data were available and applicable.

For the analysis of death certification practice, Swedish data from the Patient Register and Swedish Cancer Registry databases were used.

2.3.1. Incident date

Assessing data, from NCRAS and Sweden's Cancer Registry, the National Board of Health and Welfare, Stockholm (2010 incidence data for breast, colorectal, lung and ovarian cancer) respectively indicated a similar proportion of registrations could be assigned an earlier incidence date across jurisdictions.

One-year survival was calculated using the different incidence dates available in the baseline data. Incidence date based upon pathological confirmation of cancer was used to calculate the baseline measurement, consistent with ENCR guidelines [6]. Other definitions of incidence date were then selected and one-year survival compared with the baseline.

Estimates prioritising the incidence date in primary care used two methods: the first only included cases diagnosed within 6 months of the baseline date; the second used all cases including those diagnosed greater than 6 months from the baseline date[3].

2.3.2. Death certificate handling

Analyses using the baseline date (pathology based incidence date prioritised) were performed with and without inclusion of the DCO cases. All jurisdictions except for Sweden were able to supply their proportion of DCOs (more information available in Supplementary Material 3).

We investigated death certificates in Sweden arising in 2008–2012 that mentioned ICBP tumour sites that were unmatched to the cancer registry database. Unmatched DCOs were then 'traced-back' using information from the records of the Patient Register not routinely available in Swedish cancer registration practice. The Patient Register contains information on hospital activities but does not include records from primary care [19]. Where enough information was available from the Patient Register to provide supporting evidence of a incidence date for the cancer mentioned on the death certificate, the case was categorised as a DCI and added to the cohort of registered tumours in the Cancer Registry for that tumour site. The impact of the addition of DCIs on one-year survival was reported.

2.3.3. Registration of multiple primaries

All participating registries except Ontario,[4] prior to 2010, and England registered multiple primary tumours in accordance with IARC guidelines [20]. Based on IARC Guidelines, 2nd or higher-order primary tumours could be registered if they occurred at a different anatomical site, or at the same topographical site providing they were not from the same tumour group (e.g. adenocarcinoma, lymphoma etc.) as the preceding tumour(s) [20]. To assess the significance of pre-2010 Ontario multiple primary registration rules on incidence we first calculated the average proportion of 2nd or higher-order primaries registered in Ontario. This was then compared to the highest percentage of registered 2nd or higher-order primaries from the other Canadian registries that participated in the ICBP [8].

The 1st, 2nd, 3rd etc. diagnosed tumours for each patient were identified from the NCRAS cohort. For the same tumour sites used in the ICBP benchmark [8], one-year survival estimates were calculated both including and excluding 2nd or higher order primary tumours. The percentage point difference in one-year survival between including and excluding 2nd or higher-order primaries was calculated and then adjusted by the average proportion described above for the four tumour sites. This estimated the effect on one-year survival calculations, based on registration practice in Ontario.

3. Results

3.1. Key informant exercise

Differences in the definition of incidence date, death certificate case handling and registration of multiple primary tumours were highlighted as areas with the greatest potential to impact one-year survival

[3] This was done to simulate the practice of some registries in the ICBP (Supplementary Material 1).

[4] Previously the Ontario Cancer Registry Information System (OCRIS) did not permit registration of a second tumour of the same body site, laterality was not recognized, and a subsequent cancer of the same histology type was not counted as a new primary. Subsequent primaries that were of a different body part, and were not the same histology were almost always counted as new primaries, although with constraints present because the core cancer identification logic used ICD-9. From 2010 onwards, Ontario started using a Surveillance, Epidemiology and End Results (SEER) based system for the registration of multiple primaries that allowed for the registration of 2nd or higher-order primaries at different anatomical sites [21].

Table 1
[5]One-year overall survival with prioritisation of different incidence date definitions for the four tumour sites studied. Percentage point differences in (). Change in median days survived compared to baseline in []. Using data from NCRAS, Eastern Office 2010.

