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Xie, Shao-Hua; Lagergren, Jesper

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Time trends in the incidence of oesophageal cancer in Asia: variations across populations and histological types

Authors: Shao-Hua Xie [a,*] and Jesper Lagergren [a, b]

Affiliations: [a] Upper Gastrointestinal Surgery, Department of Molecular Medicine and Surgery, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden; [b] Section of Gastrointestinal Cancer, Division of Cancer Studies, King's College London, United Kingdom

[*]**Corresponding authour:** Upper Gastrointestinal Surgery, Department of Molecular Medicine and Surgery, Karolinska Institutet, NS 67, 2nd Floor, 17176 Stockholm, Sweden. Tel: +46 8 517 70917; Fax: +46 8 517 76280.

E-mail address: shaohua.xie@ki.se (S.-H. Xie).

Abstract

Objective: We aimed to assess temporal trends in incidence rates of oesophageal cancer in Asian countries.

Materials and Methods: Using data from the Cancer Incidence in Five Continents series, we examined the temporal trends in incidence rates of oesophageal cancer by population and histological type in seven Asian countries in 1988 to 2007. Age-period-cohort analyses estimated the overall annual percentage changes (net drifts) and their 95% confidence intervals (CIs) in incidence rates.

Results: The age-standardised incidence rate of oesophageal cancer declined in most Asian populations, but remained relatively unchanged in Japan and Israel. The rate of oesophageal squamous cell carcinoma decreased in Hong Kong, Singapore and Israel, but was stable in Japan. The net drifts were statistically significant in men in Hong Kong (-3.4%, 95% CI: -6.1%, -0.7%) and in women in Singapore (-10.1%, 95% CI: -14.4%, -5.5%). The age-standardised incidence rates of oesophageal adenocarcinoma were below 2 and 0.5 per 100 000 in men and women, respectively, across all periods in the all registers containing valid data on histological type. The age-standardised incidence rate of oesophageal adenocarcinoma slightly increased in Japan, Singapore, and Israel, although the net drift was statistically significant only in Israeli men (4.9%, 95% CI: 0.8%, 9.1%).

Conclusion: The overall incidence rates of oesophageal cancer declined in most Asian countries, which is due to a decrease in oesophageal squamous cell carcinoma incidence. However, attention needs to be paid to a probable beginning of an increasing incidence of oesophageal adenocarcinoma in Asia.

Key words: Oesophageal cancer; Incidence; Epidemiology; Adenocarcinoma; Asia

Abbreviations: ASR, age-standardized incidence rates; BMI, body mass index; CI, confidence interval; OAC: oesophageal adenocarcinoma; OSCC: oesophageal squamous cell carcinoma; *H. pylori*, *Helicobacter pylori*.

1. Background

Oesophageal cancer is the eighth most common type of malignancy and the sixth leading cause of cancer deaths globally [1, 2]. It was estimated that there were 456 000 new cases of oesophageal cancer worldwide in 2012, among which 340 000 (75%) occurred in Asia. Men in Eastern Asia have the highest incidence rate of oesophageal cancer globally (17 per 100 000) [2].

The risk factors for the two main histological types of oesophageal cancer, squamous cell carcinoma and adenocarcinoma, differ greatly. Oesophageal squamous cell carcinoma is mainly associated with tobacco smoking, heavy alcohol use, and certain dietary factors, while the main risk factors for oesophageal adenocarcinoma include gastro-oesophageal reflux disease , obesity, and *Helicobacter pylori* (*H. pylori*) infection (inverse association) [3-6]. Oesophageal squamous cell carcinoma is the predominant type in Asia, Africa and South America, and accounts for approximately 90% of all oesophageal cancer cases worldwide [2, 3]. In contrast, oesophageal adenocarcinoma has become the predominant type in most North American and European countries. The past four decades have witnessed a rapidly increased incidence of oesophageal adenocarcinoma in Western populations, particularly in white males [3-5].

Asian societies have experienced substantial socio-economic development with changes in the exposures in relation to cancer risk during the past several decades [7, 8]. A decreasing prevalence of tobacco smoking may have, for example, contributed to a declining risk of oesophageal squamous cell carcinoma, while an increased prevalence of obesity or reflux may have led to a rise in the incidence of oesophageal adenocarcinoma. To provide an update on potential differences in incidence of oesophageal cancer between Asian countries and changes in incidence over time, we analysed the incidence of oesophageal cancer in selected Asian countries by histological type using data from the *Cancer Incidence in Five Continents* series.

2. Methods

2.1. Data sources

We extracted data on the incidence of oesophageal cancer and population sizes from the *Cancer Incidence in Five Continents* (CI5) series volumes VII to X. These are published by the International Agency for Research on Cancer (IARC) and contain information on cancer incidence worldwide where good quality data are available [9-12]. We followed the geographical definition of the United Nations, which was also in line with the practice in CI5 series [13]. We included registers in seven Asian countries with available data in all four CI5 volumes during the period 1988-2007: China (Shanghai and Hong Kong), Japan (Miyagi, Nagasaki, and Osaka), India (Chennai and Mumbai), Thailand (Chiang Mai), Singapore, Philippines (Manila), and Israel. We pooled the numbers of cases and population sizes at risk from multiple regional registers within the country for Japan and India. Evaluation of incidence by histological type was restricted to registers with a microscopically verified percentage of cases of over 80% in each of the four CI5 volumes (Supplementary Figure 1).

2.2. Statistical analyses

We first calculated the sex-specific crude and age-standardised incidence rates (ASRs) by population and histological type for each CI5 volume in five-year calendar periods. The ASRs were calculated using the direct method with the World Health Organisation (WHO) World Standard Population 2000 as the reference [14]. The 95% confidence intervals (CIs) of crude rates were computed under the assumption of Poisson distribution, while CIs for ASRs were estimated based on the gamma distribution, as it assumes that the standardised rate is a weighted sum of independent Poisson random variables [15, 16]. All these statistical analyses were performed using the statistical software SAS version 9.4 (SAS Institute, Cary, NC).

