

SUPPLEMENTARY METHODS:

Countries Included

Data from 42 countries were included in this analysis: Africa: Uganda; Asia: China, India, Korea, Japan, the Philippines, and Thailand; Europe: Austria, Bulgaria, Croatia, Cyprus, the Czech Republic, Denmark, Estonia, France, Germany, Iceland, Ireland, Italy, Lithuania, Malta, the Netherlands, Norway, Poland, Slovakia, Slovenia, Spain, Switzerland, and the United Kingdom; the Middle East: Bahrain, Kuwait, Israel, Turkey; North America: Canada, the United States; Oceania: Australia and New Zealand; and Central/South America: Brazil, Chile, Colombia, Costa Rica, Ecuador, and Martinique. We chose to analyze data from 1993-2012 given that many countries, particularly from Asia, lacked data prior to 1993.

Human Development Index

The Human Development Index (HDI) for each country was obtained from the United Nations Development Program using the data from the year 2000 (United Nations Development Programme (UNDP). Human Development Report 2020. UNDP; 2020. Accessed November 16, 2021. <https://hdr.undp.org/en/content/human-development-index-hdi>). Correlations with OPC net drift were assessed in both men and women

Anatomic Site and Histology Codes

Cancers were grouped according to International Classification of Disease codes. For head and neck cancers, all histologies were included, given that >95% of these are squamous cell carcinomas (SCC). OPC included base of tongue (C01.9, C02.4), tonsil (C09.0-C09.9), soft

palate/uvula (C05.1-C05.2), and other oropharyngeal sites (C10.0-C10.9, C14.2). C02.8, C02.9, C05.8, C05.9, C14.0, and C14.8 were considered ambiguous codes that could represent either OPC or other head and neck cancer sites, so were excluded from this analysis. We also analyzed incidence trends in lung SCC, representing a cancer driven primarily by smoking (C34.0-C34.9, histology codes 8050-8094), and OCCs (mucosal lip (C00.3-C00.5), oral tongue (C02.0-C02.3), alveolar ridge (C03.0, C03.1, C03.9), floor of mouth (C04.0-C04.9), hard palate (C05.0), buccal mucosa (C06.0-C06.1), retromolar trigone (C06.2), other oral cavity (C06.8-C06.9)), representing cancers driven by both tobacco and alcohol.

Supplementary Table 1. Summary of net drifts calculated by age-period-cohort modeling for male cancer incidence in countries with significantly increasing oropharyngeal cancer incidence as assessed by log-linear regression (annual percentage change). Net drifts for different cancer types with compared using a 1-df Wald test.

Country	Net Drift (95% CI)			Net Drift Comparison		
	Lung SCC	Oral Cavity Cancer	Oropharyngeal Cancer	OPC vs. Lung (p-value)	OPC vs. OCC (p-value)	OCC vs. Lung (p-value)
Australia	-4.15 (-4.83 to -3.48)	-0.34 (-0.86 to 0.18)	2.48 (1.95 to 3.01)	<0.001	<0.001	<0.001
Austria	-3.19 (-3.76 to -2.61)	-0.46 (-1.44 to 0.54)	0.51 (-0.27 to 1.30)	<0.001	0.135	<0.001
Brazil	-3.00 (-4.81 to -1.16)	-1.59 (-3.69 to 0.55)	1.09 (-0.91 to 3.13)	0.003	0.073	0.322
Canada	-4.96 (-5.75 to -4.17)	-1.35 (-1.83 to -0.87)	2.34 (1.79 to 2.89)	<0.001	<0.001	<0.001
China	-0.05 (-1.21 to 1.13)	0.69 (-1.67 to 3.11)	2.58 (-0.22 to 5.45)	0.09	0.319	0.585
Czech Republic	-4.85 (-5.41 to -4.28)	0.39 (-0.25 to 1.04)	1.67 (1.10 to 2.23)	<0.001	0.004	<0.001
Denmark	-2.95 (-3.74 to -2.16)	-0.06 (-0.92 to 0.80)	3.12 (2.30 to 3.94)	<0.001	<0.001	<0.001
Ireland	-2.77 (-3.77 to -1.76)	-0.57 (-1.77 to 0.65)	1.45 (0.28 to 2.63)	<0.001	0.02	0.006
Italy	-5.97 (-6.87 to -5.05)	0.66 (-0.71 to 2.05)	1.53 (0.35 to 2.72)	<0.001	0.351	<0.001
Japan	-1.04 (-1.93 to -0.14)	5.71 (4.65 to 6.79)	5.06 (3.75 to 6.38)	<0.001	0.448	<0.001
Korea	-4.55 (-5.31 to -3.79)	-0.03 (-1.27 to 1.23)	1.70 (0.60 to 2.80)	<0.001	0.042	<0.001
Lithuania	-3.12 (-3.78 to -2.46)	0.86 (-0.26 to 1.99)	1.88 (0.82 to 2.94)	<0.001	0.197	<0.001
New Zealand	-3.37 (-4.05 to -2.67)	0.13 (-1.03 to 1.30)	3.48 (2.30 to 4.67)	<0.001	<0.001	<0.001
Norway	-2.43 (-3.03 to -1.83)	-0.96 (-1.91 to -0.01)	2.94 (1.94 to 3.94)	<0.001	<0.001	0.01
Slovakia	-2.59 (-2.95 to -2.24)	-1.87 (-2.65 to -1.09)	1.15 (0.46 to 1.85)	<0.001	<0.001	0.1
The Netherlands	-5.17 (-5.50 to -4.84)	0.31 (-0.13 to 0.74)	0.80 (0.32 to 1.28)	<0.001	0.132	<0.001
United Kingdom	-4.43 (-5.00 to -3.84)	2.06 (1.67 to 2.45)	6.12 (5.66 to 6.59)	<0.001	<0.001	<0.001
United States	-3.78 (-4.35 to -3.22)	-2.71 (-3.06 to -2.36)	0.99 (0.63 to 1.35)	<0.001	<0.001	0.002