	Prioritised Incidence Date					
	Date of first pathology report (Baseline)	Date of first imaging report	Date of first consultation / admission to hospital	Date first referred to secondary care	Date of first diagnosis by a physician (excluding dates more than 6 months before the baseline)	Date of first diagnosis by a physician (including dates more than 6 months before the baseline)
Breast	93.7%	93.7% (+0.0) [0]	93.8% (+0.1) [+8]	93.9% (+0.2) [+15]	93.9% (+0.2) [+20]	94.5% (+0.8) [+98]
Colorectal	73.2%	73.3% (+0.1) [0]	73.3% (+0.1) [+10]	74.0% (+0.8) [+15]	74.0% (+0.8) [+17]	76.0% (+2.8) [+44]
Lung	29.3%	29.6% (+0.3) [+3]	30.4% (+1.1) [+13.5]	30.7% (+1.4) [+18]	31.1% (+1.8) [+22]	36.6% (+7.3) [+55]
Ovary	67.3%	67.4% (+0.1) [0]	67.6% (+0.3) [0]	68. % (+0.8) [0]	68.1% (+0.8) [+1]	69.9% (+2.6) [+142]

estimates. Key informants also reported differences in cancer registration that did not impact or had a negligible effect on survival calculations (e.g. staging systems).

3.1.1. Definition of incidence date

The IARC and the ENCR rules and hierarchies for the defining incidence date by participating jurisdictions are displayed [Fig. 1]. Prioritisation of definitions for the incidence date varied, with many registries prioritising incidence dates that typically occur before histological confirmation. However, it is acknowledged that for some cancers histological information is not always available (e.g. patient and presentation characteristics, influence whether a lung tumour is histologically confirmed).

3.1.2. Death certificate case handling

Some jurisdictions investigate DCOs and add information gathered from clinical data sources. Access and availability to these data sources are reported to vary (Supplementary Material 1). All jurisdictions, except Sweden and Ontario, have a central source from which death certificates can be received and investigated. For legal reasons, traceback of DCO cases on a routine basis is not possible in Sweden, whilst Ontario will not actively trace back cases as long as their DCO proportion is less or equal to 2% (in line with national targets).

3.1.3. Registration of multiple primaries

Ontario reported that prior to 2010 they only registered a single morphological group as defined by IARC, per patient rather than per topographical site. England reported that in addition to the IARC rules, multiple breast tumours with different morphologies but within the same IARC morphological groupings were registered (e.g. ductal and lobular carcinomas).

3.2. Modelling

3.2.1. Definition of incidence date

Using NCRAS and Swedish Cancer Registry data, we found that a similar proportion of registrations using earlier incidence dates could change in each cancer registry. Within the NCRAS data, 46.5% of registrations would have an earlier incidence date when prioritising a clinical incidence date over the date of histological confirmation compared with 45.0% in the Swedish data.

The largest differences in one-year survival were seen when prioritising incidence date based on date seen in primary care (Table 1). The differences in one-year survival were greatest for lung cancer (7.3 percentage points; Norway), and lowest for breast cancer (0.1 percentage points; NSW, Ontario and Sweden).

Table 2
One-year survival by tumour site based on inclusion or exclusion of DCO cases, NCRAS, East of England region 2010 data.

DCO Cases	Breast	Colorectal	Lung	Ovary
Excluded	93.8%	73.5%	29.3%	67.1%
Included	93.7%	73.4%	29.3%	67.1%

3.2.2. Death certificate case-handling

Jurisdictions reported annual DCO proportions after all other cases had been traced back (data collected in April 2014, N/A in Sweden). Proportions of DCO varied from 0.3% (Scotland, Northern Ireland), 0.5% (Manitoba), 1.0% (Norway), 1.4% (New South Wales and Wales), 1.7% (Victoria) and 2.0% (Ontario, no active trace back if DCO proportion less than or equal to 2%) and 2.6% (England, regional variation 0.1% to 4.1%).