We further performed age-period-cohort regressions on the incidence of oesophageal cancer by population and histological type for each sex using a web tool, newly developed by the National Cancer Institute (NCI), United States [17]. This web tool fits the age-period-cohort model which attempts to differentiate the effects of age, calendar period, and birth cohort on disease rates, and estimates the overall annual percentage changes (net drifts) in ASRs in addition [17, 18]. The central age group, calendar period, and birth cohort were defined as the reference in all age-period-cohort analyses.

3. Results

3.1. Oesophageal cancer of all histological types

In total, 53 206 men and 18 382 women were diagnosed with oesophageal cancer as recorded in all included registers during the period 1988-2007. The ASRs in men were generally highest in Eastern Asia, followed by India and Singapore, and were relatively low in Thailand, Philippines, and Israel (Table 1). The ASRs in women were highest in India, followed by China, and were lower (<3 per 100 000 person-years) in the other populations (Table 1).

The ASRs of oesophageal cancer declined in both sexes in most Asian populations during the study period, but remained relatively stable in Japan and Israel (Figures 1). The decreases in net drifts were statistically significant in men in Shanghai (-3.4%, 95% CI: -5.3%, -1.4%), Hong Kong (-6.2%, 95% CI: -7.8%, -4.6%), and India (-1.9%, 95% CI: -3.7%, -0.1%). The net drifts in women showed decreasing incidence rates with statistical significance in all populations, except for Japan (2.9%, 95% CI: -1.5%, 7.6%) and Israel (-0.4%, 95% CI: -4.1%, 3.5%) (Figure 2 and Supplementary Table 1).

3.2. Oesophageal squamous cell carcinoma

The incidence rates of oesophageal squamous cell carcinoma were the highest in Hong Kong and Japan, followed by Singapore, and were the lowest in Israel (Figure 3 and Supplementary Table 2).

The ASRs of oesophageal squamous cell carcinoma declined in Hong Kong, Singapore and Israel, but remained stable in Japan in both sexes (Figure 3). The net drifts were statistically significant in men in Hong Kong (-3.4%, 95% CI: -6.1%, -0.7%) and in women in Singapore (-10.1%, 95% CI: -14.4%, -5.5%) (Figure 3 and Supplementary Table 1).

3.3. Oesophageal adenocarcinoma

No evident difference in the incidence rates of oesophageal adenocarcinoma between the studied Asian populations was seen except for relatively higher rates in Israel since 1993. The ASRs of oesophageal adenocarcinoma were below 2 and 0.5 per 100 000 in men and women, respectively, across calendar periods in all studied Asian populations (Figure 3 and Supplementary Table 3).

The incidence rates increased in Japan, Singapore, and Israel, although only the net drift in Israeli men was statistically significant (4.9%, 95% CI: 0.8%, 9.1%). The percentages of oesophageal adenocarcinoma in all cases of oesophageal cancer increased from 3.6% to 11.0% and from 13.1% to 37.0% in Singapore and Israel, respectively, from the period 1988-1992 to the period 2003-2007 (Supplementary Figure 1). On the contrary, the ASRs of oesophageal adenocarcinoma significantly declined in both sexes in Hong Kong during the study period (net drifts -8.8% and -8.5% in men and in women, respectively).

3.4. Unspecified and other histological types

The rate of unspecified histology slightly declined with later calendar periods, while the rate of other histological types remained stable over time. However, the rate of unspecified histology was low and did not substantially influence the findings for squamous cell carcinoma or adenocarcinoma (Supplementary Figure 1).

4. Discussion

The present study provided an update on the changing incidence of oesophageal cancer over a 20-year period in Asia, and revealed variations across populations and histological types. The incidence of oesophageal cancer declined in most Asian countries included in this analysis, but remained stable in Japan and Israel. This decline was predominantly in oesophageal squamous cell carcinoma. There was a seeming trend towards a rise in the incidence of oesophageal adenocarcinoma in Singapore and Israel.

The observed decline in the incidence of oesophageal cancer predominantly in oesophageal squamous cell carcinoma is likely to be associated with the decreasing prevalence of tobacco smoking over the past few decades in these Asian populations [19-21]. However, the stable incidence of oesophageal cancer in Japan did not parallel the decreasing prevalence of smoking in this population. It is possible that the influence of a decreasing prevalence of smoking has been neutralised by the considerable rise in alcohol consumption in the Japanese population [21, 22]. The annual alcohol consumption per capita in people aged 15 and above in Japan increased from less than 5 litres in the 1960s to 8 litres in 2003-2005 [22]. Moreover, consumption of spirits, which is more strongly associated with the risk of oesophageal squamous cell carcinoma than other alcoholic beverages, alone accounted for over half of the total alcohol consumption in Japan [23]. Therefore, efforts to reduce the alcohol use could decrease the burden of oesophageal cancer in the Japanese population.