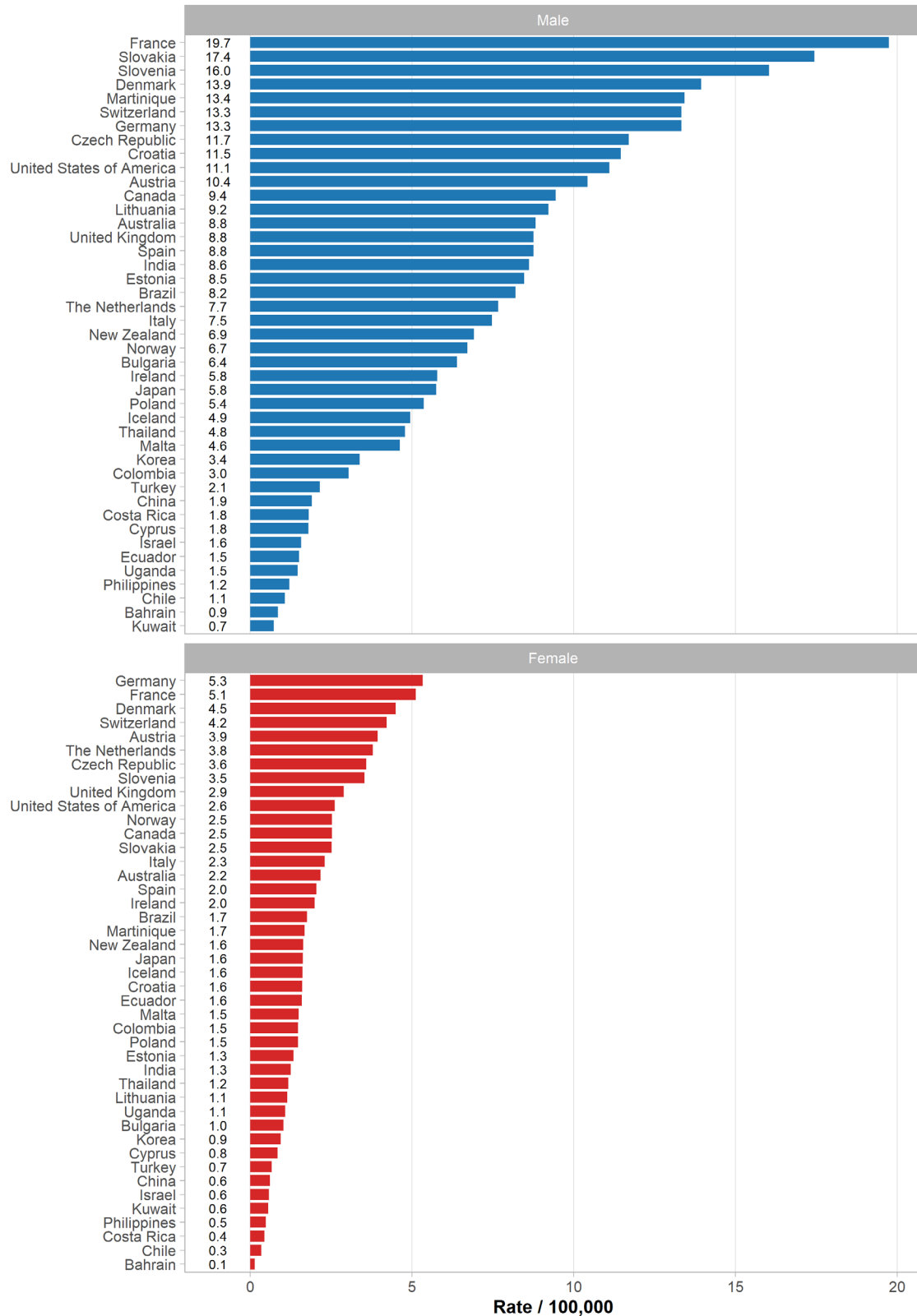
CI: confidence interval; OCC: oral cavity cancer; OPC: oropharyngeal cancer; SCC: squamous cell carcinoma

Supplementary Table 2. Summary of net drifts calculated by age-period-cohort modeling for female cancer incidence in countries with significantly increasing oropharyngeal cancer incidence as assessed by log-linear regression (annual percentage change). Net drifts for different cancer types with compared using a 1-df Wald test.

