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International Trends in Oesophageal Cancer Survival by Histological Subtype between 1995 and 2014

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Abstract

Introduction: Survival from oesophageal cancer remains poor, even across high-income countries. Ongoing changes in the epidemiology of the disease highlight the need for survival assessments by its two main histological subtypes, adenocarcinoma (AC) and squamous cell carcinoma (SCC).

Methods: The ICBP SURVMARK-2 project, a platform for international comparisons of cancer survival, collected cases of oesophageal cancer diagnosed 1995-2014, followed until 31st December 2015, from cancer registries covering seven participating countries with similar access to health care (Australia, Canada, Denmark, Ireland, New Zealand, Norway and the UK). 1- and 3-year age-standardised net survival alongside incidence rates were calculated by country, subtype, sex, age group and period of diagnosis.

Results: 111,894 cases of AC and 73,408 cases of SCC were included in the analysis. Marked improvements in survival were observed over the 20-year period in each country, particularly for AC, younger age groups and 1-year after diagnosis. Survival was consistently higher for both subtypes in Australia and Ireland followed by Norway, Denmark, New Zealand, the UK and Canada. During 2010-2014, survival was higher for AC compared to SCC, with 1-year survival ranging from 46.9% (Canada) to 54.4% (Ireland) for AC and 39.6% (Denmark) to 53.1% (Australia) for SCC.

Conclusion: Marked improvements in both oesophageal AC and SCC survival suggest advances in treatment. Less marked improvements 3 years after diagnosis, among older age groups and patients with SCC, highlight the need for further advances in early detection and treatment of oesophageal cancer alongside primary prevention to reduce the overall burden from the disease.

Summary Box

What is already known about this subject?

- Survival from oesophageal cancer remains poor, even across high-income countries.
- In light of differences in the descriptive epidemiology and the degree of treatment advances of the two main histological groups (adenocarcinoma and squamous cell carcinoma), it is important to assess survival stratified by subtype and to benchmark this across countries and over time.

What are the new findings?

- Using data from high-quality population-based cancer registries from countries with similar healthcare access (Australia, Canada, Denmark, Ireland, New Zealand, Norway, and the United Kingdom (UK), this study investigates trends in survival of oesophageal cancer by histological subtype.

- Overall, improvements in survival in both subtypes were observed during the 20-year study period, with some countries showing greater improvements than others. Marked survival increases more noted for adenocarcinoma, younger age groups and at 1-year post-diagnosis.

- Certain geographical variations in survival were observed, with consistently higher survival for both subtypes in Australia and Ireland followed by Norway, Denmark, New Zealand, the UK and Canada.

How might it impact on clinical practice in the foreseeable future?

- These study findings highlight the impact of treatment advances on oesophageal cancer survival, and the importance of continued advances in treatment options, particularly among older patients, as well as continued surveillance to benchmark survival across countries.

- While oesophageal cancer survival has been increasing across countries in recent years, it remains low for both disease subtypes. As such, future research into early detection and treatment, alongside primary prevention is warranted to improve survival and reduce the disease burden.

Introduction

Oesophageal cancer is the seventh most common cancer worldwide with close to 600,000 new cases diagnosed in 2018 and the sixth most common cause of cancer mortality, with more than half a million deaths.[1] The disease is predominantly categorised by two main histological subtypes with distinct aetiologies: adenocarcinoma (AC), which is typically located in the lower third of the oesophagus and

linked to Barrett's oesophagus (characterised by metaplastic epithelium), and squamous cell carcinoma (SCC), which develops in the native oesophageal epithelium. While SCCs are associated with smoking and alcohol consumption, ACs mainly occur in patients with a history of gastro-oesophageal reflux disease (GORD), which in turn is associated with obesity. [2,3] Recent studies have shown that although SCC is the more common type of oesophageal cancer globally, incidence rates of AC have surpassed SCC rates in high-income countries.[4] These changes may relate to an increasing prevalence of obesity and GORD and a concurrent decline in *Helicobacter pylori* infection (changes in AC incidence) and declines in tobacco smoking prevalence (changes in SCC incidence).

Over the last two decades there have been marked advances in the diagnosis and treatment of oesophageal cancer with an increasing use of multimodality treatments. Recent randomised controlled trials have reported improvements in survival for patients with clinically-resectable cancer undergoing neoadjuvant chemoradiotherapy plus surgery, compared to surgery alone.[5,6] Subsequent to these trials, preoperative chemotherapy plus chemoradiotherapy followed by surgery has become a standard treatment modality, with more intensive perioperative chemotherapy used since publication of the MRC Adjuvant Gastric Infusional Chemotherapy (MAGIC) trial in 2007[7] and the FLOT trial in 2019.[8] In addition, positron emission tomography computed tomography (PET-CT) scanning has been found to improve staging of oesophageal cancer and this has provided better guidance for stage-specific treatment.[9]

Notwithstanding, overall survival from oesophageal cancer remains low - 5-year survival peaks 24% in high-income countries - as a result of a large proportion of patients with advanced stage at diagnosis, with some not undergoing radical treatment due to comorbidities.[10] Previous population-based studies have suggested that 1-year survival is higher among patients diagnosed with AC compared to patients with SCC, but these studies have been conducted either at an individual country level, [11–14] or have not had sufficiently recent follow-up to reflect recent changes in treatment.[15]

The ICBP SURVMARK-2 project, a multidisciplinary partnership gathering experts and data from seven countries characterised by having similar access to healthcare, aims to investigate and elucidate differences in cancer survival across high-income settings. In this paper, we report trends in oesophageal cancer incidence and survival by histological subtype for seven countries with over 20 years of data, investigating subtype-specific survival differences by period of diagnosis, country, age group and sex.

Methods

Data collection

As part of the ICBP SURVMARK-2 project data for primary cancers of the oesophagus were obtained from 21 population-based cancer registries spanning seven countries: Australia (New South Wales, Victoria, Western Australia), Canada (Alberta, British Columbia, Manitoba, New Brunswick, Newfoundland and Labrador, Nova Scotia, Ontario, Prince Edward Island, Quebec, Saskatchewan), Denmark, Ireland, New Zealand, Norway and the UK (England, Scotland, Wales and Northern Ireland). Cases diagnosed during 1995-2014 (Ireland 1995-2013) and followed up until 31st December 2015 were included in the analysis. Data from two Canadian registries were excluded as data were only available from 2000 (Quebec) or death linkage was not systematically carried out prior to 2005

(Newfoundland and Labrador). A total of 19 jurisdictions from seven countries thus contributed data in the present analyses.

Case Definition

Primary malignant oesophageal tumours (ICD-10: C15) were included. Histological groups were based on the International Classification of Diseases for Oncology, third edition (ICD-O-3) [16] and defined as ACs: 8140-8141, 8143-8145, 8190-8231, 8260-8263, 8310, 8401, 8480-8490, 8550-8551, 8570-8574 and 8576; SCCs: 8050-8078 and 8083-8084; Unspecified: 8000-8005. All remaining morphology codes were grouped as "Other", with the exception of gastrointestinal stromal (ICD-O-3: 8936) and neuroendocrine tumours (ICD-O-3: 8013, 8041-8045, 8150-8158, 8240-8247, 8249, and 8574) which were excluded from all analyses as they differ in their aetiology and prognosis from other oesophageal tumours.

In total, 216,689 cases of oesophageal cancer were provided from the 19 included jurisdictions, of which 185,796 patients diagnosed with either AC or SCC were identified. Cases younger than 15 or older than 99 years at diagnosis, cases diagnosed based on death certificates only (DCOs) or at autopsy as well as those with multiple primaries at the same site, were excluded (n=494; 0.3%). This resulted in a total of 185,302 patients included in the survival analyses.

Ethical approval was obtained from the International Agency for Research on Cancer (IARC) Ethics Committee, as well as from the relevant ethics committees in each participating jurisdiction, as required.

Statistical analysis

Trends in age-standardised incidence rates per 100,000 person-years were calculated for the two main histological subgroups (AC and SCC) of oesophageal cancer using the World Standard Population.[17] Net survival, defined as the survival of patients from the specific cancer under study after controlling for other causes of death, was used to benchmark across countries. Age-standardised net survival estimates at 1 and 3 years after diagnosis and their 95% confidence intervals (CIs) were calculated for AC and SCC and for each 5-year period of diagnosis by age group (15-64 years, 65-74 years and 75-99 years), sex and country; the unbiased Pohar Perme estimator [18] was used to take into account the higher competing risks of death among the older populations. Analyses were performed using the *stnet* command in Stata version 14.2 and the International Cancer Survival Standard (ICSS) weights were used for age standardization.[19]

The *cohort* approach was used for the earlier three periods of diagnosis (1995-1999, 2000-2004 and 2005-2009) where complete follow-up was available, whereas the *period* approach [20] was used for the most recent diagnosis period (2010-2014) to estimate 3-year survival for patients without the complete three years follow-up.

Life tables were constructed for each jurisdiction for all-cause mortality in the general population by sex, single year of age and calendar year during 1995-2014. As it is possible that some cancers of the lower oesophagus may have been incorrectly recorded or misclassified as cancers of the gastric cardia

(ICD-10: C16.0), additional incidence and survival analyses were performed by histological subtype combining C15 and C16.0 together for cases diagnosed 2010-2014.

Patient and Public Involvement

As this work is a retrospective study involving examination of secondary cancer data only, patients were not involved in the design and conduct of this research.

Results

In total, 111,894 new cases of AC and 73,408 cases of SCC diagnosed 1995-2014 were included in the survival analysis. While AC was more common in males than females, sex-specific differences were less marked for SCC (**Table 1**). The median age at diagnosis ranged from 66 to 72 years (across countries) for AC and from 65 to 75 years for SCC. During the period of diagnosis 1995-1999, SCC was the most common subtype across all countries, except for the UK. Subsequently the proportion of AC increased over time and became the most common subtype in all countries during the most recent period (2010-2014), ranging from 50.9% of all cases in Ireland to 59.9% in the UK, whereas the proportion of SCC concomitantly decreased over time, with proportion ranging from 29.8% in the UK to 43.3% in Denmark (2010-2014) (**Figure 1**). While the proportion of other histological types were relatively small and constant over time, cases with unspecified histology were relatively high in some countries, particularly during earlier periods of diagnosis, ranging from 9.5% of cases in Norway to 21.7% of cases in the UK during 1995-1999, with decreasing proportions observed thereafter.

Age-standardised incidence rates of oesophageal AC increased in all seven countries over the 1995-2014 period, surpassing the rates of SCC which were in decline in all countries except Denmark (**Supplementary Figure S1**). In 2014, age-standardised incidence rates of oesophageal AC were highest in the UK (7.7 per 100,000 person-years) and oesophageal SCC rates highest in Denmark (3.6 per 100,000 person-years). In 2013 (incidence data available from all participating countries), oesophageal SCC rates were highest in Ireland (4.4 per 100,000 person-years). Canada had the lowest incidence of both oesophageal AC and SCC in 2014 (2.7 and 1.2 per 100,000 person-years, respectively). Sensitivity analyses showed that the increasing incidence rates of oesophageal AC were similar to the corresponding trends of AC of the gastric cardia over time, except for the UK, where incidence rates decreased rather than increased to 2.5 per 100,000 person-years in 2014.