The incidence of oesophageal adenocarcinoma has increased rapidly in many Western populations, including North America and Europe, during the past four decades [4, 5], whereas data from Asian countries are limited. Earlier studies have shown a statistically non-significant rise in the incidence of oesophageal adenocarcinoma in Singapore [24], declined incidence of oesophageal adenocarcinoma and ratio of adenocarcinoma versus squamous cell carcinoma in Hong Kong [25], and a stable incidence in Japan and Taiwan during the past few decades [26, 27]. A recent systematic review of Barrett's oesophagus, regarded as a pre-malignant condition for adenocarcinoma of the oesophagus, suggested an increasing prevalence of this condition in Eastern Asian countries between 1991 and 2014 [28]. The present study with updated data till the year 2007 indicates a rise in the incidence of oesophageal adenocarcinoma and considerably increased ratio of adenocarcinoma versus squamous cell carcinoma in Singapore and Israel. This may be explained by the associated rise in the prevalence of reflux and obesity, and the decreased prevalence of *H. pylori* infection in these populations [29-32]. On the other hand, the observed increase may, at least partially, be explained by the improvements in histological typing and diagnostic procedures over time as shown in other populations [5, 33]. Such speculation is also supported by some statistically significant period effects in males from age-period-cohort regressions (Supplementary Figure 2). However, these statistical findings need to be interpreted with caution given the known co-linearity between effects from calendar periods and birth cohorts [17, 18]. Possible misclassification between adenocarcinomas of the oesophagus and gastric cardia might have affected the reported incidence rates, but does not seem to influence an overall interpretation of the time trends for either of these cancer sites [34]. The decreasing trend in the incidence of oesophageal adenocarcinoma in Hong Kong differs from observations in Western and other Asian populations, and is also unexpected in a population with an increasing prevalence of gastro-oesophageal reflux disease and obesity [29, 35], and a decreasing prevalence of *H. pylori* infection [36]. The only most plausible explanation would be the decreasing prevalence of tobacco smoking since the 1980s in Hong Kong [20], although there is only a moderately strong association between tobacco smoking and the risk of oesophageal adenocarcinoma [37]. We were not able to assess the incidence trends of oesophageal adenocarcinoma in Shanghai due to lack of complete data on histology. An earlier study from a high-risk region of China has shown virtually no cases of oesophageal adenocarcinoma in this area [38]. Previous reports from a high-risk area of Iran also suggested that oesophageal adenocarcinoma remained uncommon in this area [39, 40]. Nevertheless, considering the fact that the two major risk factors for oesophageal adenocarcinoma, obesity and reflux, are becoming more common in Asian populations, together with the lessons from Western countries, a rise in the incidence of oesophageal adenocarcinoma is expected in the coming decades in Asia. However, the link between the changing prevalence of reflux, obesity and *H. pylori* infection and the increasing incidence of oesophageal adenocarcinoma has been mainly generated in Western populations. The aetiology of oesophageal adenocarcinoma in Asian countries, which may differ from that in Western societies, remains to be better understood in the future.

The present study has some strengths and limitations. The data from the cancer registers used were of good quality in terms of completeness of coverage and accuracy, which lend validity to the findings. In addition, the time trends in the incidence of oesophageal cancer were further assessed by histological type in several populations. We also performed age-period-cohort analyses to estimate the overall annual percentage changes (net drifts) in ASRs, which represent the temporal trend with adjustment for age and non-linear birth cohort effects. Therefore, the net drifts may be considered superior to the annual percentage changes in cross-sectional ASRs when interpreting the time trends of disease rates, although the net drifts are virtually analogous to the latter [17, 18]. A limitation of this study is that the analyses were restricted only to selected cancer registers containing data for the 20-year study period. Furthermore, we could perform analyses by histological type in only some countries or regions (Hong Kong, Japan, Singapore and Israel) due to lack of complete information on histological typing elsewhere. Thus, the results may not be representative for all Asian countries, or even for all involved countries, e.g. data from Shanghai not representing the whole China. Racial-ethnic disparities, e.g. Jews versus non-Jews in Israel or Chinese versus non-Chinese in Singapore, were not within the scope of this study, but need to be addressed in future studies. Finally, any trends in women are difficult to interpret given the low incidence rates, resulting in limited statistical precision. Possible explanations for a lower risk of oesophageal squamous cell carcinoma in women may be lower prevalence of smoker and heavy alcohol use in women, while the reasons for a more striking male predominance of oesophageal adenocarcinoma remain incompletely understood [4, 41].

In conclusion, the incidence of oesophageal cancer has decreased in some, but not all Asian populations from 1988 to 2007. The decrease is attributable to a decline in the incidence of oesophageal squamous cell carcinoma, which in turn is likely to be due to the decreasing prevalence in tobacco smoking. Oesophageal adenocarcinoma remains uncommon in Asian countries. However, there appears to be a trend towards a rise in the incidence of oesophageal adenocarcinoma in some Asian populations. This increase might be associated with the increasing prevalence of reflux and obesity and the decreasing prevalence of *H. pylori* infection, in these populations. More attention needs to be paid to a possible increase in the incidence of oesophageal adenocarcinoma in Asia in the future.

Competing interests statement

None declared.

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Table 1

Crude and age-standardised incidence rates (ASRs) with 95% confidence intervals (CIs) of oesophageal cancer per 100 000 person-years in selected Asian countries and calendar periods during 1988-2007

Calendar periods	Males			Females		
	N	Crude rate (95% CI)	ASR (95% CI) *	N	Crude rate (95% CI)	ASR (95% CI) *
China (Shanghai)						
1988-1992	2855	15.71 (15.14, 16.30)	14.29 (13.75, 14.86)	1338	7.70 (7.29, 8.12)	5.53 (5.23, 5.84)
1993-1997	2355	14.34 (13.77, 14.94)	11.20 (10.74, 11.68)	1189	7.51 (7.09, 7.95)	4.63 (4.37, 4.91)
1998-2002	2291	14.40 (13.81, 15.00)	10.96 (10.50, 11.44)	965	6.22 (5.84, 6.63)	3.63 (3.40, 3.88)
2003-2007	2017	12.96 (12.40, 13.54)	7.79 (7.45, 8.15)	791	5.16 (4.81, 5.53)	2.42 (2.25, 2.60)
China (Hong Kong SAR)						
1988-1992	2179	14.91 (14.29, 15.55)	15.72 (15.05, 16.42)	565	4.05 (3.72, 4.40)	3.62 (3.33, 3.94)
1993-1997	2145	13.78 (13.21, 14.38)	13.03 (12.48, 13.60)	553	3.58 (3.29, 3.89)	2.95 (2.71, 3.22)
1998-2002	2030	12.41 (11.88, 12.97)	10.54 (10.08, 11.01)	455	2.69 (2.45, 2.95)	2.02 (1.83, 2.22)
2003-2007	1780	10.89 (10.39, 11.41)	7.96 (7.59, 8.34)	493	2.78 (2.54, 3.03)	1.84 (1.67, 2.02)
Japan (Miyagi, Nagasaki, and Osaka)						
1988-1992	4114	13.46 (13.05, 13.87)	11.34 (11.00, 11.7)	955	3.00 (2.81, 3.19)	1.98 (1.85, 2.11)
1993-1997	5256	17.07 (16.61, 17.53)	12.26 (11.93, 12.60)	1100	3.41 (3.21, 3.62)	1.95 (1.84, 2.07)
1998-2002	6530	21.15 (20.64, 21.67)	12.96 (12.65, 13.28)	1273	3.91 (3.70, 4.13)	1.96 (1.85, 2.08)