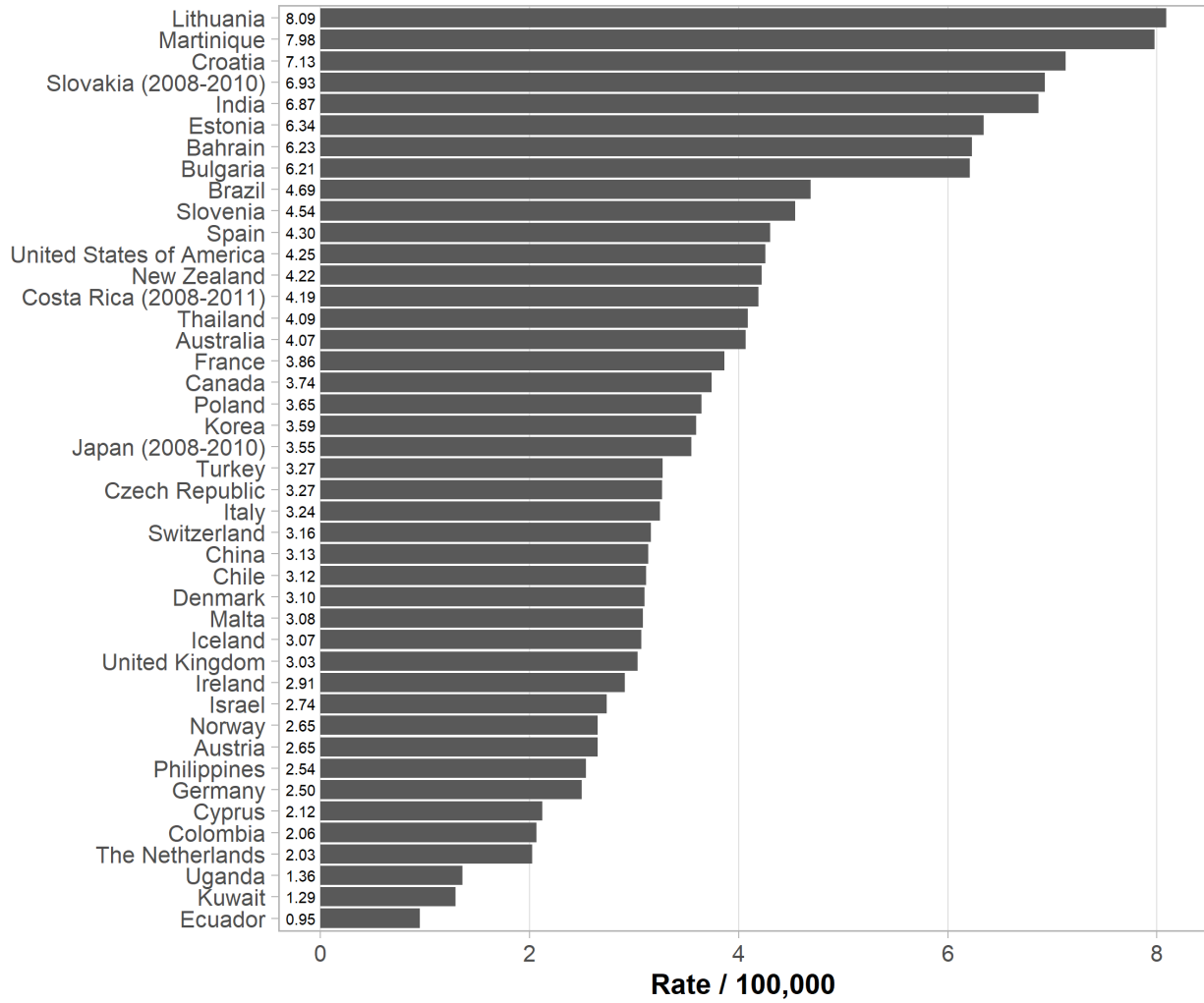
Country	Net Drift (95% CI)			Net Drift Comparison		
	Lung SCC	Oral Cavity Cancer	Oropharyngeal Cancer	OPC vs. Lung (p-value)	OPC vs. OCC (p-value)	OCC vs. Lung (p-value)
Australia	-2.14 (-3.07 to -1.20)	0.49 (-0.26 to 1.24)	1.63 (0.70 to 2.57)	<0.001	0.062	<0.001
Austria	3.05 (1.97 to 4.14)	2.74 (0.96 to 4.56)	2.20 (0.75 to 3.67)	0.364	0.649	0.776
Bulgaria	5.13 (3.84 to 6.45)	4.12 (1.88 to 6.42)	4.44 (1.73 to 7.22)	0.655	0.861	0.45
Canada	-3.18 (-3.78 to -2.59)	-0.72 (-1.29 to -0.14)	0.97 (0.26 to 1.69)	<0.001	<0.001	<0.001
Croatia	0.89 (-0.06 to 1.84)	1.78 (0.06 to 3.54)	2.07 (0.24 to 3.94)	0.263	0.823	0.375
Czech Republic	0.62 (-0.24 to 1.50)	4.29 (3.21 to 5.39)	5.19 (4.13 to 6.26)	<0.001	0.251	<0.001
Denmark	-1.76 (-2.74 to -0.78)	1.64 (0.59 to 2.70)	2.36 (1.26 to 3.48)	<0.001	0.354	<0.001
France	1.89 (0.36 to 3.43)	1.63 (0.20 to 3.07)	3.02 (1.53 to 4.53)	0.3	0.188	0.809
Germany	1.09 (-0.40 to 2.61)	0.10 (-1.79 to 2.02)	3.84 (1.89 to 5.82)	0.029	0.007	0.421
Ireland	0.96 (-0.06 to 2.00)	2.17 (0.51 to 3.87)	1.84 (-0.13 to 3.85)	0.442	0.801	0.227
Italy	-0.36 (-1.76 to 1.06)	2.98 (1.01 to 5.00)	4.35 (2.17 to 6.58)	<0.001	0.366	0.007
Japan	0.43 (-1.44 to 2.33)	5.63 (4.14 to 7.14)	9.71 (6.88 to 12.61)	<0.001	0.012	<0.001
Korea	-3.64 (-4.99 to -2.26)	-0.25 (-1.98 to 1.51)	1.15 (-0.76 to 3.10)	<0.001	0.292	0.003
New Zealand	-0.64 (-1.50 to 0.24)	1.21 (-0.28 to 2.71)	2.74 (0.62 to 4.90)	0.004	0.25	0.036
Norway	1.64 (0.64 to 2.64)	0.11 (-1.10 to 1.32)	2.82 (1.25 to 4.41)	0.215	0.007	0.057
Slovakia	2.89 (1.83 to 3.97)	1.17 (-0.56 to 2.94)	3.28 (1.54 to 5.04)	0.714	0.096	0.101
Slovenia	3.24 (1.85 to 4.66)	3.28 (1.15 to 5.45)	1.78 (-0.07 to 3.67)	0.222	0.304	0.979
Spain	3.31 (1.63 to 5.01)	2.99 (1.60 to 4.40)	4.82 (2.67 to 7.03)	0.281	0.164	0.775
The Netherlands	0.31 (-0.22 to 0.84)	1.49 (0.92 to 2.06)	1.80 (1.11 to 2.49)	<0.001	0.504	0.003
United Kingdom	-2.89 (-3.38 to -2.41)	3.21 (2.76 to 3.67)	5.59 (5.02 to 6.15)	<0.001	<0.001	<0.001