Excluding DCOs as is normally the case for international survival comparisons, from the NCRAS baseline data resulted in small increases (0.1 percentage points) in one-year survival estimates for breast and colorectal cancer (Table 2). The small increases were due to the low DCO proportion in the NCRAS, East of England, indicating many cases are "traced back" to produce DCI registrations. We therefore looked at data from Sweden where death certificates cannot be used to 'trace back' cases.

When death certificate trace back is performed on Swedish data, an overall decrease in one-year survival is observed for colorectal, lung and ovarian tumours (Table 3). In Sweden the effect of excluding DCOs registered with unknown primaries and secondary cancers had a greater impact on one-year survival estimates for ovarian cancer than for lung and colorectal cancer, because further investigation of these cases revealed that the primary tumour site stated on the death certificate in some cases was different to that recorded in the patient register (e.g. mesothelioma and lung cancers). The analysis excluded DCOs where other information indicated a different primary site.

[5] In a separate analysis of the Swedish data only, comparing the incidence dates from date of first pathology and date of first consultation, changed the median days survived by tumour site, by +2 days for breast and colorectal, +15 days for lung and 0 days for ovary.

Table 3
One-year overall survival for Swedish 2008–2012 cases comparing cases only registered in cancer register and combined registered and unregistered cases. Percentage point difference in brackets. (National Board of Health and Welfare, Stockholm, Sweden).

Tumour Site	Number of Registered cases in Cancer Register (Group A)	Number of death certificates with correct tumour registerable from Patient Register (Group B)	Combined total of Group A and B	One-year survival (Group A)	One-year survival (Group B)	One-year survival (Group A and B combined)
Breast	33,855	237	34,092	96.0%	49.8%	95.7% (-0.3)
Colorectal	28,205	1,561	29,766	80.6%	19.1%	77.3% (-3.3)
Lung	18,504	2,891	21,395	43.9%	18.3%	40.4% (-3.5)
Ovary	3,855	263	4,118	81.6%	38.0%	78.8% (-2.8)

Table 4
Percentage of adults diagnosed during 1995–2007 whose cancer was a second or higher-order primary by cancer and jurisdiction (5).

	% of adults (15-99 years) diagnosed during 1995-2007 whose cancer was a 2nd or higher-order primary.			
	Breast	Colorectal	Lung	Ovary
Alberta	8.7	13.0	14.5	12.0
British Columbia	9.9	14.6	14.7	10.4
Manitoba	11.0	14.8	17.9	13.5
Ontario	*4.9*	*8.1*	*8.7*	*8.5*
Proportion recorded in Ontario compared to highest	*44.5%*	*54.7%*	*48.6%*	*62.9%*

3.2.3. *Registration of multiple primaries*

Ontario had a significantly lower percentage of 2nd or higher-order primaries recorded in their registry compared to other Canadian registries (Table 4). This was statistically significant for all four ICBP tumour sites (Z-test, $p = < 0.01$). The inclusion of further multiple primary breast tumours in England compared to the IARC guidelines would either have no effect on or reduce one-year survival estimates.

Excluding patients diagnosed with 2nd or higher-order primary tumours in the NCRAS data from 1996 to 2012 reduced one-year overall survival by 1.2–6.2 percentage points for 2nd and higher order primaries, compared to 1st order primaries only (Table 5).

3.3. *Summary of sensitivity analyses*

Figures from Table 1 are used to calculate percentage point change in incidence date, Swedish DCO inclusion figures are taken from Table 3, and figures from multiple primaries inclusion are taken from Table 5. The changes to the estimated survival using this method were most pronounced in colorectal and lung cancers. Depending on tumour site and jurisdiction, the largest differences between unadjusted (survival estimates from previous ICBP survival data) and adjusted (survival estimates recalculated taking into account differences in registration practice) for one-year survival by cancer site, were 1.3% for breast, 3.4% for colorectal, 7.3% for lung and 2.6% for ovary.

The one-year survival estimates for New South Wales, Norway, Ontario and Sweden were affected by this adjustment. While the adjusted one-year survival was lower for Sweden and Ontario, they were still the jurisdictions with the highest survival for breast and ovarian cancer respectively. For lung cancer, after adjustment, Victoria and Manitoba had the highest adjusted one-year survival estimate at 42.7%, compared to Sweden's previous highest unadjusted estimate of 43.6%, and adjusted of 39.0%. For colorectal cancer, Victoria's estimate of 85.1% was not changed by the adjustment and remained the highest amongst the jurisdictions included.