Adenocarcinoma vs squamous cell carcinoma survival

1-year and 3-year survival increases were greater for AC, reaching 21.9 (Ireland) and 14.5 (Denmark) percentage points over the 20-year period, respectively, compared with 15.6 (Ireland) and 13.3 (Norway) percentage points for SCC (Figure 2, Supplementary Table S1). In the most recent period, 1-year survival tended to be greater for AC than SCC across countries with the observed differences greater in Norway (53.2% vs. 40.0%, 13.2% point difference), Denmark (50.7% vs. 39.6%, 11.1% difference) and in the UK (50.6% vs. 43.4%, respectively or 7.2% difference). Subtype differences were less apparent at 3 years after diagnosis.

Survival from adenocarcinoma of the oesophagus

There were marked improvements in 1-year net survival from AC across countries in patients diagnosed during 2010-2014 relative to 1995-1999, with increases ranging from 7.5 to 21.9 percentage

points, with the largest increases observed in Ireland, Norway, Denmark and the UK. In the most recent period, 1-year net survival was highest in Ireland (54.4%), Australia (53.6%) and Norway (53.2%) but somewhat lower in Canada (46.9%) and New Zealand (48.2%) (**Figure 2, Supplementary Table S1**). Absolute improvements in 3-year survival from AC ranged from 6.0 (Canada) to 14.5 (Denmark) percentage points, with the highest survival observed in Australia (29.1%) and Ireland (28.4%), with somewhat lower survival estimates seen in Canada (21.5%) and the UK (22.8%) in 2010-2014.

Survival varied considerably by age at diagnosis. While 1-year net survival from AC ranged from 51.7% (New Zealand) up to 69.0% (Ireland) in patients diagnosed at age 15-64 years in 2010-2014, the range was 36.9% (Denmark and UK) to 44.1% (Australia) in those aged 75 years and above. Marked improvements were observed in 1-year survival from AC in patients below 65 years (ranging from 9.2 (Canada) to 30.3 (Ireland) percentage points across the seven countries) and 65-74 years at diagnosis (ranging from 6.1 (Canada) to 22.4 (Denmark) percentage points) over the 1995-2014 period (**Figure 3a, Supplementary Table S4**). Less marked improvements in 1-year survival over time were observed in the oldest age group (75+ years) with the greatest improvements in Norway and the smallest observed in New Zealand (14.1 and 4.9 percentage points, respectively). Similar results were seen for survival at three years, where improvements were largest in the two younger age groups (**Figure 3b, Supplementary Table S5**).

Improvements in 1- and 3-year net survival were observed in both males and females over time with higher survival observed in males compared to females in the majority countries (Canada, the UK, Denmark and Ireland) (**Supplementary Table S3**). Improvements in both 1-year and 3-year net survival were also observed at the jurisdiction level within countries, with the greatest absolute survival improvements among diagnoses 2010-2014 compared to 1995-1999 observed in Saskatchewan, Canada (27.8 percentage point increase at 1 year) and Northern Ireland, UK (11.9 percentage points at 3 years). Within country survival differences of up to 17.7 percentage points were observed at 1 year in Canada ranging from 36.1% in Prince Edward Island to 53.8% in Saskatchewan in 2010-2014 (**Supplementary Table S2**).

Survival from squamous cell carcinoma of the oesophagus

Improvements in 1-year net survival from oesophageal SCC were observed in all countries with survival increases ranging from 3.4 to 15.6 percentage points in Canada and Ireland, respectively (**Figure 2, Supplementary Table S1**). Improvements were slightly less pronounced at 3 years after diagnosis, with survival increases ranging from 3.1 percentage points (Canada) to 13.3 percentage points (Norway). In the most recent period, both 1- and 3-year survival from SCC was highest in Australia (53.1% and 28.5%, respectively).

Survival from SCC 1 year after diagnosis particularly improved among patients aged under 65 years and between 65 and 74 years, with marked improvements seen in the UK and Denmark as well as in Norway and Ireland (the latter two countries only for 65-74 year olds) (**Figure 3a, Supplementary Table S4**). Improvements were also observed in Australia, Ireland, New Zealand and the UK for patients aged 75 years and older at diagnosis, with the increases ranging from 10.1 to 15.2 percentage point in 1-year survival. Overall, similar trends were observed in 3-year survival, although only minor improvements were seen among SCC patients diagnosed at ages 75 and older (**Figure 3b, Supplementary Table S5**).

For both sexes, 1- and 3-year net survival from SCC improved over the 20-year period (**Supplementary Table S3**). Survival estimates were higher in females compared to males, most notably in Australia (39.0% versus 22.3% 3-year survival, respectively) and the UK (24.1% versus 16.4% 3-year survival; 48.1% versus 39.0% 1-year survival, respectively).

Improvements in both 1-year and 3-year net survival from SCC were also observed at the individual jurisdiction level by up to 22.4 percentage points at 1 year (New Brunswick, Canada) and 18.7 percentage points at 3 years (Victoria, Australia) over the 20-year period. Within-country differences in survival were observed in the most recent period of up to 34.1 percentage points at 1 year in Canada, ranging from 23.6% in Nova Scotia to 57.7% in New Brunswick (**Supplementary Table S2**).

Sensitivity analyses: Survival from oesophageal adenocarcinoma and gastric cardia cancer

Similar patterns in 1-year survival of oesophageal AC across countries were observed when cancers of the gastric cardia were additionally included in the analyses and compared with survival from oesophageal AC alone. There was minor change in survival estimates for the 2010-14 period when 7,390 gastric cardia cancers were included, with the largest increase of 3 percentage points seen in AC survival in Australia (56.6%) (**Supplementary Figure S2**).

Discussion

With the incidence of AC of the oesophagus rising over the past 20 years, the subtype has become the most common type of oesophageal cancer in all seven high-income countries included in this study. In contrast, the incidence of SCC has been steadily decreasing over the same period. We report that survival from both oesophageal AC and SCC have improved substantially across all countries, with survival from AC generally more favourable than that of SCC, with differences of up to 13.2 percentage points for 1-year survival for patients diagnosed in 2010-2014. Generally, improvements in survival were most pronounced in patients diagnosed with AC compared to SCC among patients aged <75 years at diagnosis, and for 1-year survival compared to 3-year survival. Similar improvements were seen within countries, for example in New South Wales, Australia 1-year survival of AC improved by over 12 percentage points compared to an improvement of less than 2 percentage points in SCC patients. Whilst improvements in 1-year net survival of AC were greatest in Ireland, Norway and Denmark, recent survival estimates were highest in Ireland, Australia and Norway. Similar patterns were observed for oesophageal SCC with some within-country variation.

Survival from AC was higher relative to that of SCC, particularly at 1-year after diagnosis. Similar findings have been reported previously [15,21], with the differences in the aetiology and consequent comorbidity postulated as one possible explanatory factor: as smoking is a strong risk factor of SCC, and is often associated with other comorbidities such as cardiovascular and respiratory disease, this might in part influence survival of these patients and explain the poorer prognosis.[22] Future studies are needed to investigate survival differences between the two subtypes with an assessment of comorbidities. Furthermore, patients with Barrett's oesophagus (a precursor lesion of AC) who undergo endoscopic surveillance may be diagnosed at an earlier stage, which may in turn partially account for the relatively higher AC survival.[23,24] The true impact of active surveillance using endoscopy remains unclear however, with a previous meta-analysis of non-randomized studies reporting only a small benefit in survival, although these results are susceptible to confounding biases.[25] Recent studies have shown the promise of less invasive techniques (e.g. sponges) for the

early detection of oesophageal AC [26] which may also prove useful in the detection of oesophageal squamous dysplasia, a precursor to oesophageal SCC. [27]

Nonetheless, survival for both oesophageal cancer types remains poor. As such, it is important that international initiatives and campaigns targeting obesity control through healthy diet and regular physical activity, alongside continued reduction of smoking and the harmful use of alcohol,[28] continue to be promoted to further reduce the overall incidence of oesophageal cancer. Further research on chemopreventative therapies[29] such as aspirin and proton-pump inhibitors as well as endoscopic intervention and ablative therapies for precancerous conditions may also prove beneficial in reducing the burden of disease.

The marked improvements in survival from both subtypes are likely related to the improvement and further development of treatments for oesophageal cancer that have been adopted in recent years, including the use of neo-adjuvant therapy for resectable, locally-advanced oesophageal cancers [5,7,30,31] as well as better supportive care in terms of nutrition. The main curative treatment strategy for oesophageal cancer (both AC and SCC) relies on surgical approaches, or in some cases definitive chemo-radiotherapy for SCC,[32] with recent randomised trials showing improved survival with the addition of neoadjuvant chemotherapy or chemo-radiotherapy.[5,30–33] The CROSS trial has shown that compared with surgery alone, treatment of locally advanced oesophageal cancer with chemo-radiotherapy followed by surgery improved overall 5-year survival from 33.3% to 43.3% and from 30.2% to 61.0% in resectable patients with AC and SCC, respectively.[5] Furthermore, the more intensive perioperative MAGIC regimen, may have contributed to improved survival in oesophageal AC patients over the last decade,[7] and the recent FLOT randomised trial highlights potential continued progress in this context.[8]

A second key factor may be increased centralisation of oesophageal cancer surgery.[11] Many of the countries involved in this study such as Denmark (2007), Norway (2013), England and Wales (2000; 2007) and Ireland (2006) have undergone major national health reforms. These reforms have resulted in increased expenditure on cancer services and centralisation of surgery resulting in a shortening of time until diagnosis and the fast-tracking of treatment and ultimately improvements in population-based survival.[34–38] Survival differences observed within countries could be due to limited availability of specialised care in oesophageal cancer services in lower incidence regions and warrant further investigation. In addition, improvements in diagnostic and staging procedures through the use of PET-CT [39] could also have contributed to improved prognosis as a result of more accurate staging of patients which has been a possible explanation for improved survival in a previous study.[11] An in-depth investigation of how survival differences in oesophageal cancer could partly be explained by variation in the proportion of histological subtype and earlier diagnosis, i.e. stage at diagnosis, is the subject of a separate ICBP SURVMARK-2 paper. Future studies should aim to diagnose cases in high-risk populations earlier and identify biomarkers that aid the characterisation of high-risk SCC patients. [27] In addition, the recent identification of mutational signatures of oesophageal AC, show promise for early detection, and more targeting of treatments for patients [40] which may further improve survival outcomes.