CI: confidence interval; OCC: oral cavity cancer; OPC: oropharyngeal cancer; SCC: squamous cell carcinoma

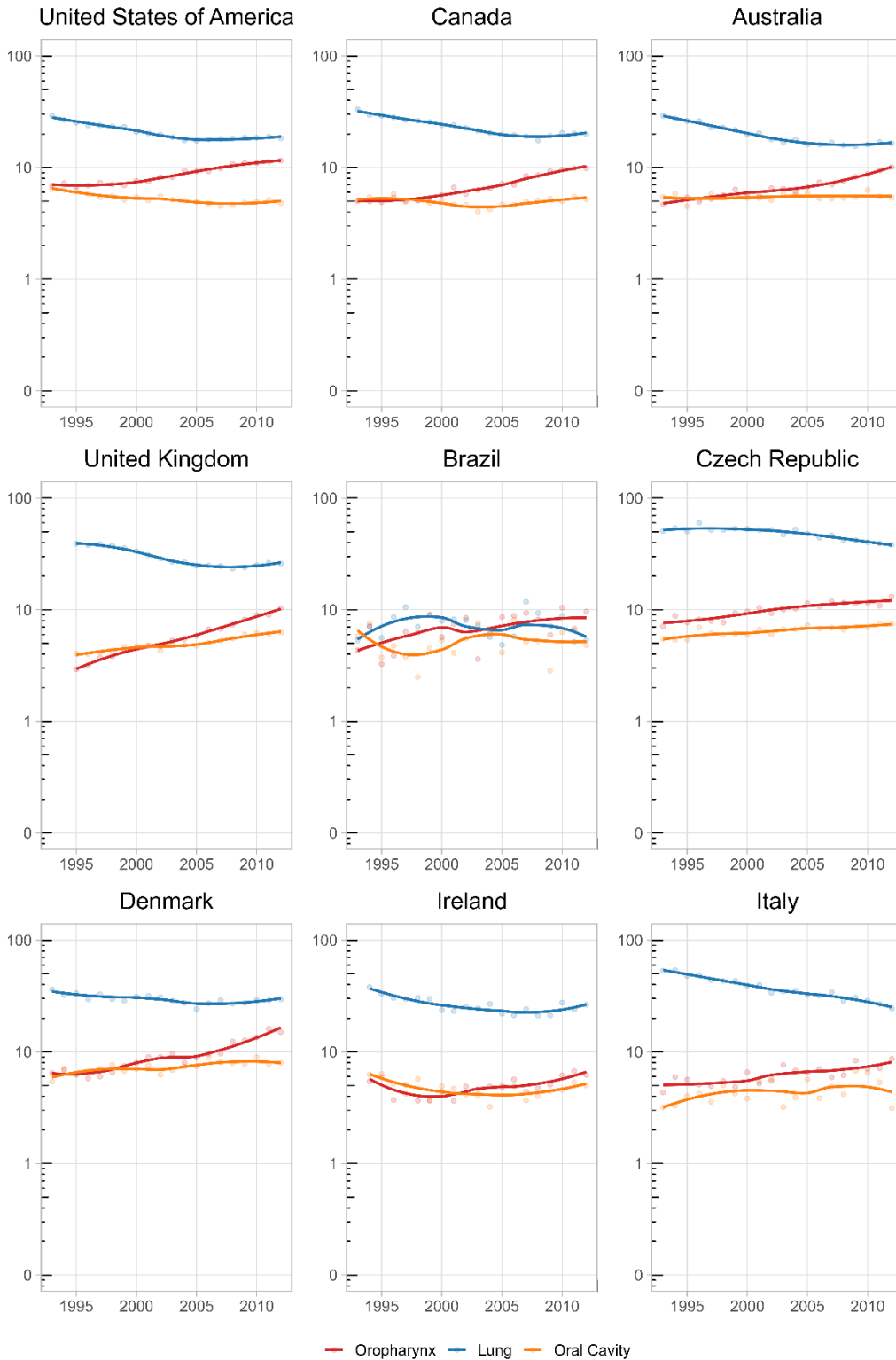
SUPPLEMENTARY FIGURE 2. Standardized incidence rates (per 100,000 persons) for oropharyngeal cancers in men and women from 2008-2012.