2003-2007	7595	24.45 (23.9, 25.01)	12.93 (12.63, 13.23)	1494	4.51 (4.28, 4.74)	2.08 (1.97, 2.20)
India (Chennai and Mumbai)						
1988-1992	2053	5.59 (5.35, 5.83)	10.39 (9.91, 10.89)	1389	4.47 (4.24, 4.71)	7.82 (7.40, 8.26)
1993-1997	2043	5.12 (4.90, 5.35)	9.41 (8.98, 9.86)	1406	4.16 (3.94, 4.38)	7.16 (6.78, 7.56)
1998-2002	2177	4.98 (4.78, 5.20)	8.18 (7.82, 8.54)	1384	3.74 (3.55, 3.94)	5.36 (5.07, 5.65)
2003-2007	1999	4.22 (4.03, 4.41)	6.59 (6.30, 6.89)	1272	3.18 (3.01, 3.36)	4.25 (4.02, 4.50)
Thailand (Chiang Mai)						
1988-1992	68	1.98 (1.54, 2.51)	2.54 (1.96, 3.22)	47	1.41 (1.03, 1.87)	1.74 (1.27, 2.31)
1993-1997	73	2.05 (1.61, 2.58)	2.36 (1.85, 2.98)	38	1.07 (0.76, 1.47)	1.20 (0.85, 1.65)
1998-2002	84	2.27 (1.81, 2.81)	2.49 (1.98, 3.09)	31	0.82 (0.56, 1.17)	0.85 (0.58, 1.22)
2003-2007	64	1.74 (1.34, 2.22)	1.60(1.23, 2.05)	22	0.57 (0.36, 0.87)	0.48 (0.30, 0.74)
Singapore						
1988-1992	408	5.95 (5.38, 6.55)	8.67 (7.83, 9.56)	149	2.23 (1.89, 2.62)	2.65 (2.24, 3.11)
1993-1997	389	5.05 (4.56, 5.58)	6.63 (5.98, 7.33)	116	1.54 (1.28, 1.85)	1.66 (1.37, 2.00)
1998-2002	390	4.84 (4.37, 5.35)	5.79 (5.22, 6.41)	110	1.37 (1.12, 1.65)	1.40 (1.15, 1.68)
2003-2007	335	3.89 (3.48, 4.33)	4.10 (3.66, 4.57)	83	0.95 (0.76, 1.18)	0.82 (0.65, 1.02)
Philippines (Manila)						
1988-1992	143	1.34 (1.13, 1.57)	3.49 (2.90, 4.16)	91	0.80 (0.65, 0.98)	1.96 (1.56, 2.42)
1993-1997	158	1.27 (1.08, 1.49)	3.49 (2.92, 4.12)	85	0.65 (0.52, 0.81)	1.59 (1.26, 1.96)

1998-2002	195	1.51 (1.30, 1.73)	3.47 (2.96, 4.03)	61	0.46 (0.35, 0.59)	0.90 (0.68, 1.16)
2003-2007	193	1.34 (1.16, 1.55)	2.97 (2.52, 3.46)	83	0.56 (0.44, 0.69)	1.05 (0.82, 1.30)
Israel						
1988-1992	220	1.87 (1.63, 2.13)	1.91 (1.66, 2.18)	161	1.35 (1.15, 1.58)	1.18 (1.00, 1.38)
1993-1997	352	2.56 (2.30, 2.85)	2.71 (2.43, 3.02)	212	1.51 (1.32, 1.73)	1.23 (1.07, 1.41)
1998-2002	358	2.36 (2.12, 2.62)	2.38 (2.14, 2.65)	228	1.47 (1.29, 1.68)	1.08 (0.94, 1.24)
2003-2007	357	2.17 (1.95, 2.41)	2.09 (1.87, 2.32)	243	1.45 (1.27, 1.64)	1.05 (0.92, 1.20)

* Standardised to the World Health Organization (WHO) World Standard Population 2000.