While marked survival improvements were observed in the younger age groups diagnosed below the age of 75 years, improvements in older patients were less evident. As older patients are more likely to present with comorbidities than younger patients, treatment decisions or adherence to treatment

in this age group often differ, which may reduce the prospects of treatment-related improvements in survival.[41] A lack of clinical guidelines for this age group across jurisdictions might also impact survival outcomes. Age-related inequalities have been identified for colon cancer[42] and the survival gap between elderly and middle-aged patients has been widening in Europe, particularly after the first year of diagnosis, an indication of differing treatment decisions in this cohort.[43] As around 40% of AC and SCC patients are diagnosed at ages greater than 75 years, there is a need for randomised controlled trials targeting older cancer patients to investigate the efficacy of cancer treatments in this age group and for clinicians to use comprehensive geriatric assessments when making treatment decisions in these patients.[44]

This international study, part of the ICBP SURVMARK-2 project, has a number of strengths. As an international partnership, data have been collected from 21 high-quality cancer registries allowing assessment of cancer survival among a large number of AC and SCC patients over a 20-year period. The procedures in place under this collaborative project have ensured that data are of both optimal quality and comparability across countries. Detailed protocols for the collection and linkage of data were established and each registry dataset was examined to confirm adherence, with any queries discussed with each registry and re-evaluated datasets submitted, where necessary; frequent discussions with local leads and clinicians were also scheduled. Although measures have been put in place to ensure data are consistent, it is possible that differences in clinical practices and cancer registration practices including coding and classification may have contributed to the observed differences in survival across countries. It may be that as diagnostic techniques have improved, the quality of cancer registrations has further increased, which in turn may have led to the observed decline of the proportions of oesophageal cancers with unspecified histology. However, the proportion of unspecified oesophageal cancers is relatively low particularly for the more recent time periods, ranging from 4.5% in Denmark to 11.4% in New Zealand among patients diagnosed in 2010-2014. As such, the major conclusions of our paper are likely to remain valid.

It is also possible that some AC of the lower oesophagus and gastro-oesophageal junction were misclassified as cancers of the gastric cardia (ICD-10 C16.0) which were not included in the main analyses, as it was not possible to differentiate these cases without information on Siewert type.[45,46] However, after including cases coded as C16.0, which includes both gastric cardia and gastro-oesophageal junction cancers, there was little impact on survival estimates and overall patterns across countries for both histological subtypes. To avoid misclassification of cancers of the gastro-oesophageal junction, a new topography code for these cancers to separate from gastric cardia cancers should be considered. Lastly, this study did not have treatment-specific data to directly quantify the impact of specific treatment advances on improved survival over time.

In conclusion, the international variation observed in survival from oesophageal AC and SCC points to a large role of improved treatment and management of cases across the seven countries included in the ICBP SURVMARK-2 project. Given the ongoing changes in the epidemiology and treatment of oesophageal cancer, with the incidence of AC surpassing that of SCC and constant advances in therapeutic modalities, ongoing surveillance and additional studies are warranted, particularly those that focus on older patients, for whom survival has least improved. An increasing emphasis on the early detection of precancerous changes and early cancers to identify AC among high-risk groups, as well as broad prevention measures, are crucial to reduce the number of oesophageal cancer diagnoses and improve survival among patients in future years.

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Contributorship statement

Study concept and design: EM, IS, FB, MA. Data collection and interpretation of data: HT, LS, RW, SK, AL, PD, VT, GE, AG, EM, PW, SV, CJ, BM, OB. Data analysis: EM, MR, AB, JF. Drafting the manuscript: EM, IS, MA. Critical revision of the manuscript for manuscript for important intellectual content: all authors.

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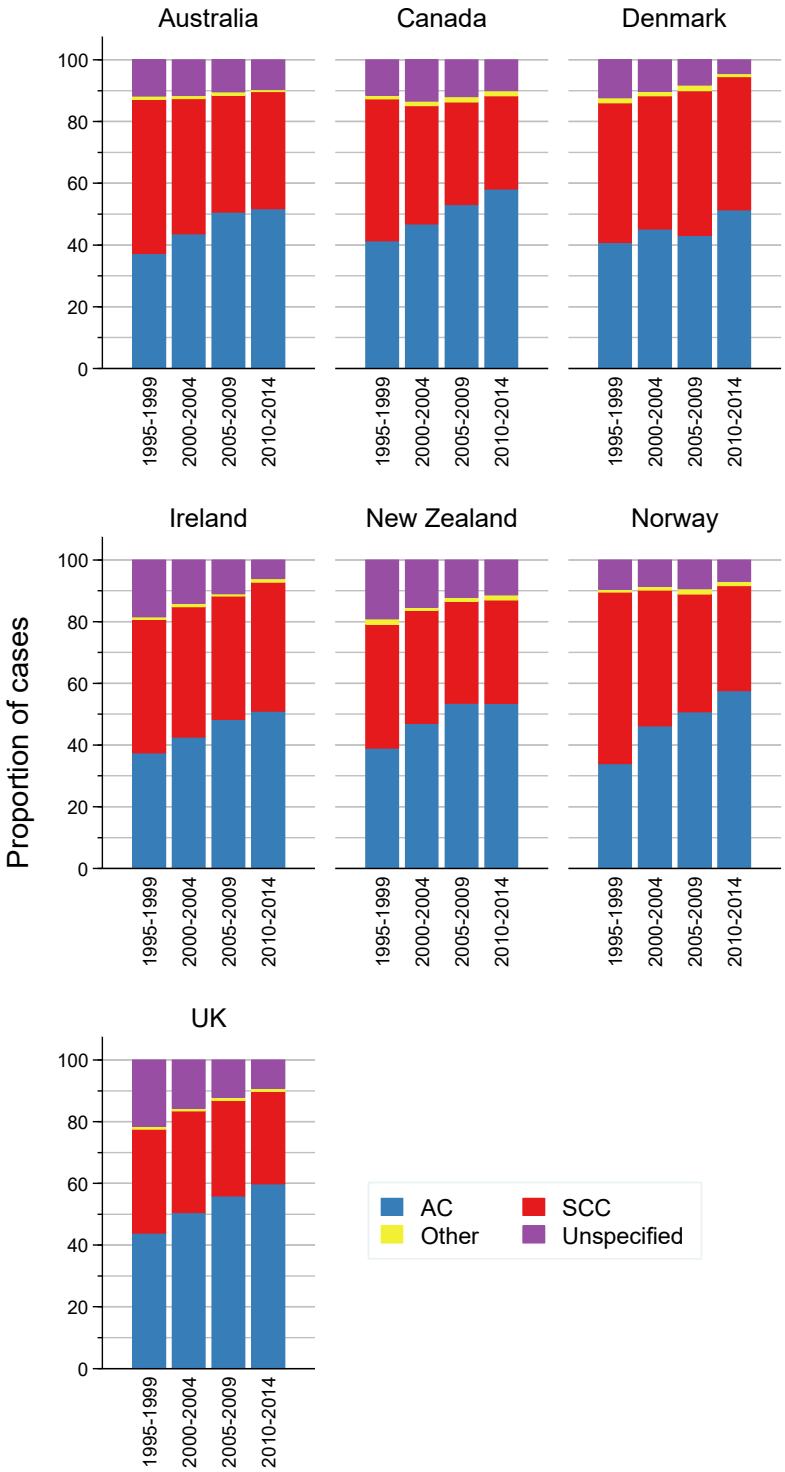

Figure 1: Proportion of oesophageal cancer cases by histological subtype and period of diagnosis, 1995-2014

*Morphological subtype categorised as AC: Adenocarcinoma of the oesophagus, SCC: Squamous cell carcinoma of the oesophagus, Other and Unspecified

Table 1: Number and characteristics of new cases of oesophageal cancer (C15) by histological subtype, period of diagnosis and country, 1995-2014

		Adenocarcinoma (AC)				Squamous cell carcinoma (SCC)				Other				Unspecified			
Country	**Period of diagnosis**	**Cases**	**Cases included (%)***	**Median age**	**% males**	**Cases**	**Cases included (%)***	**Median age**	**% males**	**Cases**	**Cases included (%)***	**Median age**	**% males**	**Cases**	**Cases included (%)***	**Median age**	**% males**
Australia	1995-1999	1251	1249(99.8%)	71	82	1690	1686(99.8%)	71	49	33	33(100%)	72	58	399	360(90.2%)	75.5	59
	2000-2004	1662	1654(99.5%)	70	82	1672	1668(99.8%)	72	51	38	37(97.4%)	67	65	441	375(85%)	76	59
	2005-2009	2145	2142(99.9%)	70	83	1604	1600(99.8%)	73	54	43	43(100%)	70	74	444	381(85.8%)	78	62
	2010-2014	2418	2410(99.7%)	69	84	1779	1772(99.6%)	72	53	34	34(100%)	70	71	451	352(78%)	77	62
Canada	1995-1999	1900	1898(99.9%)	69	85	2119	2119(100%)	69	59	52	52(100%)	68	75	531	464(87.4%)	75	61
	2000-2004	2524	2521(99.9%)	68	85	2030	2026(99.8%)	70	58	75	75(100%)	69	72	617	536(86.9%)	75	66
	2005-2009	3355	3352(99.9%)	67	84	2026	2025(100%)	70	61	112	112(100%)	67	78	646	571(88.4%)	75	68
	2010-2014	4324	4306(99.6%)	66	85	2215	2197(99.2%)	70	61	119	115(96.6%)	69	73	648	549(84.7%)	74	72
Denmark	1995-1999	702	688(98%)	70	82	778	753(96.8%)	65	63	29	29(100%)	67	83	213	198(93%)	73	68
	2000-2004	880	875(99.4%)	70	81	843	837(99.3%)	66	62	28	27(96.4%)	60	85	200	190(95%)	74.5	72
	2005-2009	863	860(99.7%)	71	79	940	933(99.3%)	65	65	37	36(97.3%)	66	61	166	162(97.6%)	71.5	65
	2010-2014	1275	1274(99.9%)	69	80	1074	1074(100%)	67	66	22	22(100%)	70	77	112	107(95.5%)	72	71
Ireland	1995-1999	553	553(100%)	69	76	642	640(99.7%)	70	50	12	12(100%)	59	67	273	232(85%)	78	56
	2000-2004	690	689(99.9%)	70	80	688	685(99.6%)	69	47	16	16(100%)	67.5	81	230	196(85.2%)	76	53
	2005-2009	869	869(100%)	68	78	719	718(99.9%)	70	49	15	15(100%)	68	67	198	183(92.4%)	79	62
	2010-2014	757	754(99.6%)	69	80	623	618(99.2%)	71	49	17	17(100%)	66	59	90	82(91.1%)	76	59
New Zealand	1995-1999	373	373(100%)	71	82	386	385(99.7%)	71	55	17	17(100%)	74	65	184	179(97.3%)	75	58
	2000-2004	554	553(99.8%)	71	83	432	431(99.8%)	72	47	12	12(100%)	71	50	180	172(95.6%)	78	61
	2005-2009	690	690(100%)	71	82	428	426(99.5%)	75	45	15	15(100%)	61	80	158	145(91.8%)	78	58
	2010-2014	761	761(100%)	71	84	479	479(100%)	72	49	23	23(100%)	69	87	162	156(96.3%)	77	69
Norway	1995-1999	277	277(100%)	72	82	454	450(99.1%)	69	68	8	8(100%)	70	88	78	72(92.3%)	76	75
	2000-2004	406	403(99.3%)	72	75	389	386(99.2%)	70.5	67	10	10(100%)	67	80	76	71(93.4%)	77	65
	2005-2009	494	493(99.8%)	70	81	371	369(99.5%)	68	64	17	17(100%)	68	65	91	83(91.2%)	75	65
	2010-2014	721	717(99.4%)	69	82	425	420(98.8%)	68	68	18	18(100%)	78	50	88	77(87.5%)	74	62
UK	1995-1999	14959	14925(99.8%)	71	75	11520	11480(99.7%)	71	45	249	248(99.6%)	69	65	7393	6857(92.7%)	77	55
	2000-2004	18778	18742(99.8%)	72	77	12225	12195(99.8%)	72	45	273	273(100%)	69	65	5855	5359(91.5%)	77	57
	2005-2009	22223	22181(99.8%)	71	78	12299	12269(99.8%)	72	46	349	347(99.4%)	70	67	4863	4365(89.8%)	77	59
	2010-2014	25731	25685(99.8%)	71	79	12811	12767(99.7%)	72	47	474	472(99.6%)	71	63	3959	3480(87.9%)	79	60

*Reasons for exclusion include DCOs, cases diagnosed at autopsy, data inconsistencies (dates, invalid age), under 15 or over 99 years at diagnosis, missing/ incomplete dates.