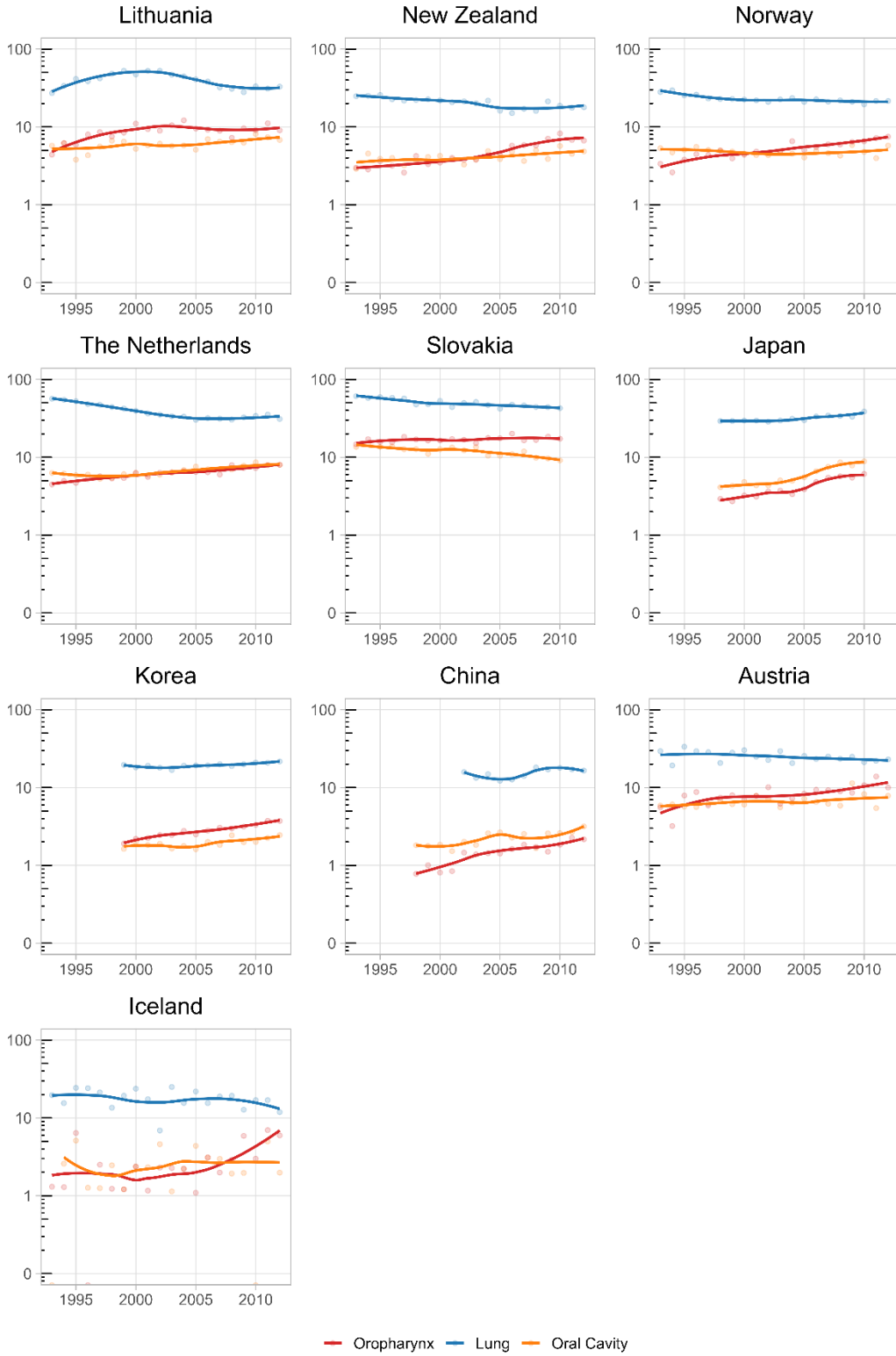
SUPPLEMENTARY FIGURE 3. Male:female ratio of standardized incidence rates (per 100,000 persons) for oropharyngeal cancers in men and women from 2008-2012.



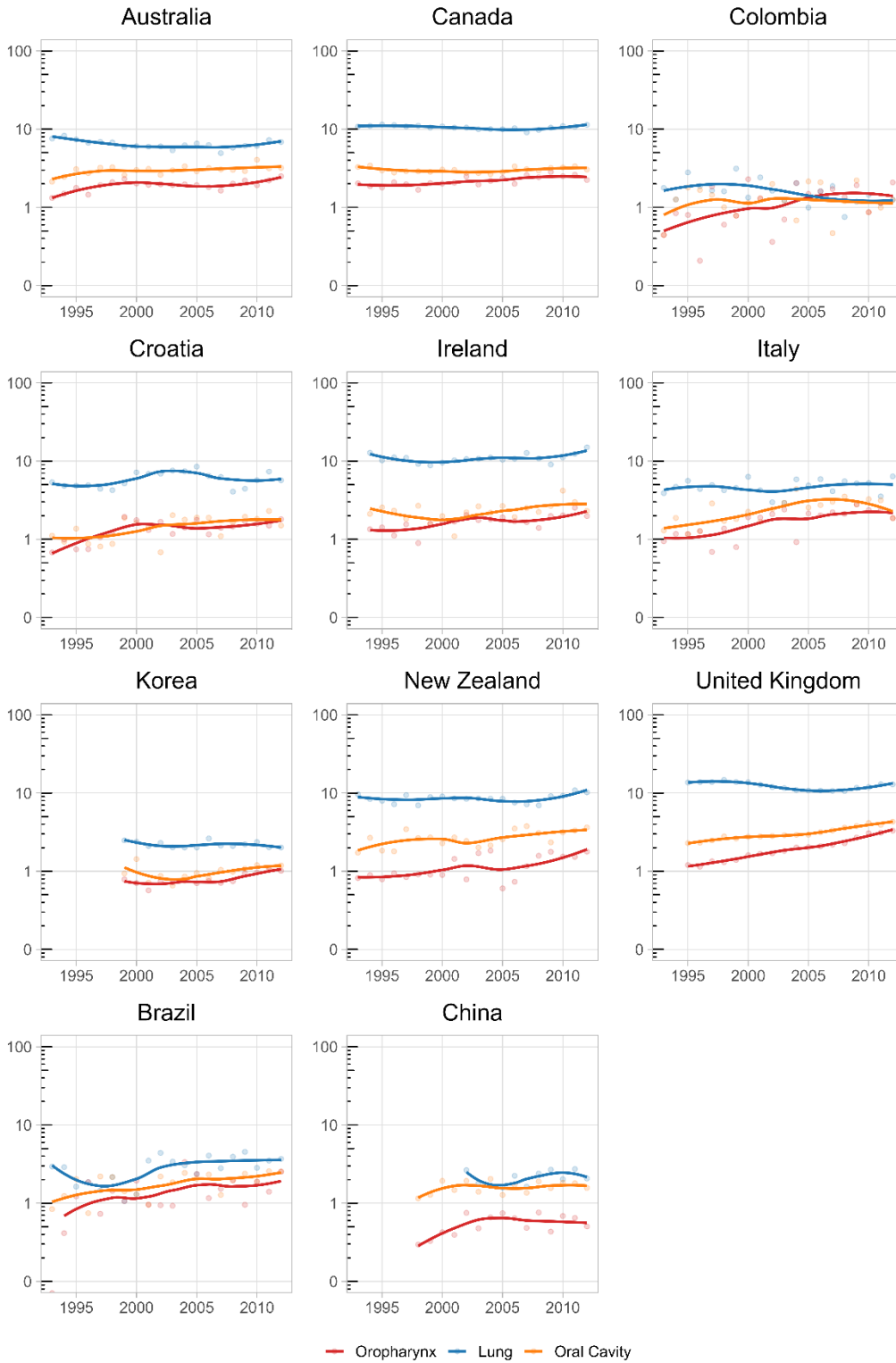
SUPPLEMENTARY FIGURE 4. Standardized incidence rates (per 100,000 persons) for oropharyngeal cancers (OPC), oral cavity cancer, larynx/hypopharynx cancer, and lung squamous cell carcinoma in men in countries with significantly increasing OPC annual percentage change.