This adjustment reduces the survival gap between the jurisdictions with the original highest one-year survival and the lowest (Wales for all four cancer types) by 8.7% for breast, 30.0% for lung, 0.0% for colorectal and 13.6% for ovarian (Table 6) Fig. 2.

4. Discussion

4.1. *Main findings*

Prioritising earlier events for the incidence date ahead of the date of the histology leads to increases in one-year survival that were most marked when jurisdictions prioritised the date of first diagnosis by a physician. The effect was greatest for lung and colorectal cancers (7.3 and 3.4 percentage points respectively). The magnitude of the change was dependent upon the proportion of cases that had a incidence date available that was significantly earlier than the date of histological confirmation. This reflects the typical patient pathway for the diagnosis of colorectal and lung cancer [22,23], with a period of weeks to months of clinical investigations prior to the definitive histological confirmation. Patient or presentation characteristics may also influence histological confirmation. This contrasts with breast cancer pathways in all jurisdictions that ensure there is a minimal lag time between clinical and pathological diagnosis of cancer [22,24,25].

Though routinely excluded from international survival comparisons, previous studies have demonstrated the impact of inclusion of DCOs on survival for particular registries and regions. Robinson et al. (2007) showed five-year relative survival for colorectal, lung, breast and

Table 5
Comparison of one-year overall survival between 1st order only and 1st or higher order tumours. (NCRAS East of England region 1996–2012 data).

	% One-year overall survival			
	1st order tumours only	1st or higher order tumours	Percentage point difference	Percentage point difference multiplied by average proportion recorded in Table 5
Breast	92.1	89.5	2.6	1.2
Colorectal	86.8	83.4	3.4	1.9
Lung	68.7	55.9	12.8	6.2
Ovary	85.8	83.0	2.8	1.8

Table 6

Simulated change in one-year survival gap specific to ICBP jurisdictions prior to 2010, compared to Wales (jurisdiction with the lowest survival across all tumours sites). Based on NCRAS, Eastern Office 2010 data and ICBP Module 1 data[8] covering tumours diagnosed 2005-2007. ICBP Module 1 did not include ovarian cancer survival data from Sweden, as such no other registration practice figures are included here. (*X*)- Figures from Table 1,(Y) - figures from Table 3,(Z) – figures from Table 5.