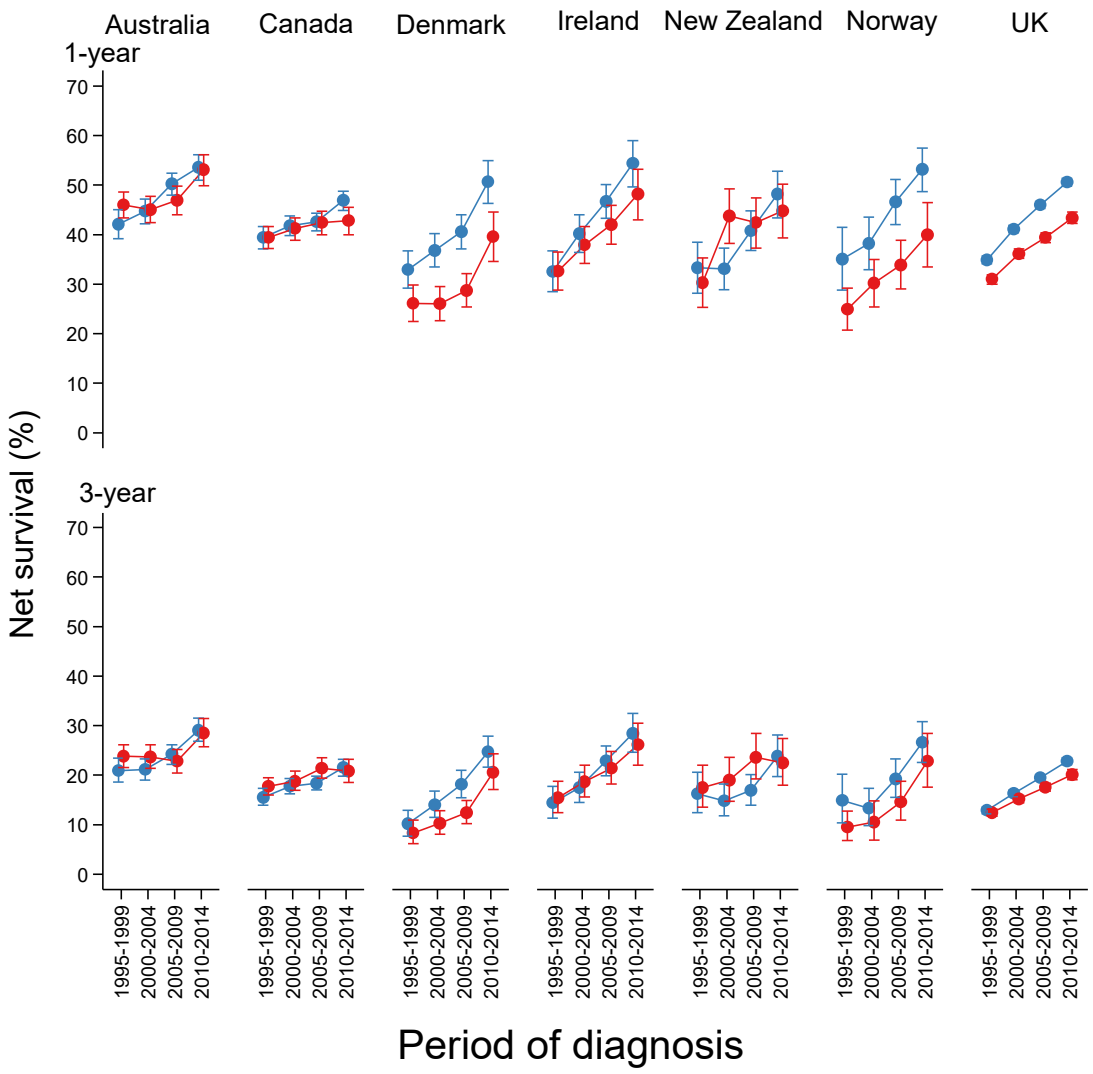

Figure 2: Age-standardized 1- and 3-year net survival estimates and corresponding 95% confidence limits of oesophageal adenocarcinoma (blue) and squamous cell carcinoma (red) by country and period of diagnosis

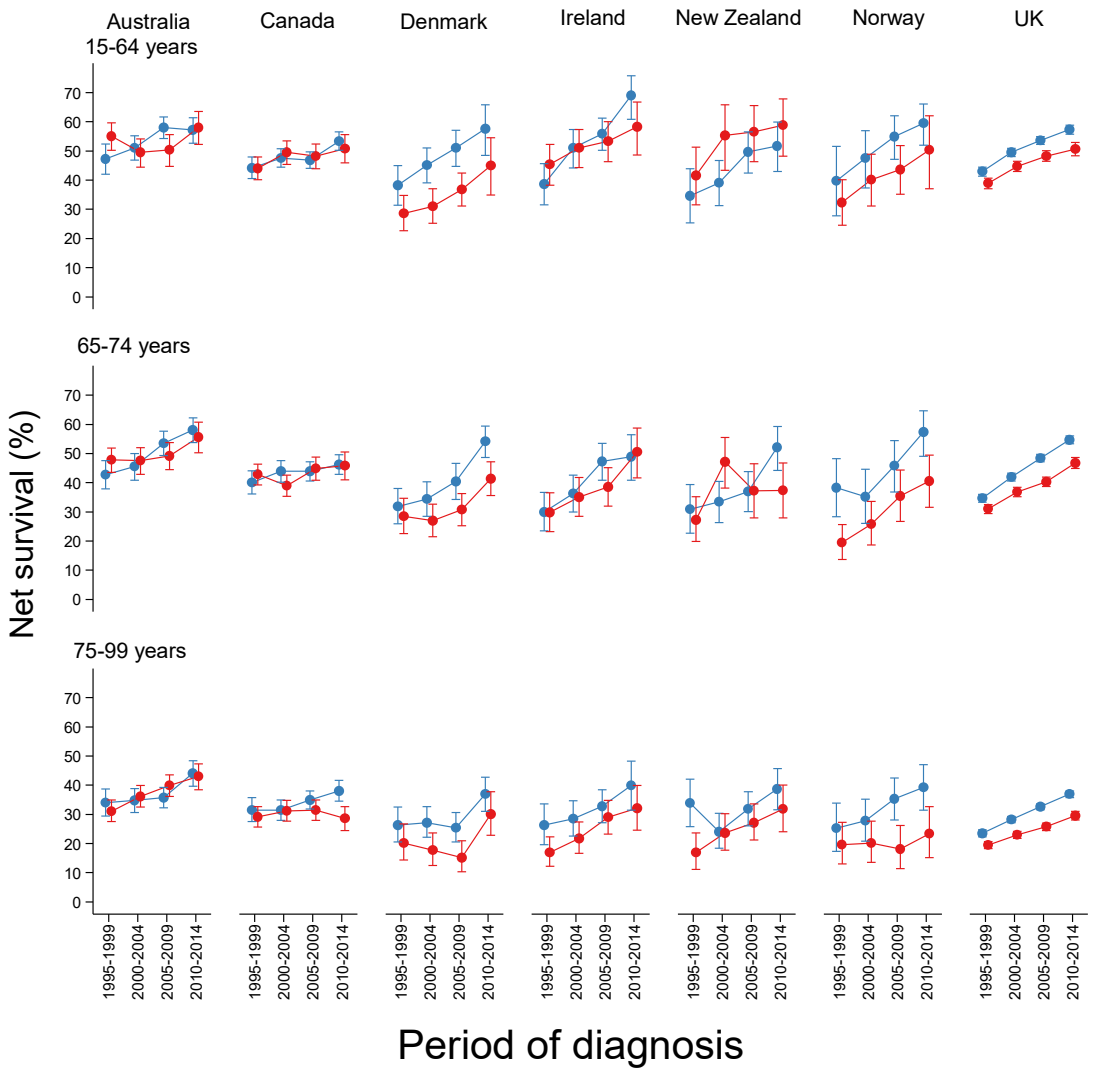

Figure 3a: One-year net survival estimates and corresponding 95% confidence limits of oesophageal adenocarcinoma (blue) and squamous cell carcinoma (red) by country, age group and period of diagnosis