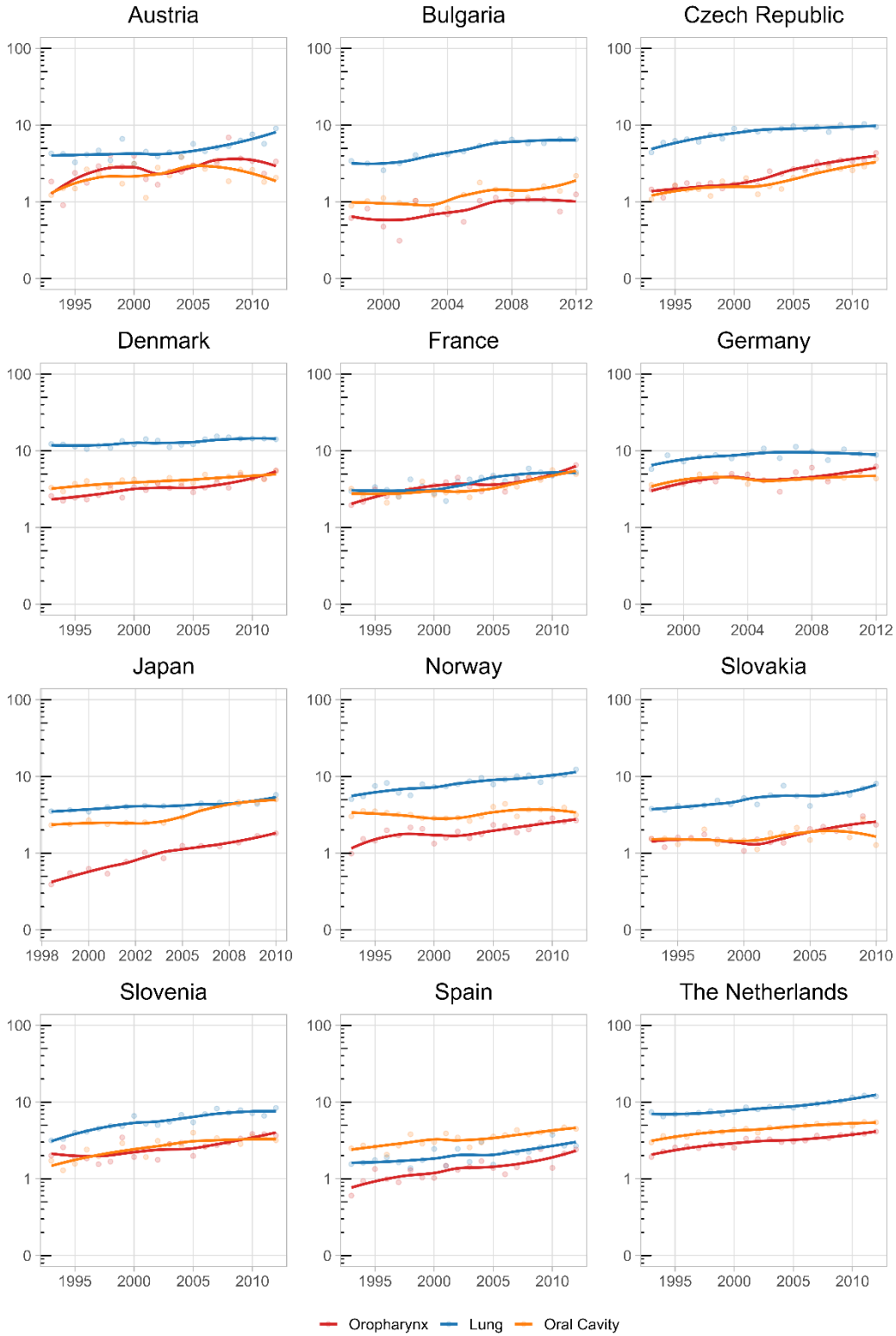
SUPPLEMENTARY FIGURE 4. Cont'd.