				Percentage point change by registration practice						
	Jurisdiction	Unadjusted original survival by jurisdiction (Q)	Original Survival Gap (% Points) (M = Q-A)	Definition of incidence date (X)	DCO Inclusion (Y)	Multiple primary inclusion (Z)	% Point Change (P = X +Y + Z)	Adjusted estimated one-year survival (%) N = Q-P	New Survival Gap (N-A)	Survival gap bridged (P/M)
Breast										
Wales	England	94.3	0.9	–	–	–	–	94.3	No change	–
Original one-	Manitoba	96.7	3.3	–	–	–	–	96.7	No change	–
year survival:	NSW	96.5	3.1	0.1	–	–	0.1	96.4	3.0	3.2%
93.4% (A)	NI	95.0	1.6	–	–	–	–	95.0	No change	–
	Norway	96.6	3.2	0.8	–	–	0.8	95.8	2.4	25.0%
	Ontario*	96.1	2.7	0.1	–	1.2	1.3	94.8	1.4	48.1%
	Sweden	98.0	4.6	0.1	0.3	–	0.4	97.6	4.2	8.7%
	Victoria	97.1	3.7	–	–	–	–	97.1	No change	–
Colorectal										
Wales	England	74.7	1.1	–	–	–	–	74.7	No change	–
Original one-	Manitoba	82.1	8.5	–	–	–	–	82.1	No change	–
year survival:	NSW	84.7	11.1	0.1	–	–	0.1	84.6	11.0	0. 9%
73.6% (A)	NI	76.2	2.6	–	–	–	–	76.2	No change	–
	Norway	82.4	8.8	2.8	–	–	2.8	79.6	6.0	31.8%
	Ontario	83.9	10.3	0.1	–	1.9	2.0	81.9	8.3	19.4%
	Sweden	83.8	10.2	0.1	3.3	–	3.4	80.4	6.8	33.3%
	Victoria	85.1	11.5	–	–	–	–	85.1	No change	–
Lung										
Wales	England	29.7	1.2	–	–	–	–	29.7	No change	–
Original one-	Manitoba	42.7	14.2	–	–	–	–	42.7	No change	–
year survival:	NSW	42.9	14.4	1.1	–	–	1.1	41.8	13.3	7.6%
28.5% (A)	NI	30.6	2.1	–	–	–	–	30.6	No change	–
	Norway	39.2	10.7	7.3	–	–	7.3	31.9	3.4	68.2%
	Ontario	43.4	14.9	1.1	–	6.2	7.3	36.1	7.6	49.0%
	Sweden	43.6	15.1	1.1	3.5	–	4.6	39.0	10.5	30.5%
	Victoria	42.7	14.2	–	–	–	–	42.7	No change	–
Ovary										
Wales	England	65.4	4.9	–	–	–	–	65.4	No change	–
Original one-	Manitoba	68.0	7.5	–	–	–	–	68.0	No change	–
year survival:	NSW	73.3	12.8	0.1	–	–	0.1	73.2	12.7	0.8%
60.5% (A)	NI	63.9	3.4	–	–	–	–	63.9	No change	–
	Norway	75.2	14.7	2.6	–	–	2.6	72.6	12.1	17.7%
	Ontario	75.9	15.4	0.3	–	1.8	2.1	73.8	13.3	13.6%
	Sweden	Data not supplied	–	–	–	–	–	–	–	–
	Victoria	73.7	13.2	–	–	–	–	73.7	No change	–

ovarian cancers decreased by 4 to 14 percentage points by including DCO cases [7].

Our data shows that not using death certification for case ascertainment and 'trace back', as occurs in Sweden [26–29], was found to have a significant impact on one-year survival estimates. The Association of the Nordic Cancer Registries (NORDCAN) has identified this as one possible cause for lower incidence rates, especially in older patients and for more lethal tumours, resulting in higher survival estimates because incident cases with short survival may have been excluded [30].

The death certificate trace back simulation using Swedish data, showed a significant reduction in one-year survival in lung, colorectal and ovarian cancers (−3.5, −3.3 and −2.8 percentage points respectively). This reduction may reflect the typical pathway of these cancers where many patients present with late stage disease and are too unwell to undergo diagnostic tests to confirm cancer diagnosis. These results may impact other international survival comparisons where ovarian cancer survival is reported for Sweden [9,10].

The exclusion of 2^{nd} or higher order tumours with similar morphology to the first-order tumour as seen in Ontario, leads to the exclusion of cases with less favourable survival outcomes therefore inflating one-year survival in Ontario. A study by Heinavaara et al. 2002, showed that overall relative survival for 2^{nd} order primaries was worse than those with a respective single cancer only [31]. This was quantified in a study by Brenner et al. 2005, showing that for the tumour sites analysed in ICBP, the exclusion of 2^{nd} and higher order primaries increased five-year relative survival in the 1993-7 cohort by an average of 1 percentage point [32].

Buiatti et al. looked at the incidence of second primary cancers in Italian cancer registries. They identified an increased risk for developing rectal cancer in breast cancer patients and an increased risk of developing ovarian cancer in female colorectal cancer patients [33]. Therefore, exclusion of second or higher order primaries in the four tumour sites studied here, would be expected to more selectively reduce the number of rectal and ovarian cancers in female patients with a first order breast or colorectal cancers.