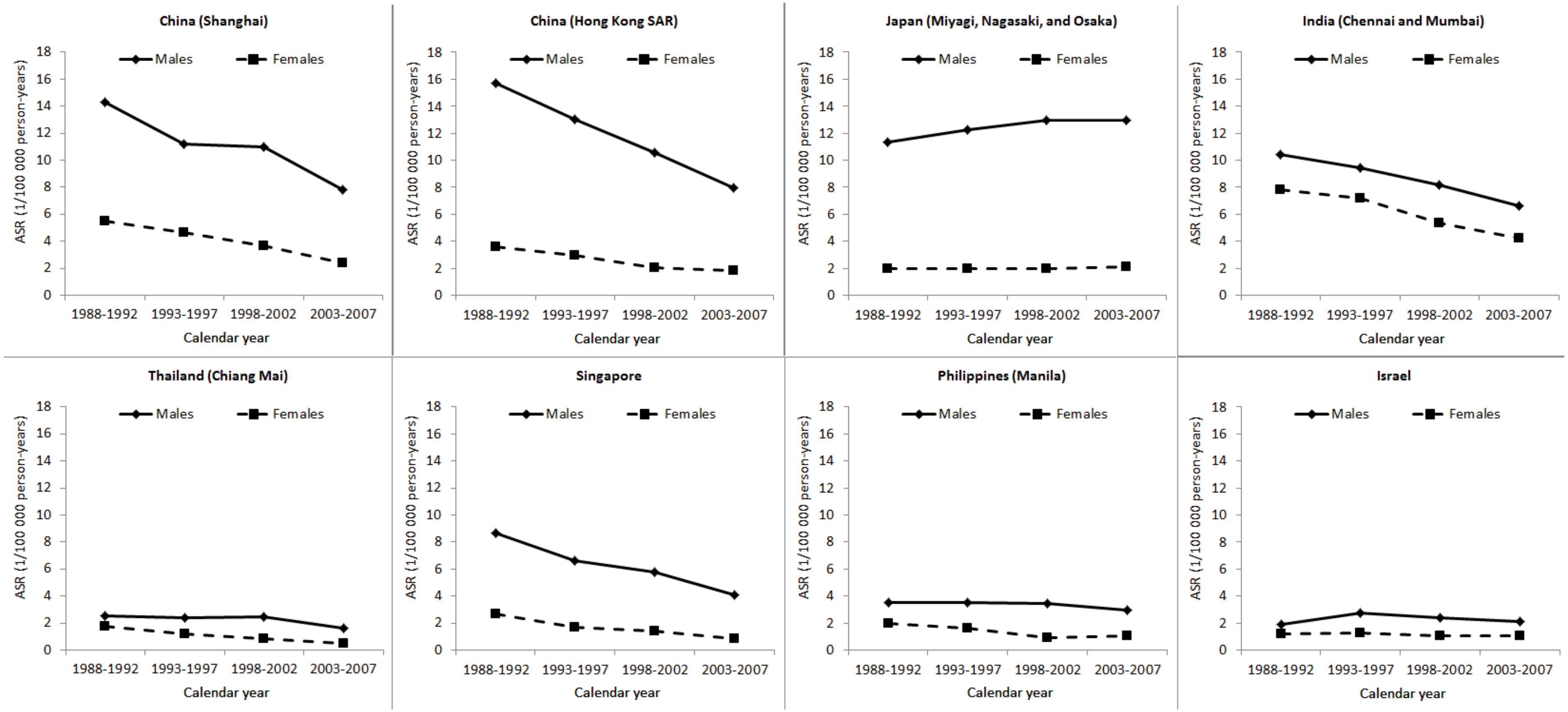


Fig. 1. Age-standardised incidence rates of oesophageal cancer by sex in selected Asian populations in 1988-2007 using the WHO World Standard Population 2000 as reference.

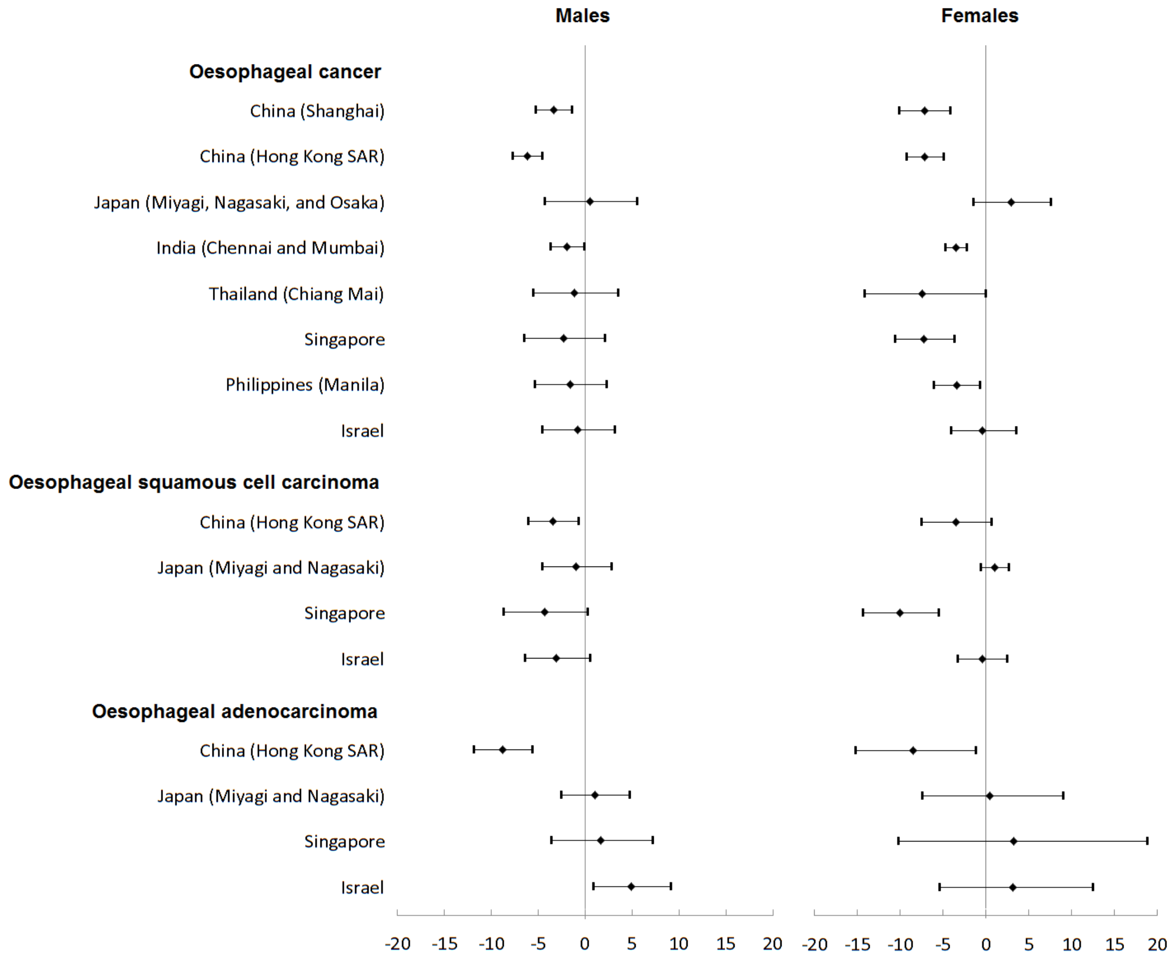


Fig. 2. The overall annual percentage changes (net drifts) and their 95% confidence intervals in the incidence of oesophageal cancer by sex and histological type in selected Asian populations in 1988-2007.

