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



CONCE

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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 1988–2007. 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.

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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

http://dx.doi.org/10.1016/j.canep.2016.08.002 1877-7821/© 2016 Elsevier Ltd. All rights reserved. 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

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*.

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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–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 Fig. 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

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.

$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$	Calendar periods	Males			Females			
China (Shanghai) U <thu< th=""> U <thu< th=""> <</thu<></thu<>		Ν	Crude rate (95% CI)	ASR (95% CI) ^a	N	Crude rate (95% CI)	ASR (95% CI) ^a	
1988-1992 2855 15.71 (15.14, 15.30) 14.29 (13.75, 14.86) 1338 7.70 (7.29, 8.12) 5.53 (5.23, 5.84) 1993-1997 2255 14.34 (13.77, 14.94) 112.01 (0.74, 11.68) 1189 7.51 (7.09, 7.95, 14.53) 3.63 (3.40, 3.88) 2003-2007 2017 12.96 (12.40, 13.54) 7.79 (7.45, 8.15) 7.91 5.16 (4.81, 5.53) 2.24 (2.25, 2.60) China (Hong Kong SAR) 1993-1997 21.45 13.78 (12.21, 14.38) 13.03 (12.44, 13.40) 553 3.53 (2.9, 3.80) 2.95 (2.71, 3.22) 2003-2007 17.80 10.88 (10.39, 11.41) 7.96 (7.59, 8.34) 433 2.78 (2.54, 3.03) 1.84 (16.7, 2.22) 2003-2007 17.80 10.88 (10.39, 11.41) 7.96 (7.59, 8.34) 430 2.78 (2.54, 3.03) 1.84 (16.7, 2.20) 1993-1997 52.56 17.07 (16.1, 17.53) 12.26 (11.93, 12.20) 1100 3.41 (3.21, 3.22, 1.95) 1.98 (18.5, 2.11) 1993-1997 52.56 17.07 (16.61, 17.53) 12.26 (12.63, 13.28) 1273 3.91 (3.70, 4.13) 1.96 (18.5, 2.08) 1993-1997 52.55 1.57 (5.53, 5.58) 12.96 (12.63, 13.28) 1273 3.91 (3.70, 4.14) 2.08 (19.7, 2.09) <td>China (Shanghai)</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td>	China (Shanghai)							
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	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)	
1998-2002 2291 14.40 (13.81, 15.00) 10.96 (10.50, 11.44) 965 6.22 (5.84, 6.63) 3.63 (2.40, 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) 1984-1992 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 (32.9, 32.98) 2.95 (2.71, 3.22) 2003-2007 1780 10.89 (10.39, 11.41) 7.96 (7.59, 8.34) 433 2.76 (2.54, 3.03) 1.84 (16.2, 0.2) Japan (Myagi, Nagasaki, and Osaka) 1 1.98 (1.102, 11.75) 12.26 (11.93, 12.60) 1100 3.41 (3.21, 3.62) 1.95 (1.84, 2.07) 1984-1992 2053 5.59 (5.35, 5.83) 10.39 (9.91, 10.89) 1384 4.51 (42.8, 4.74) 2.06 (1.97, 2.20) India (Chennai and Mumbai) 1988 1992 2053 5.59 (5.35, 5.83) 10.39 (9.91, 10.89) 1384 4.77 (42.4, 4.71) 7.82 (7.40, 8.26) 1993-1997 2043 5.12 (4.90, 5.35)	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)	
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	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)	
$\begin{array}{ c c c c c c c c c c c c c c c c c c c$	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)	
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	China (Hong Kong SAR)							
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	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)	
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	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)	
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	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)							
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	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)	
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	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)	
2003-2007 7595 24.4s ² (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) 1998-1992 68 1.98 (1.54, 2.51) 2.54 (1.96, 3.22) 47 1.41 (103, 1.87) 1.74 (127, 2.31) 1998-1992 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) 2.57 (0.36, 0.87) 0.48 (0.30, 0.74) 1988-1992 408 5.95 (5.38, 6.55) 6.67 (7.83, 9.56) 149 <td>1998-2002</td> <td>6530</td> <td>21.15 (20.64, 21.67)</td> <td>12.96 (12.65, 13.28)</td> <td>1273</td> <td>3.91 (3.70, 4.13)</td> <td>1.96 (1.85, 2.08)</td>	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)	
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) 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) 1 1 1.44 (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) 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) 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 (5.58, 6.55) 8.67 (7.83, 9.56) 149 2.23 (1.89, 2.62) 2.65 (2.24, 3.11) 1993–1997 389 5.95 (5.38, 6.55) 8.67 (7.83, 9.56) 149 2.23 (1.89, 2.62) 2.65 (1.52, 2.43, 1.1	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)	
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) 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) 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) 6.67 (7.83, 9.56) 149 2.23 (1.89, 2.62) 2.65 (2.24, 3.11) 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	India (Chennai and Mumbai)							