The EUROCARE working group also studied the impact of the inclusion of patients with multiple cancers on five-year survival, for all cancers combined the average difference was −0.4% in women and −0.7% in men, with variation by cancer site and the proportion of multiple primaries [14]. From 2010 onwards, Ontario started using a SEER based system for the registration of multiple primaries that

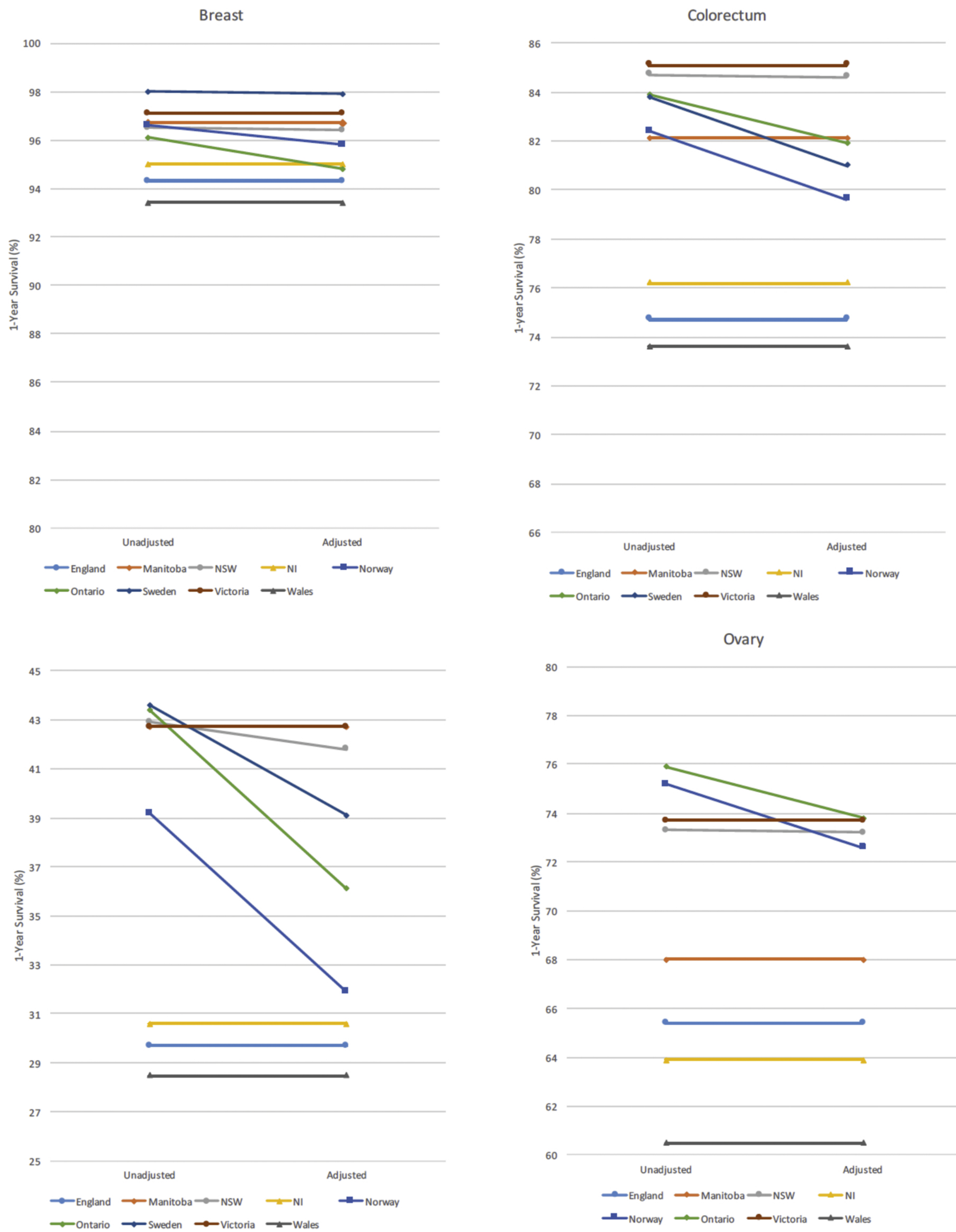

Fig. 2. Adjusted and unadjusted 1-year survival estimates calculated in Table 8 by tumour site and jurisdiction. Note: y-axis has been truncated for each cancer site. (Adjustment is made taking into account differences in DCO handling, prioritised date of diagnosis and registration of multiple tumours.).

allowed for the registration of 2nd or higher-order primaries at different anatomical sites [21].