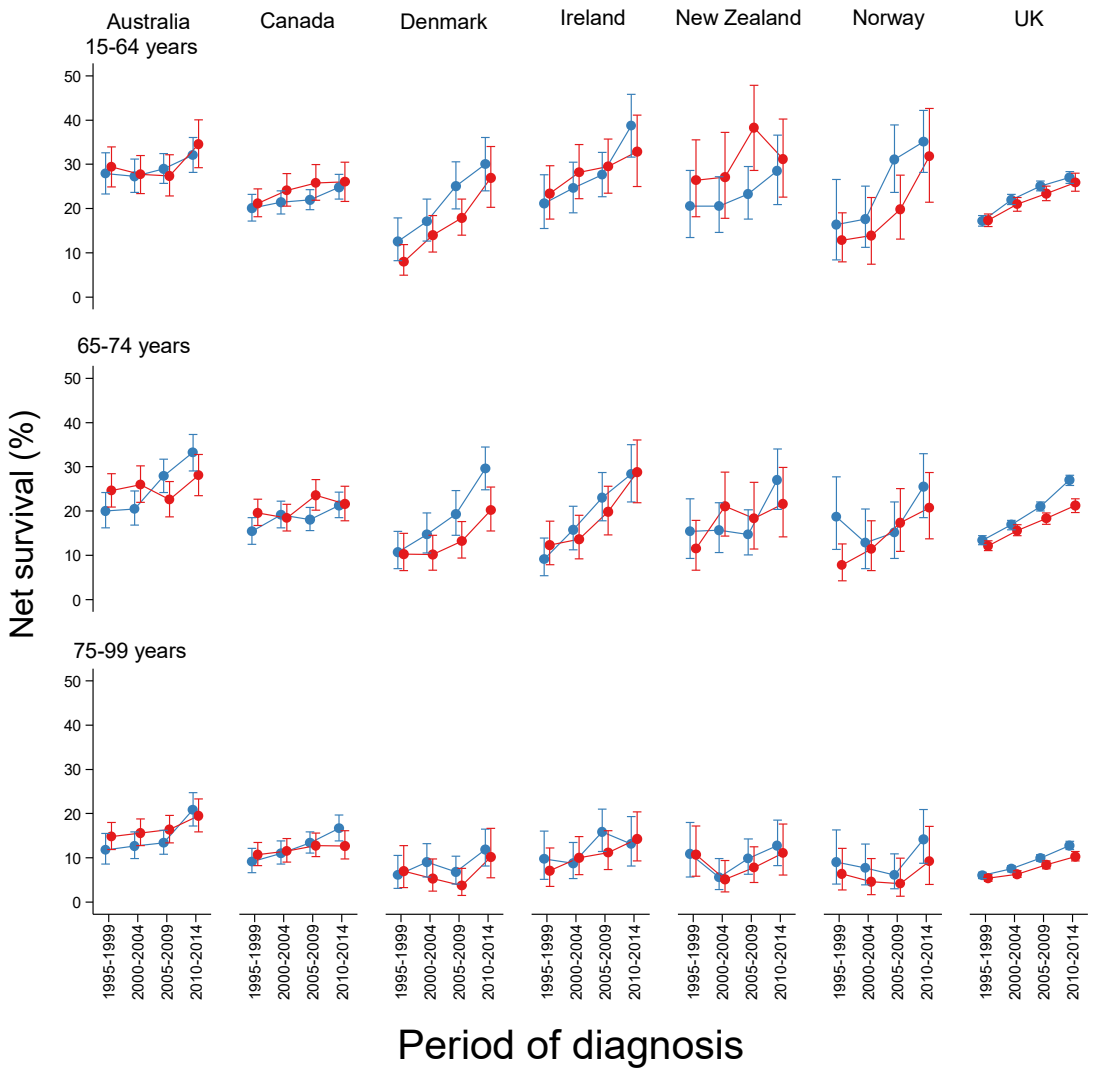

Figure 3b: Three-year net survival estimates and corresponding 95% confidence limits of oesophageal adenocarcinoma (blue) and squamous cell carcinoma (red) by country, age group and period of diagnosis

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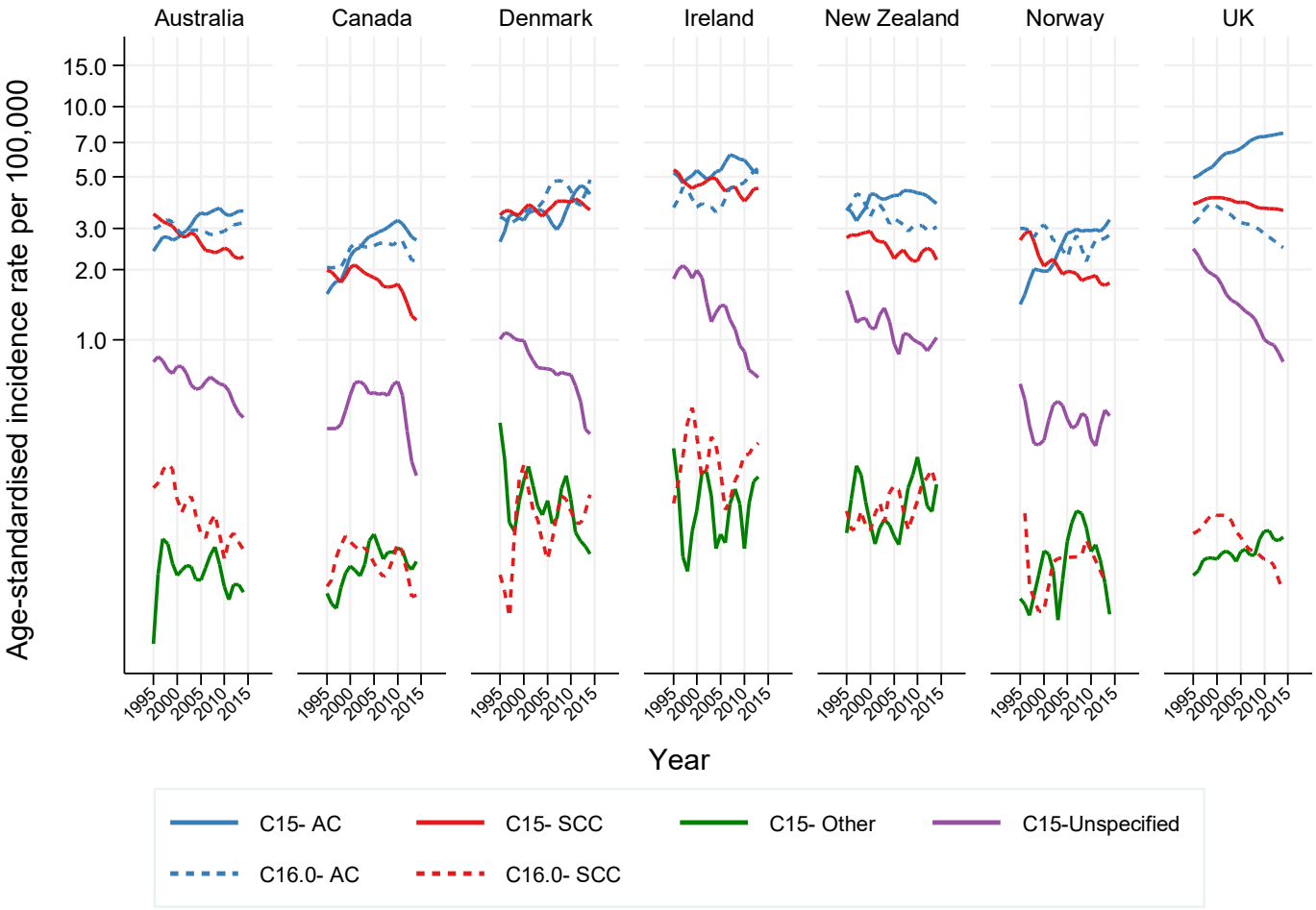

Figure S1: Trends in age-standardised incidence rate per 100,000 of oesophageal (C15) and gastric cardia (C16.0) cancer by histological subtype by country and year of diagnosis, 1995-2014

Table S1: One- and three-year age-standardised net survival (%) and corresponding 95% confidence limits from oesophageal cancer by histological subtype, country and period of diagnosis

		1-year survival (95% CI)				3-year survival (95% CI)			
Country	**Period of diagnosis**	**AC**		**SCC**		**AC**		**SCC**	
Australia	1995-1999	42.1	(39.2,45.0)	46.0	(43.4,48.6)	20.9	(18.6,23.4)	23.8	(21.5,26.1)
	2000-2004	44.7	(42.2,47.2)	45.0	(42.4,47.7)	21.1	(19.0,23.3)	23.7	(21.4,26.1)
	2005-2009	50.3	(48.0,52.4)	46.9	(44.0,49.8)	24.2	(22.2,26.1)	22.8	(20.4,25.2)
	2010-2014	53.6	(51.0,56.1)	53.1	(49.9,56.1)	29.1	(26.8,31.5)	28.5	(25.7,31.4)
Canada	1995-1999	39.4	(37.1,41.6)	39.4	(37.2,41.6)	15.5	(13.9,17.3)	17.7	(16.0,19.5)
	2000-2004	41.8	(39.8,43.8)	41.2	(38.9,43.4)	17.7	(16.2,19.3)	18.8	(16.9,20.8)
	2005-2009	42.6	(40.8,44.3)	42.4	(40.0,44.7)	18.4	(17.0,19.8)	21.4	(19.4,23.5)
	2010-2014	46.9	(44.9,48.8)	42.8	(40.0,45.5)	21.5	(19.8,23.2)	20.8	(18.5,23.2)
Denmark	1995-1999	32.9	(29.2,36.7)	26.1	(22.5,29.8)	10.2	(7.7,12.9)	8.3	(6.2,10.9)
	2000-2004	36.8	(33.5,40.2)	26.0	(22.6,29.5)	14.0	(11.5,16.8)	10.3	(8.1,12.8)
	2005-2009	40.6	(37.1,44.0)	28.7	(25.4,32.1)	18.1	(15.4,21.0)	12.4	(10.2,14.9)
	2010-2014	50.7	(46.3,54.9)	39.6	(34.6,44.6)	24.7	(21.6,27.9)	20.6	(17.1,24.3)
Ireland	1995-1999	32.5	(28.5,36.7)	32.6	(28.8,36.5)	14.4	(11.3,17.7)	15.4	(12.4,18.8)
	2000-2004	40.2	(36.4,44.0)	37.9	(34.2,41.6)	17.5	(14.5,20.6)	18.7	(15.6,22.0)
	2005-2009	46.7	(43.3,50.1)	42.0	(38.1,45.9)	22.9	(19.9,25.9)	21.4	(18.2,24.8)
	2010-2014	54.4	(49.6,59.0)	48.2	(43.0,53.2)	28.4	(24.6,32.5)	26.1	(22.0,30.5)
New Zealand	1995-1999	33.3	(28.2,38.5)	30.3	(25.3,35.3)	16.2	(12.4,20.6)	17.5	(13.5,22.0)
	2000-2004	33.1	(28.9,37.3)	43.8	(38.2,49.2)	14.8	(11.8,18.2)	19.0	(14.7,23.6)
	2005-2009	40.8	(36.8,44.8)	42.4	(37.3,47.4)	16.9	(13.9,20.1)	23.6	(19.2,28.4)
	2010-2014	48.2	(43.4,52.8)	44.8	(39.3,50.2)	23.8	(19.7,28.1)	22.5	(18.0,27.4)
Norway	1995-1999	35.1	(28.8,41.5)	24.9	(20.7,29.2)	14.9	(10.4,20.2)	9.5	(6.8,12.7)
	2000-2004	38.2	(32.9,43.5)	30.2	(25.4,35.0)	13.3	(9.8,17.3)	10.5	(6.9,14.8)
	2005-2009	46.6	(42.0,51.1)	33.9	(29.0,38.9)	19.2	(15.5,23.3)	14.6	(10.9,18.8)
	2010-2014	53.2	(48.7,57.5)	40.0	(33.5,46.5)	26.6	(22.6,30.8)	22.8	(17.6,28.4)
UK	1995-1999	34.9	(34.1,35.7)	31.0	(30.0,31.9)	12.9	(12.2,13.5)	12.4	(11.7,13.1)
	2000-2004	41.1	(40.4,41.9)	36.1	(35.2,37.1)	16.3	(15.7,16.9)	15.2	(14.4,15.9)
	2005-2009	46.0	(45.3,46.7)	39.4	(38.4,40.4)	19.5	(18.9,20.1)	17.6	(16.8,18.4)
	2010-2014	50.6	(49.8,51.4)	43.4	(42.3,44.6)	22.8	(22.1,23.5)	20.1	(19.1,21.1)