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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) 1 1 1 1 1.74 (1.03, 1.87) 1.74 (1.27, 2.31) 1998-1992 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) 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 (4.36, 5.58) 6.67 (7.83, 9.56) 149 2.23 (1.89, 2.62) 2.65 (2.24, 3.11) 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)	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)	
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) 1993-2002 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 (3.64, 6.57) 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) <td>1998-2002</td> <td>2177</td> <td>4.98 (4.78, 5.20)</td> <td>8.18 (7.82, 8.54)</td> <td>1384</td> <td>3.74 (3.55, 3.94)</td> <td>5.36 (5.07, 5.65)</td>	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)	
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) Singapre	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)	
Image (mar) 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	Thailand (Chiang Mai)							
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 988-1992 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, 0.92) Philippines (Manila) 91 0.80 (0.65, 0.98) 1.96 (1.56, 2.42) 1.98 (1.26, 1.96) 1.99 (1.56, 2.42) 1.99 (1.26, 1.96) 1.99 (1.26, 1.96) 1.99 (1.26, 1.96) 1.99 (1.26, 1.96) 1.99 (1.26, 1.96) 1.99 (1.26, 1.96) 1.99 (1.26, 1.96) 1.95 (1.26, 1.96) 1.99 (0.68, 1.16) 1.91 (1.66, 2.18	1988–1992	68	198 (154 251)	2 54 (196 3 22)	47	141 (103 187)	174 (127 231)	
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) 198 193-1997 158 1.27 (1.08, 1.49) 3.49 (2.90, 4.16) 91 0.80 (0.65, 0.98) 1.96 (1.56, 2.42) 1998-1992 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 (2.90, 4.16) 91 0.48 (0.35, 0.59) 0.90 (0.68, 1.16) 2003-2007	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)	
2003-2007 64 1.74 (134, 2.22) 1.60(1.23, 2.05) 22 0.57 (0.36, 0.87) 0.48 (0.30, 0.74) Singapore	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)	
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 (2.90, 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 (2.90, 4.16) 91 0.80 (0.65, 0.98) 1.96 (1.56, 2.42) 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, 1.69) 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)	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)	
Disperse 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) 1998-1992 143 1.34 (1.13, 1.57) 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) 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) <tr< td=""><td>Singapore</td><td></td><td></td><td></td><td></td><td></td><td></td></tr<>	Singapore							
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 Israel Israel Israel Israel Israel Israel Israel Israel <td>1988–1992</td> <td>408</td> <td>5 95 (5 38 6 55)</td> <td>867 (783 956)</td> <td>149</td> <td>2 23 (189 262)</td> <td>2 65 (2 24 3 11)</td>	1988–1992	408	5 95 (5 38 6 55)	867 (783 956)	149	2 23 (189 262)	2 65 (2 24 3 11)	
Instruction State	1993-1997	389	5.05 (4.56, 5.58)	663 (598, 733)	116	154(128, 185)	166(137,200)	
Autor Autor <th< td=""><td>1998-2002</td><td>390</td><td>4 84 (4 37 5 35)</td><td>579(522,641)</td><td>110</td><td>137 (112, 165)</td><td>140(115, 168)</td></th<>	1998-2002	390	4 84 (4 37 5 35)	579(522,641)	110	137 (112, 165)	140(115, 168)	
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 Issae 1998–1992 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)	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)	
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 Israel Israel Israel Israel 1.987 (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)	Philippines (Manila)							
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Instruction	1993-1997	158	127(108, 149)	349(2.92, 4.12)	85	0.65(0.52, 0.81)	159 (126, 196)	
100 100 <td>1998-2002</td> <td>195</td> <td>151(130,173)</td> <td>347(2.96,4.03)</td> <td>61</td> <td>0.46(0.35, 0.59)</td> <td>0.90 (0.68, 1.16)</td>	1998-2002	195	151(130,173)	347(2.96,4.03)	61	0.46(0.35, 0.59)	0.90 (0.68, 1.16)	
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)	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)	
1988-19922201.87 (1.63, 2.13)1.91 (1.66, 2.18)1611.35 (1.15, 1.58)1.18 (1.00, 1.38)1993-19973522.56 (2.30, 2.85)2.71 (2.43, 3.02)2121.51 (1.32, 1.73)1.23 (1.07, 1.41)1998-20023582.36 (2.12, 2.62)2.38 (2.14, 2.65)2281.47 (1.29, 1.68)1.08 (0.94, 1.24)2003-20073572.17 (1.95, 2.41)2.09 (1.87, 2.32)2431.45 (1.27, 1.64)1.05 (0.92, 1.20)	Israel							
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)	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)	
1998-2002 358 2.36 (2.1, 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)	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)	
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)	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)	

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

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