4.2. Strengths and limitations

This is the first study to estimate the impact of multiple cancer registration differences on international cancer survival comparisons.

A strength of the sensitivity analysis was the use of parameters based on cancer registry data that in some areas incorporated data from multiple jurisdictions, combined with information on day-to-day cancer registration practice (Supplementary Material 1).

Properties of the baseline data from NCRAS that underpinned the sensitivity analysis were assumed to be like baseline data that could have been collected from other jurisdictions. This was based on the comparability of the jurisdictions in the criteria outlined in the methods, including equality of case ascertainment between registries.

To validate this assumption future research could obtain more data from different jurisdictions to add to the baseline data.

Investigating the impact that varying availability of data sources, have on short-term survival estimates requires analysis of diagnostic and treatment processes that are often not exclusive to cancer across various medical, surgical and diagnostic disciplines, and an assessment of the quality of these data sources, which is more suited to a high-resolution study.

The analysis was limited by the complexity of interaction between areas of cancer registration practice that affect comparability identified by Parkin and Bray 2009, in particular the availability of data sources and their impact on selecting an incidence date [18]. The differences in one-year survival following adjustment for cancer registration practice should be interpreted with carefully. For example, we assumed the date of diagnosis in Norway were from primary or secondary health care, but almost all information in Norway is collected from secondary health care, thus the adjusted estimates based on definition of incidence date for Norway is probably too low. We also assumed that definition of a pathological confirmation was consistent across jurisdictions, though it is acknowledged that the date could refer to the date of specimen collection, laboratory receipt or report authorisation date [5,32].

5. Conclusion

We show that differences in cancer registration practices impact international comparisons of one-year survival. Changes in one-year survival varied across jurisdictions and cancer types, dependant on registration practices locally. In the original survival estimates Sweden had the highest one-year survival for breast and lung cancer, Victoria for colorectal cancer and Ontario for ovarian cancer. After adjustments were made, Sweden no longer had the highest one-year survival for lung cancer and the size of the survival gap between England and several jurisdictions was diminished though the general ranking of jurisdictions remained the same. Cancer registration differences can account for part of the survival gap reported between jurisdictions.

Population-based cancer survival comparison results can be adversely affected by registration and detection biases which have been particularly highlighted in Sweden and Ontario. Efforts should be made ahead of international comparisons to assess differences in cancer registration practices and their potential impact on cancer outcomes, extending also to other tumour sites such as kidney and lymphoma. To this end, Norway, Wales, Sweden and England are taking steps to collect multiple sources of data such as different dates of diagnosis based on ENCR definitions. Future international comparison studies, should address registration and detection biases by using these multiple sources of data and the findings of this study to assist the interpretation of differences in one-year cancer survival or provide appropriate warnings about biases with accompanying data on incidence and mortality.

The results of this study should be used to foster transparency with regards to the standardisation of registry data. The nature of cancer registries is rapidly evolving, particularly with the advent of personalised medicine and as such any agreement would need to evolve at similar pace. Phase 2 of the ICBP will use this analysis and insight from key informants as a framework for future analysis of cancer registration protocols, as it expands to cover further tumour sites.

Authorship contribution

ME and JR planned the study design. ME, SH, MG, ML, DP, AG, DHB, YL, TBJ, RLM, HF, DN, MJK, DWH, JW, DT, CR, and JR were involved in the data collection. ME carried out the analyses. ME, JR and SH wrote the draft manuscript. ME, SH, MG, ML, DP, AG, DHB, YL, TBJ, RLM, HF, DN, MJK, DWH, JW, DT, CR, MP, JR were responsible for the interpretation of the data, and have participated in writing and approving the final manuscript version.

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Conflicts of interest

None.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.canep.2018.10.019.

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