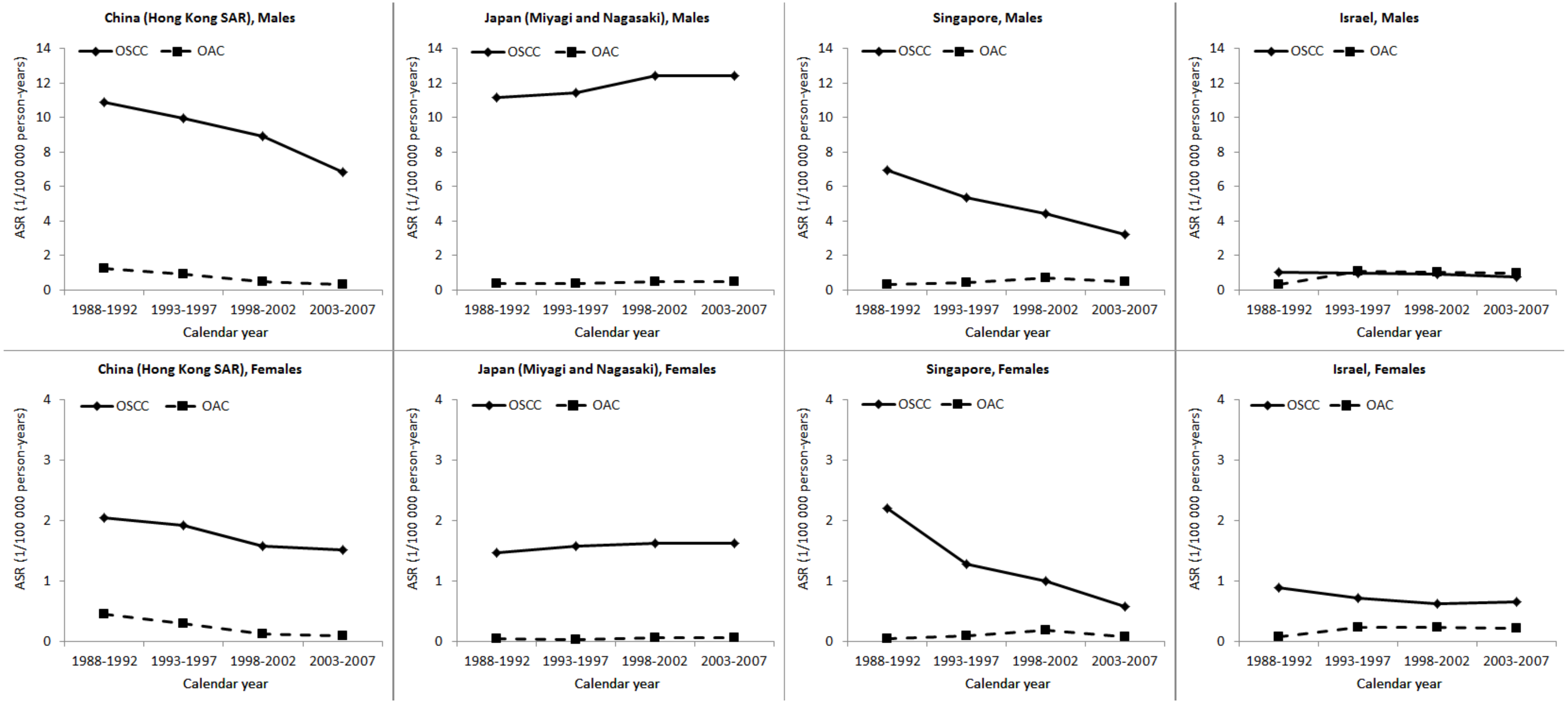


Fig. 3. Age-standardised incidence rates (ASRs) of oesophageal squamous cell carcinoma (OSCC) and adenocarcinoma (OAC) by sex in selected Asian populations in 1988-2007 using the WHO World Standard Population 2000 as reference.

Supplementary Table 1. Crude and age-standardised incidence rates (ASRs) with 95% confidence intervals (CIs) of oesophageal squamous cell carcinoma per 100 000 person-years by country and calendar period in Asia, 1988-2007