Table S2: Age-standardized one- and three-year net survival (%) and corresponding 95% confidence limits from oesophageal cancer by histological subtype, jurisdiction and period of diagnosis

Country/ Jurisdiction		Period of diagnosis	1-year survival (95% CI)				3-year survival (95% CI)			
			AC		SCC		AC		SCC	
Australia	NSW	1995-1999	40.0	(35.7,44.3)	47.7	(44.1,51.2)	20.0	(16.6,23.7)	25.4	(22.0,28.9)
		2000-2004	42.9	(39.2,46.5)	41.3	(37.6,45.0)	21.8	(18.7,25.0)	22.1	(18.9,25.4)
		2005-2009	47.1	(43.9,50.2)	44.3	(40.3,48.2)	24.0	(21.3,26.8)	21.5	(18.3,24.8)
		2010-2014	52.3	(48.2,56.2)	49.4	(45.0,53.6)	27.5	(23.7,31.4)	24.5	(20.9,28.3)
	VIC	1995-1999	44.4	(39.7,48.9)	44.5	(39.7,49.2)	22.5	(18.6,26.6)	21.9	(18.0,25.9)
		2000-2004	46.4	(42.3,50.4)	51.3	(46.7,55.7)	20.0	(16.7,23.5)	28.6	(24.6,32.7)
		2005-2009	52.4	(48.7,56.0)	48.7	(43.5,53.7)	24.1	(20.9,27.4)	24.5	(20.3,29.0)
		2010-2014	54.0	(49.8,58.1)	60.5	(55.8,64.9)	31.4	(27.6,35.3)	40.6	(36.3,45.0)
	WA	1995-1999	43.8	(35.6,51.8)	42.7	(35.6,49.6)	20.2	(14.1,27.0)	21.9	(16.2,28.2)
		2000-2004	46.2	(39.8,52.3)	43.0	(35.7,50.0)	21.6	(16.5,27.2)	17.2	(12.0,23.2)
		2005-2009	55.3	(49.5,60.8)	51.9	(43.3,59.8)	25.1	(20.1,30.4)	23.8	(17.8,30.2)
		2010-2014	58.2	(51.6,64.3)	57.1	(48.9,64.5)	30.2	(24.5,36.1)	34.8	(27.5,42.2)
Canada	AB	1995-1999	46.2	(37.7,54.3)	29.2	(21.9,36.8)	20.4	(14.1,27.5)	11.0	(6.9,16.3)
		2000-2004	37.4	(30.6,44.1)	38.0	(31.3,44.7)	17.0	(12.2,22.4)	19.3	(13.9,25.3)
		2005-2009	42.2	(37.2,47.1)	33.8	(27.6,40.1)	15.2	(11.7,19.1)	12.6	(8.4,17.6)
		2010-2014	41.5	(36.4,46.5)	45.3	(37.1,53.1)	19.8	(15.9,23.9)	25.9	(19.2,33.1)
	BC	1995-1999	38.2	(33.3,43.1)	37.4	(32.1,42.7)	13.4	(10.1,17.2)	16.5	(12.9,20.6)
		2000-2004	39.0	(34.6,43.3)	42.1	(37.2,46.9)	16.3	(13.1,19.8)	18.3	(14.2,22.8)
		2005-2009	45.3	(41.0,49.4)	42.6	(36.5,48.6)	20.9	(17.5,24.5)	22.9	(18.5,27.5)
		2010-2014	47.6	(43.1,52.0)	48.2	(42.8,53.4)	21.0	(17.0,25.3)	24.3	(19.2,29.6)
	MB	1995-1999	35.3	(23.1,47.8)	43.8	(33.7,53.4)	11.3	(4.8,20.9)	12.9	(7.1,20.5)
		2000-2004	35.2	(25.4,45.1)	34.2	(24.2,44.4)	14.6	(8.1,23.1)	8.8	(3.5,17.0)
		2005-2009	41.2	(32.6,49.5)	39.7	(27.5,51.6)	16.0	(10.1,23.2)	11.0	(4.9,19.9)
		2010-2014	44.1	(34.9,52.9)	37.9	(26.2,49.6)	22.0	(13.5,32.0)	10.5	(4.3,20.1)
	NB	1995-1999	27.8	(16.5,40.2)	35.3	(24.7,45.9)	7.7	(2.4,17.3)	17.6	(9.6,27.6)
		2000-2004	38.5	(28.4,48.5)	45.2	(31.7,57.7)	16.1	(9.7,23.9)	15.8	(6.9,27.9)
		2005-2009	41.1	(32.1,49.8)	39.3	(25.7,52.6)	11.8	(6.4,18.9)	23.8	(13.2,36.2)
		2010-2014	51.7	(40.5,61.9)	57.7	(39.1,72.4)	16.1	(9.1,24.8)	31.7	(15.6,49.1)

AC, Adenocarcinoma; SCC, Squamous cell carcinoma; NSW, New South Wales; VIC, Victoria; WA, Western Australia; AB, Alberta; BC, British Columbia; MB, Mantioba; NB, New Brunswick; NS, Nova Scotia; ON, Ontario; PE, Prince Edward Island; SK, Saskatchewan; ENG, England; NIR, Northern Ireland; SCO, Scotland; WAL, Wales.

Table S2 *continued*: Age-standardized one- and three-year net survival (%) and corresponding 95% confidence limits from oesophageal cancer by histological subtype, jurisdiction and period of diagnosis

Country/ Jurisdiction		Period of diagnosis	1-year survival (95% CI)				3-year survival (95% CI)			
			AC		SCC		AC		SCC	
UK	NS	1995-1999	35.3	(24.9,45.9)	38.6	(27.7,49.4)	13.9	(7.2,22.7)	14.6	(7.7,23.7)
		2000-2004	32.7	(24.6,41.1)	35.5	(24.4,46.8)	14.2	(8.7,21.0)	15.4	(8.0,25.1)
		2005-2009	42.9	(35.6,50.0)	42.5	(29.5,55.0)	15.9	(10.4,22.5)	23.0	(13.0,34.7)
		2010-2014	50.3	(42.3,57.8)	23.6	(13.1,35.9)	23.4	(16.6,30.9)	12.9	(5.8,23.0)
	ON	1995-1999	41.6	(38.4,44.7)	42.2	(39.0,45.3)	16.9	(14.5,19.4)	19.9	(17.4,22.6)
		2000-2004	46.1	(43.3,48.9)	42.9	(39.7,46.0)	19.7	(17.4,22.0)	20.2	(17.6,23.0)
		2005-2009	42.5	(40.0,45.0)	44.7	(41.6,47.8)	19.5	(17.5,21.5)	24.1	(21.1,27.2)
		2010-2014	47.7	(44.8,50.6)	42.5	(38.6,46.3)	22.7	(20.1,25.3)	20.7	(17.5,24.1)
	PE	1995-1999	16.6	(3.7,37.7)	35.5	(11.8,60.5)			13.0	(1.2,39.1)
		2000-2004	38.5	(15.7,61.1)	18.1	(2.8,44.3)	25.1	(8.1,46.8)	18.7	(2.8,45.5)
		2005-2009	23.5	(9.3,41.3)	50.3	(19.1,75.2)	18.2	(6.3,35.2)	13.5	(1.6,38.2)
		2010-2014	36.1	(20.8,51.6)	52.2	(16.5,79.1)	23.4	(11.7,37.5)	9.9	(0.2,42.4)
	SK	1995-1999	26.0	(17.2,35.6)	32.7	(23.5,42.2)	13.5	(7.1,22.0)	7.4	(2.7,15.6)
		2000-2004	31.3	(22.0,41.1)	31.3	(20.7,42.5)	11.2	(5.5,19.3)	13.7	(7.2,22.3)
		2005-2009	37.9	(28.3,47.3)	32.4	(21.6,43.6)	14.7	(8.8,22.0)	13.8	(6.5,23.7)
		2010-2014	53.8	(43.8,62.8)	29.4	(15.9,44.1)	17.0	(8.5,28.0)	11.4	(4.0,23.1)
	ENG	1995-1999	34.6	(33.6,35.5)	31.2	(30.1,32.2)	12.5	(11.8,13.2)	12.2	(11.4,13.0)
		2000-2004	41.0	(40.1,41.8)	36.5	(35.4,37.6)	16.3	(15.6,16.9)	15.5	(14.7,16.4)
		2005-2009	45.9	(45.1,46.7)	39.9	(38.8,40.9)	19.7	(19.1,20.4)	18.1	(17.2,19.0)
		2010-2014	50.7	(49.8,51.6)	43.8	(42.5,45.1)	23.0	(22.3,23.8)	20.6	(19.5,21.7)
	NI	1995-1999	42.2	(36.7,47.6)	32.4	(25.8,39.1)	16.3	(12.2,20.9)	13.6	(8.9,19.4)
		2000-2004	36.7	(31.4,42.0)	34.8	(28.1,41.5)	15.5	(11.5,20.0)	17.1	(11.9,23.1)
		2005-2009	51.0	(46.2,55.5)	35.8	(29.2,42.4)	26.1	(21.9,30.5)	18.2	(13.4,23.7)
		2010-2014	54.7	(49.5,59.5)	43.6	(36.1,50.9)	28.2	(23.6,33.0)	22.4	(15.5,30.2)
	SCO	1995-1999	35.9	(33.6,38.3)	29.7	(27.2,32.3)	14.1	(12.3,16.0)	11.7	(10.0,13.6)
		2000-2004	42.5	(40.1,44.8)	34.5	(32.0,37.0)	15.9	(14.1,17.8)	13.0	(11.0,15.2)
		2005-2009	45.7	(43.3,48.0)	39.0	(35.8,42.1)	17.8	(16.0,19.7)	16.3	(13.8,18.9)
		2010-2014	50.1	(47.5,52.6)	40.3	(37.0,43.5)	21.1	(18.8,23.5)	16.7	(14.1,19.5)
	WAL	1995-1999	35.3	(31.4,39.1)	30.3	(26.3,34.4)	13.1	(10.5,15.9)	15.4	(12.4,18.8)
		2000-2004	42.0	(38.8,45.3)	35.9	(32.0,39.9)	18.1	(15.6,20.8)	14.8	(12.0,17.9)
		2005-2009	45.3	(42.1,48.5)	38.0	(33.6,42.3)	17.0	(14.7,19.5)	15.2	(12.1,18.6)
		2010-2014	48.9	(45.1,52.6)	45.7	(40.4,50.9)	20.6	(17.5,23.9)	20.9	(16.3,25.8)

AC, Adenocarcinoma; SCC, Squamous cell carcinoma; NSW, New South Wales; VIC, Victoria; WA, Western Australia; AB, Alberta; BC, British Columbia; MB, Mantioba; NB, New Brunswick; NS, Nova Scotia; ON, Ontario; PE, Prince Edward Island; SK, Saskatchewan; ENG, England; NIR, Northern Ireland; SCO, Scotland; WAL, Wales.