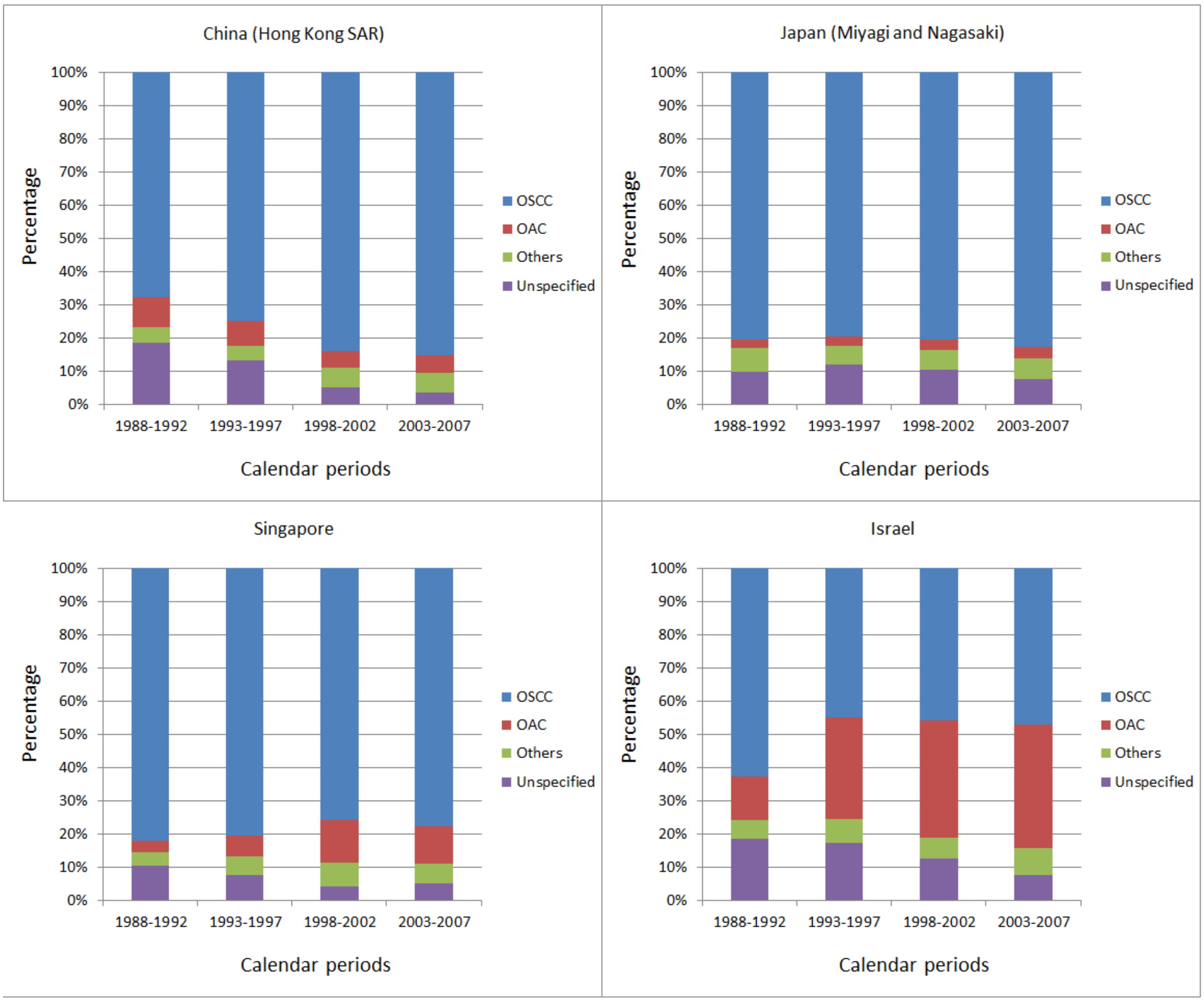
Calendar periods	Males			Females		
	N	Crude rate (95% CI)	ASR (95% CI) *	N	Crude rate (95% CI)	ASR (95% CI) *
China (Hong Kong SAR)						
1988-1992	1538	10.47 (9.95, 11.00)	10.9 (10.35, 11.47)	320	2.28 (2.04, 2.55)	2.04 (1.82, 2.29)
1993-1997	1662	10.63 (10.13, 11.16)	9.97 (9.49, 10.47)	358	2.31 (2.08, 2.56)	1.93 (1.73, 2.14)
1998-2002	1725	10.55 (10.06, 11.06)	8.94 (8.52, 9.38)	356	2.10 (1.89, 2.33)	1.59 (1.42, 1.77)
2003-2007	1533	9.38 (8.92, 9.86)	6.86 (6.52, 7.22)	400	2.25 (2.04, 2.48)	1.51 (1.36, 1.68)
Japan (Miyagi and Nagasaki)						
1988-1992	1382	15.01 (14.23, 15.82)	11.20 (10.62, 11.81)	248	2.52 (2.22, 2.85)	1.47 (1.29, 1.68)
1993-1997	1616	17.33 (16.49, 18.19)	11.44 (10.89, 12.02)	294	2.94 (2.62, 3.30)	1.58 (1.40, 1.78)
1998-2002	1991	21.28 (20.36, 22.24)	12.45 (11.90, 13.02)	338	3.36 (3.01, 3.74)	1.63 (1.45, 1.83)
2003-2007	2223	24.17 (23.18, 25.20)	12.46 (11.94, 13.01)	355	3.56 (3.20, 3.95)	1.63 (1.45, 1.84)
Singapore						
1988-1992	332	4.84 (4.33, 5.39)	6.95 (6.22, 7.75)	124	1.86 (1.54, 2.21)	2.20 (1.83, 2.63)
1993-1997	318	4.13 (3.69, 4.61)	5.39 (4.81, 6.02)	88	1.17 (0.94, 1.44)	1.28 (1.03, 1.58)
1998-2002	300	3.73 (3.32, 4.17)	4.41 (3.92, 4.95)	78	0.97 (0.77, 1.21)	1.00 (0.79, 1.25)
2003-2007	267	3.10 (2.74, 3.49)	3.22 (2.84, 3.64)	58	0.66 (0.50, 0.86)	0.58 (0.44, 0.75)
Israel						
1988-1992	118	1.00 (0.83, 1.2)	1.04 (0.86, 1.24)	121	1.02 (0.84, 1.21)	0.90 (0.74, 1.08)
1993-1997	128	0.93 (0.78, 1.11)	0.99 (0.82, 1.18)	124	0.89 (0.74, 1.06)	0.72 (0.60, 0.87)
1998-2002	137	0.90 (0.76, 1.07)	0.90 (0.76, 1.07)	132	0.85 (0.71, 1.01)	0.62 (0.52, 0.75)
2003-2007	134	0.82 (0.68, 0.97)	0.77 (0.65, 0.92)	148	0.88 (0.75, 1.04)	0.66 (0.55, 0.78)

* Standardised to the World Health Organization (WHO) World Standard Population 2000.

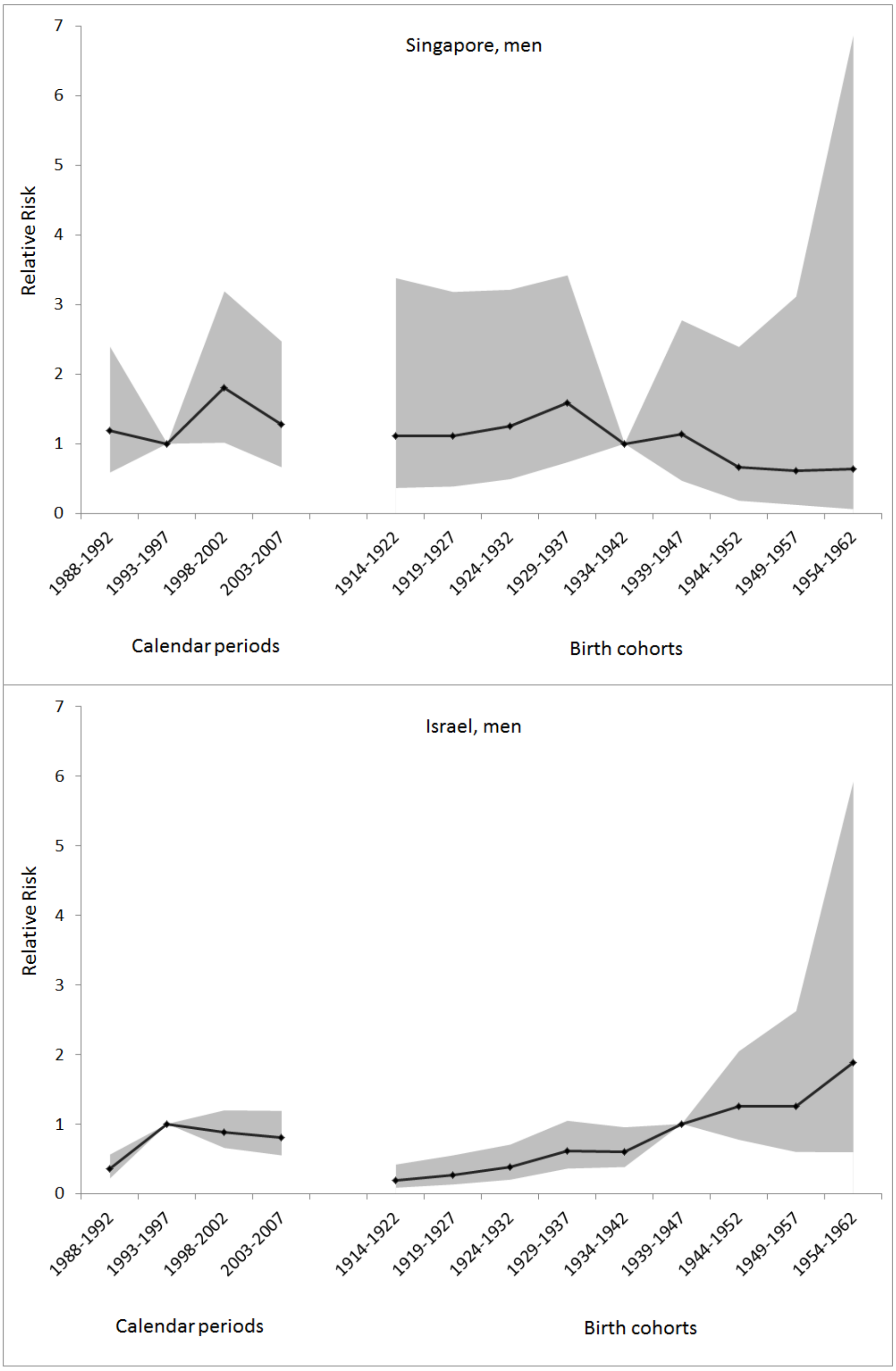
Supplementary Table 2. Crude and age-standardised incidence rates (ASRs) with 95% confidence intervals (CIs) of oesophageal adenocarcinoma per 100 000 person-years by country and calendar period in Asia, 1988-2007

Calendar periods	Males			Females		
	N	Crude rate (95% CI)	ASR (95% CI) *	N	Crude rate (95% CI)	ASR (95% CI) *
China (Hong Kong SAR)						
1988-1992	170	1.16 (0.99, 1.34)	1.27 (1.08, 1.48)	76	0.54 (0.43, 0.68)	0.46 (0.36, 0.58)
1993-1997	146	0.93 (0.79, 1.10)	0.91 (0.76, 1.07)	55	0.35 (0.27, 0.46)	0.29 (0.22, 0.38)
1998-2002	97	0.59 (0.48, 0.72)	0.52 (0.42, 0.63)	29	0.17 (0.11, 0.25)	0.12 (0.08, 0.18)
2003-2007	71	0.43 (0.34, 0.55)	0.31 (0.24, 0.40)	30	0.17 (0.11, 0.24)	0.10 (0.07, 0.15)
Japan (Miyagi and Nagasaki)						
1988-1992	46	0.50 (0.37, 0.67)	0.38 (0.28, 0.51)	8	0.08 (0.04, 0.16)	0.04 (0.02, 0.10)
1993-1997	55	0.59 (0.44, 0.77)	0.40 (0.30, 0.52)	7	0.07 (0.03, 0.14)	0.03 (0.01, 0.08)
1998-2002	75	0.80 (0.63, 1.01)	0.48 (0.37, 0.60)	12	0.12 (0.06, 0.21)	0.06 (0.02, 0.12)
2003-2007	86	0.94 (0.75, 1.15)	0.49 (0.39, 0.61)	18	0.18 (0.11, 0.28)	0.07 (0.04, 0.12)
Singapore						
1988-1992	17	0.25 (0.14, 0.40)	0.34 (0.19, 0.53)	3	0.04 (0.01, 0.13)	0.05 (0.01, 0.15)
1993-1997	25	0.32 (0.21, 0.48)	0.43 (0.28, 0.64)	7	0.09 (0.04, 0.19)	0.10 (0.04, 0.20)
1998-2002	49	0.61 (0.45, 0.80)	0.73 (0.53, 0.96)	15	0.19 (0.10, 0.31)	0.18 (0.10, 0.30)
2003-2007	37	0.43 (0.30, 0.59)	0.48 (0.33, 0.66)	9	0.10 (0.05, 0.20)	0.08 (0.04, 0.16)
Israel						
1988-1992	39	0.33 (0.24, 0.45)	0.35 (0.25, 0.48)	11	0.09 (0.05, 0.17)	0.08 (0.04, 0.14)
1993-1997	136	0.99 (0.83, 1.17)	1.07 (0.90, 1.27)	37	0.26 (0.19, 0.36)	0.23 (0.16, 0.32)
1998-2002	156	1.03 (0.87, 1.20)	1.07 (0.90, 1.25)	50	0.32 (0.24, 0.43)	0.24 (0.18, 0.32)
2003-2007	169	1.03 (0.88, 1.20)	1.00 (0.86, 1.17)	53	0.32 (0.24, 0.41)	0.23 (0.17, 0.30)

* Standardised to the World Health Organization (WHO) World Standard Population 2000.



Supplementary Figure 1. Percentages of histological types of oesophageal cancer in selected Asian populations by calendar period during 1988-2007.



Supplementary Figure 2. Period and cohort effects and their 95% confidence intervals obtained from age-period-cohort analyses for the incidence rates of oesophageal adenocarcinoma in men in Singapore and Israel.