Table S3: Age-standardized one- and three-year net survival and corresponding 95% confidence limits from oesophageal cancer by histological subtype, sex and period of diagnosis

		1-year net survival (95% CI)								3-year net survival (95% CI)							
		Males				Females				Males				Females			
country	period	AC		SCC		AC		SCC		AC		SCC		AC		SCC	
Australia	1995-1999	42.0	(38.7,45.2)	40.7	(37.2,44.2)	45.2	(37.9,52.1)	53.8	(50.0,57.5)	20.9	(18.2,23.7)	18.7	(15.8,21.8)	24.1	(18.2,30.5)	31.0	(27.2,34.8)
	2000-2004	45.1	(42.3,47.8)	41.8	(38.3,45.3)	45.4	(38.9,51.6)	49.8	(45.5,53.9)	21.8	(19.5,24.2)	18.3	(15.6,21.3)	17.9	(12.8,23.7)	30.6	(26.7,34.5)
	2005-2009	50.8	(48.4,53.2)	44.2	(40.5,47.8)	50.2	(44.4,55.8)	53.0	(47.3,58.3)	24.4	(22.3,26.5)	20.5	(17.6,23.6)	25.3	(20.1,30.9)	27.6	(22.9,32.5)
	2010-2014	53.6	(50.7,56.4)	48.0	(43.9,52.0)	54.7	(48.4,60.6)	61.6	(57.0,65.8)	29.5	(26.9,32.1)	22.3	(18.9,25.7)	26.9	(21.3,32.9)	39.0	(34.6,43.4)
Canada	1995-1999	39.8	(37.3,42.2)	37.8	(34.8,40.7)	37.8	(31.6,44.0)	42.9	(39.3,46.4)	15.3	(13.5,17.2)	15.5	(13.3,17.8)	17.3	(12.6,22.7)	21.8	(18.9,24.9)
	2000-2004	42.3	(40.1,44.5)	39.5	(36.6,42.4)	38.8	(33.6,43.9)	44.2	(40.5,47.8)	17.7	(16.0,19.5)	16.5	(14.2,19.0)	18.8	(14.8,23.2)	23.8	(20.6,27.1)
	2005-2009	42.9	(41.0,44.8)	39.5	(36.5,42.4)	41.5	(36.8,46.1)	48.3	(44.4,52.0)	18.9	(17.4,20.5)	18.7	(16.2,21.3)	16.4	(13.1,20.0)	27.8	(24.1,31.6)
	2010-2014	47.3	(45.2,49.4)	41.7	(38.1,45.2)	45.5	(40.5,50.5)	44.8	(40.4,49.2)	21.3	(19.5,23.2)	18.5	(15.6,21.7)	22.4	(18.3,26.9)	24.5	(20.7,28.5)
Denmark	1995-1999	32.9	(28.8,37.1)	24.8	(20.6,29.3)	31.0	(22.1,40.2)	28.9	(21.4,36.8)	10.9	(8.2,14.0)	8.1	(5.5,11.5)	5.5	(1.8,12.1)	8.9	(5.6,13.3)
	2000-2004	36.7	(33.0,40.4)	25.3	(21.0,29.9)	38.4	(29.6,47.1)	29.3	(23.9,35.0)	13.7	(10.9,16.7)	8.5	(5.8,11.8)	17.1	(10.6,24.8)	14.3	(10.5,18.7)
	2005-2009	41.7	(37.8,45.6)	28.1	(23.8,32.5)	33.3	(24.9,41.9)	30.2	(24.8,35.8)	18.7	(15.6,22.0)	11.2	(8.5,14.2)	14.4	(9.0,20.9)	15.3	(11.2,19.8)
	2010-2014	53.4	(48.0,58.5)	36.9	(30.2,43.5)	46.2	(38.2,53.7)	44.4	(37.8,50.8)	28.4	(24.7,32.3)	17.9	(13.8,22.5)	19.6	(13.5,26.6)	25.2	(19.6,31.0)
Ireland	1995-1999	32.6	(28.0,37.3)	29.7	(24.6,35.0)	38.3	(29.2,47.3)	37.1	(31.3,42.8)	14.9	(11.4,18.9)	13.0	(9.1,17.5)	13.4	(5.2,25.3)	19.4	(14.7,24.7)
	2000-2004	41.9	(37.6,46.2)	34.2	(28.9,39.5)	33.0	(24.6,41.6)	41.9	(36.5,47.2)	18.3	(14.9,21.9)	14.9	(10.9,19.6)	13.6	(7.9,21.0)	22.4	(17.8,27.4)
	2005-2009	47.7	(43.7,51.5)	36.8	(31.4,42.2)	45.0	(36.7,53.0)	48.5	(42.7,54.0)	23.5	(20.1,26.9)	17.4	(13.4,21.9)	23.5	(16.7,31.0)	26.5	(21.6,31.7)
	2010-2014	54.7	(49.3,59.9)	44.6	(37.2,51.7)	49.9	(36.0,62.3)	53.5	(46.1,60.3)	27.6	(23.2,32.1)	22.7	(17.1,28.7)	30.8	(20.4,41.9)	31.2	(25.0,37.6)
New Zealand	1995-1999	32.3	(26.6,38.0)	23.0	(16.6,29.9)	36.4	(21.9,51.0)	40.4	(32.2,48.5)	15.1	(11.0,19.8)	12.2	(7.7,17.6)	23.1	(10.9,37.9)	25.6	(18.1,33.7)
	2000-2004	33.6	(29.1,38.2)	39.0	(31.9,46.1)	27.5	(16.9,39.2)	47.8	(40.4,54.9)	15.5	(12.1,19.2)	13.8	(9.1,19.4)	10.0	(4.4,18.4)	23.6	(17.4,30.5)
	2005-2009	39.5	(35.0,43.9)	35.4	(28.2,42.7)	43.3	(32.1,53.9)	48.6	(41.4,55.5)	16.5	(13.3,20.0)	16.8	(11.5,23.1)	14.7	(7.9,23.5)	30.4	(23.6,37.4)

	2010-2014	47.5	(42.4,52.4)	40.0	(32.2,47.7)	52.8	(38.8,65.1)	50.4	(42.3,58.0)	22.8	(18.5,27.5)	20.2	(14.0,27.2)	30.2	(19.4,41.8)	26.8	(20.1,33.9)
Norway	1995-1999	35.0	(28.2,41.8)	21.8	(17.3,26.8)	32.9	(17.5,49.1)	30.3	(21.9,39.1)	14.6	(9.8,20.4)	8.9	(6.0,12.6)	18.3	(7.6,32.6)	9.6	(4.9,16.2)
	2000-2004	37.8	(32.0,43.7)	30.2	(24.6,35.9)	39.2	(25.1,53.0)	29.2	(20.3,38.6)	14.1	(10.1,18.9)	10.7	(6.4,16.3)	10.3	(4.4,19.1)	10.2	(5.3,16.9)
	2005-2009	47.3	(42.2,52.2)	31.6	(25.5,37.9)	39.5	(27.6,51.2)	40.0	(31.4,48.4)	18.5	(14.5,22.9)	13.0	(8.5,18.5)	20.3	(11.5,30.8)	19.4	(12.9,26.8)
	2010-2014	52.2	(47.2,56.9)	38.0	(30.4,45.6)	59.2	(47.5,69.1)	44.9	(32.3,56.7)	26.1	(21.6,30.8)	21.2	(15.1,28.0)	31.8	(22.3,41.7)	26.1	(16.5,36.6)
UK	1995-1999	35.0	(34.1,36.0)	27.2	(25.9,28.6)	35.6	(33.7,37.6)	35.5	(34.1,36.8)	12.9	(12.2,13.6)	10.2	(9.3,11.2)	13.9	(12.5,15.5)	15.0	(13.9,16.1)
	2000-2004	41.9	(41.0,42.8)	31.2	(29.9,32.6)	38.9	(37.0,40.7)	41.3	(40.0,42.7)	16.4	(15.8,17.1)	11.3	(10.4,12.3)	16.1	(14.7,17.6)	19.4	(18.2,20.7)
	2005-2009	46.4	(45.5,47.2)	35.7	(34.3,37.1)	45.5	(43.8,47.2)	43.6	(42.3,45.0)	19.6	(18.9,20.3)	13.9	(12.8,15.0)	20.1	(18.6,21.6)	21.8	(20.6,23.0)
	2010-2014	51.1	(50.2,52.0)	39.0	(37.4,40.6)	49.8	(47.9,51.6)	48.1	(46.3,49.8)	22.8	(22.0,23.6)	16.4	(15.2,17.7)	23.6	(22.0,25.2)	24.2	(22.6,25.7)

Table S4: Age-standardized one-year net survival and corresponding 95% confidence limits from oesophageal cancer by histological subtype, age group and period of diagnosis

		15-64 years				65-74 years				75-99 years			
Country	**Period of diagnosis**	**AC**		**SCC**		**AC**		**SCC**		**AC**		**SCC**	
Australia	1995-1999	47.3	(42.0,52.4)	55.1	(50.2,59.7)	42.7	(37.9,47.5)	47.8	(43.5,51.9)	34.0	(29.4,38.7)	31.1	(27.5,34.9)
	2000-2004	51.1	(46.9,55.2)	49.5	(44.5,54.2)	45.5	(40.8,50.0)	47.5	(42.8,52.0)	34.8	(30.7,38.8)	36.2	(32.5,39.9)
	2005-2009	58.0	(54.3,61.6)	50.3	(44.7,55.6)	53.5	(49.3,57.6)	49.2	(44.4,53.8)	35.7	(32.2,39.2)	39.9	(36.1,43.6)
	2010-2014	57.2	(52.7,61.4)	58.1	(52.3,63.5)	58.1	(53.8,62.2)	55.6	(50.2,60.7)	44.1	(39.7,48.4)	43.0	(38.5,47.3)
Canada	1995-1999	44.2	(40.5,47.9)	44.1	(40.2,48.0)	40.1	(36.1,44.0)	42.8	(39.2,46.4)	31.5	(27.5,35.7)	29.1	(25.6,32.7)
	2000-2004	47.6	(44.4,50.7)	49.5	(45.4,53.5)	43.9	(40.2,47.5)	39.0	(35.3,42.6)	31.5	(28.0,35.0)	31.2	(27.7,34.8)
	2005-2009	46.9	(44.1,49.7)	48.2	(43.9,52.4)	43.9	(40.6,47.2)	44.9	(40.9,48.8)	35.0	(31.9,38.1)	31.4	(27.9,34.9)
	2010-2014	53.4	(50.2,56.5)	50.8	(45.9,55.6)	46.2	(42.8,49.6)	45.8	(41.0,50.5)	38.1	(34.5,41.6)	28.6	(24.5,32.7)
Denmark	1995-1999	38.2	(31.4,45.0)	28.6	(22.6,34.8)	31.8	(25.9,38.0)	28.5	(22.5,34.7)	26.3	(20.5,32.5)	20.2	(14.4,26.7)
	2000-2004	45.1	(39.0,51.0)	31.0	(25.2,37.0)	34.4	(28.5,40.3)	27.0	(21.5,32.7)	27.2	(22.1,32.6)	17.7	(12.5,23.6)
	2005-2009	51.1	(44.7,57.1)	36.8	(31.1,42.4)	40.5	(34.3,46.6)	30.7	(25.3,36.2)	25.4	(20.5,30.6)	15.2	(10.3,21.0)
	2010-2014	57.6	(48.5,65.8)	45.0	(34.9,54.6)	54.2	(48.7,59.4)	41.4	(35.6,47.1)	36.9	(31.1,42.7)	30.1	(22.8,37.7)
Ireland	1995-1999	38.7	(31.6,45.7)	45.4	(38.3,52.2)	29.9	(23.5,36.6)	29.8	(23.2,36.5)	26.4	(19.6,33.6)	16.9	(12.2,22.3)
	2000-2004	51.0	(44.2,57.4)	51.0	(44.3,57.3)	36.3	(29.9,42.6)	35.1	(28.5,41.8)	28.5	(22.6,34.7)	21.7	(16.6,27.4)
	2005-2009	55.9	(50.2,61.2)	53.4	(46.3,60.1)	47.3	(40.9,53.5)	38.6	(31.9,45.1)	32.8	(27.2,38.5)	29.0	(23.3,34.8)
	2010-2014	69.0	(60.8,75.8)	58.3	(48.6,66.8)	48.9	(40.9,56.5)	50.5	(41.7,58.7)	39.9	(31.5,48.2)	32.1	(24.6,39.9)

New Zealand	1995-1999	34.6	(25.4,43.9)	41.6	(31.6,51.3)	30.9	(22.7,39.4)	27.3	(19.9,35.2)	33.8	(25.8,42.0)	16.9	(11.1,23.7)
	2000-2004	39.1	(31.3,46.8)	55.3	(43.3,65.8)	33.4	(26.3,40.5)	47.1	(38.1,55.5)	24.1	(18.4,30.4)	23.7	(17.7,30.3)
	2005-2009	49.7	(42.4,56.6)	56.5	(46.3,65.5)	37.0	(30.1,43.8)	37.2	(27.9,46.5)	31.8	(26.0,37.7)	27.2	(21.2,33.6)
	2010-2014	51.7	(42.9,59.9)	58.8	(48.2,67.9)	52.1	(44.2,59.3)	37.3	(27.9,46.7)	38.7	(31.6,45.7)	31.9	(24.0,40.1)
Norway	1995-1999	39.8	(27.8,51.6)	32.3	(24.6,40.1)	38.3	(28.3,48.2)	19.4	(13.7,25.7)	25.2	(17.3,33.8)	19.6	(13.0,27.3)
	2000-2004	47.5	(37.3,57.0)	40.1	(31.1,48.9)	35.2	(26.0,44.6)	25.8	(18.6,33.6)	27.8	(20.8,35.2)	20.1	(13.5,27.7)
	2005-2009	55.0	(47.2,62.1)	43.7	(35.2,51.9)	45.8	(36.8,54.4)	35.4	(26.7,44.3)	35.3	(28.1,42.5)	18.2	(11.4,26.2)
	2010-2014	59.5	(52.0,66.1)	50.3	(37.0,62.1)	57.4	(49.1,64.7)	40.6	(31.6,49.4)	39.3	(31.5,47.0)	23.4	(15.2,32.6)
UK	1995-1999	43.0	(41.4,44.5)	38.9	(37.0,40.7)	34.6	(33.3,36.0)	31.0	(29.4,32.5)	23.5	(22.3,24.7)	19.5	(18.3,20.7)
	2000-2004	49.5	(48.1,50.9)	44.7	(42.9,46.5)	41.9	(40.6,43.2)	36.8	(35.2,38.4)	28.2	(27.1,29.3)	23.0	(21.8,24.2)
	2005-2009	53.6	(52.3,54.9)	48.2	(46.4,50.1)	48.4	(47.2,49.7)	40.3	(38.7,41.9)	32.6	(31.6,33.6)	25.8	(24.5,27.0)
	2010-2014	57.3	(55.8,58.8)	50.7	(48.4,52.9)	54.7	(53.4,56.0)	46.8	(44.9,48.7)	36.9	(35.7,38.1)	29.6	(28.1,31.1)

Table S5: Age-standardized three-year net survival and corresponding 95% confidence limits from oesophageal cancer by histological subtype, age group and period of diagnosis

		15-64 years				**65-74 years**				**75-99 years**			
Country	**Period of diagnosis**	**AC**		**SCC**		**AC**		**SCC**		**AC**		**SCC**	
Australia	1995-1999	27.9	(23.3,32.6)	29.4	(24.9,33.9)	20.0	(16.2,24.2)	24.6	(20.9,28.4)	11.8	(8.6,15.5)	14.8	(11.9,18.0)
	2000-2004	27.3	(23.6,31.2)	27.7	(23.4,32.0)	20.5	(16.8,24.5)	26.0	(22.0,30.2)	12.7	(9.8,15.9)	15.6	(12.8,18.8)
	2005-2009	29.0	(25.7,32.4)	27.4	(22.8,32.2)	27.9	(24.2,31.7)	22.6	(18.7,26.7)	13.4	(10.8,16.2)	16.4	(13.4,19.6)
	2010-2014	32.1	(28.2,36.1)	34.6	(29.2,40.1)	33.2	(29.1,37.3)	28.1	(23.5,32.8)	20.8	(17.2,24.7)	19.5	(15.9,23.3)
Canada	1995-1999	20.1	(17.2,23.2)	21.2	(18.1,24.4)	15.4	(12.5,18.5)	19.6	(16.7,22.7)	9.1	(6.6,12.1)	10.7	(8.2,13.5)
	2000-2004	21.4	(18.8,24.0)	24.1	(20.5,27.9)	19.1	(16.2,22.2)	18.4	(15.5,21.5)	11.0	(8.6,13.8)	11.5	(9.0,14.4)
	2005-2009	22.0	(19.7,24.3)	25.8	(21.9,29.9)	18.1	(15.6,20.8)	23.6	(20.2,27.1)	13.4	(11.1,15.9)	12.8	(10.3,15.6)
	2010-2014	24.8	(22.1,27.7)	26.0	(21.6,30.5)	21.3	(18.5,24.3)	21.6	(17.8,25.6)	16.7	(13.8,19.7)	12.7	(9.7,16.1)
Denmark	1995-1999	12.6	(8.2,17.9)	7.9	(4.9,11.8)	10.7	(7.0,15.4)	10.3	(6.5,15.0)	6.1	(3.1,10.5)	7.0	(3.3,12.8)
	2000-2004	17.1	(12.6,22.1)	14.0	(10.2,18.4)	14.7	(10.5,19.6)	10.2	(6.6,14.5)	9.0	(5.7,13.2)	5.3	(2.5,9.7)
	2005-2009	25.1	(19.9,30.6)	17.9	(14.0,22.1)	19.3	(14.5,24.6)	13.2	(9.4,17.6)	6.8	(4.1,10.4)	3.7	(1.5,7.6)
	2010-2014	30.0	(24.0,36.1)	26.9	(20.3,34.0)	29.6	(24.8,34.5)	20.2	(15.5,25.4)	11.9	(8.1,16.5)	10.2	(5.5,16.7)
Ireland	1995-1999	21.2	(15.5,27.6)	23.4	(17.6,29.7)	9.1	(5.4,13.9)	12.3	(7.9,17.7)	9.7	(5.1,16.0)	7.1	(3.5,12.2)
	2000-2004	24.6	(19.0,30.5)	28.2	(22.2,34.5)	15.8	(11.2,21.1)	13.6	(9.2,19.0)	8.8	(5.3,13.5)	10.0	(6.2,14.8)
	2005-2009	27.6	(22.7,32.7)	29.5	(23.5,35.7)	23.0	(17.8,28.7)	19.8	(14.6,25.6)	15.9	(11.4,21.0)	11.2	(7.3,16.1)
	2010-2014	38.7	(31.6,45.8)	32.9	(25.0,41.1)	28.4	(22.1,35.0)	28.8	(21.9,36.1)	13.1	(8.1,19.3)	14.3	(9.3,20.4)
	1995-1999	20.5	(13.4,28.6)	26.4	(18.1,35.5)	15.4	(9.3,22.8)	11.5	(6.6,17.9)	10.9	(5.7,18.0)	10.7	(5.8,17.2)

New Zealand	2000-2004	20.5	(14.6,27.2)	27.1	(17.8,37.2)	15.7	(10.6,21.9)	21.1	(14.3,28.8)	5.6	(2.8,9.8)	5.1	(2.3,9.4)
	2005-2009	23.3	(17.6,29.5)	38.3	(28.6,47.9)	14.7	(10.1,20.3)	18.3	(11.4,26.5)	9.8	(6.3,14.3)	7.8	(4.4,12.5)
	2010-2014	28.5	(20.9,36.6)	31.2	(22.6,40.2)	27.0	(20.4,34.0)	21.6	(14.2,29.9)	12.8	(8.2,18.5)	11.1	(6.1,17.6)
Norway	1995-1999	16.4	(8.4,26.6)	12.8	(7.9,19.0)	18.7	(11.3,27.7)	7.8	(4.2,12.6)	9.0	(4.1,16.3)	6.4	(2.7,12.1)
	2000-2004	17.6	(11.2,25.1)	13.9	(7.4,22.5)	12.8	(7.0,20.5)	11.4	(6.5,17.8)	7.7	(3.9,13.1)	4.6	(1.7,9.8)
	2005-2009	31.1	(23.6,38.9)	19.8	(13.1,27.5)	15.1	(9.3,22.1)	17.4	(10.9,25.1)	6.1	(3.0,10.9)	4.2	(1.3,9.9)
	2010-2014	35.1	(28.2,42.2)	31.8	(21.4,42.6)	25.5	(18.5,33.0)	20.7	(13.7,28.7)	14.2	(8.8,20.9)	9.2	(4.0,17.1)
UK	1995-1999	17.2	(16.0,18.4)	17.3	(15.9,18.8)	13.4	(12.4,14.4)	12.1	(11.1,13.3)	6.0	(5.3,6.7)	5.4	(4.7,6.2)
	2000-2004	22.0	(20.9,23.2)	21.0	(19.4,22.5)	16.9	(15.8,17.9)	15.6	(14.4,16.9)	7.5	(6.8,8.2)	6.3	(5.6,7.1)
	2005-2009	25.1	(24.0,26.2)	23.4	(21.8,25.1)	21.0	(20.0,22.1)	18.3	(17.0,19.6)	9.9	(9.2,10.7)	8.4	(7.5,9.3)
	2010-2014	27.0	(25.7,28.3)	25.9	(23.9,28.0)	27.0	(25.8,28.1)	21.3	(19.7,22.8)	12.8	(11.9,13.7)	10.3	(9.3,11.4)

Figure S2: Age-standardized 1- year net survival estimates and corresponding 95% confidence limits of oesophageal adenocarcinoma (AC) and the combination of oesophageal AC and gastric cardia (C16.0) cancer by country for patients diagnosed 2010-2014

Abbreviations: AUS=Australia, CAN=Canada, DEN=Denmark, IRE=Ireland, NZ=New Zealand, NOR=Norway, UK=United Kingdom