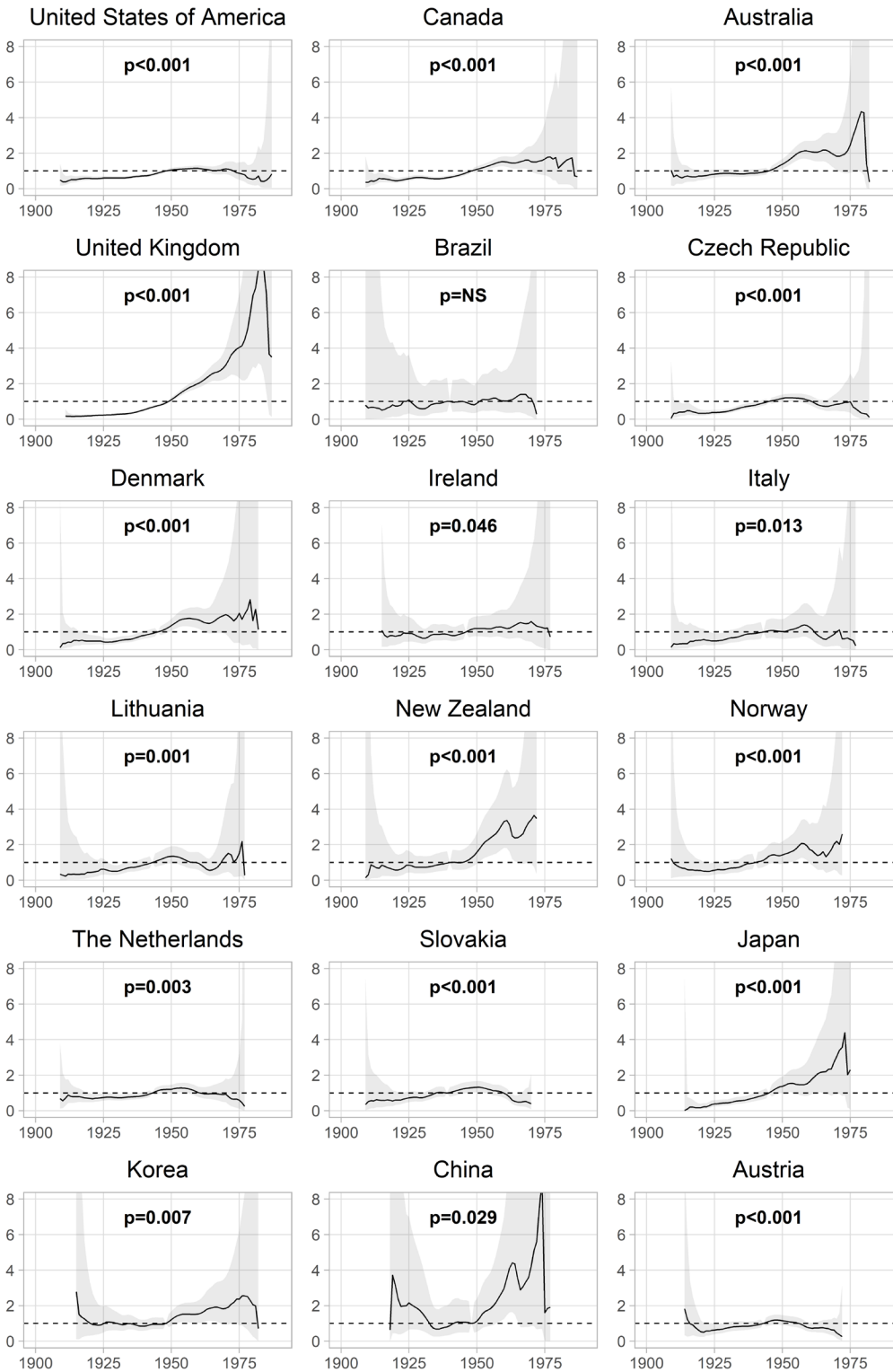
SUPPLEMENTARY FIGURE 5. Standardized incidence rates (per 100,000 persons) for oropharyngeal cancers (OPC), oral cavity cancer, larynx/hypopharynx cancer, and lung squamous cell carcinoma in women in countries with significantly increasing OPC annual percentage change.



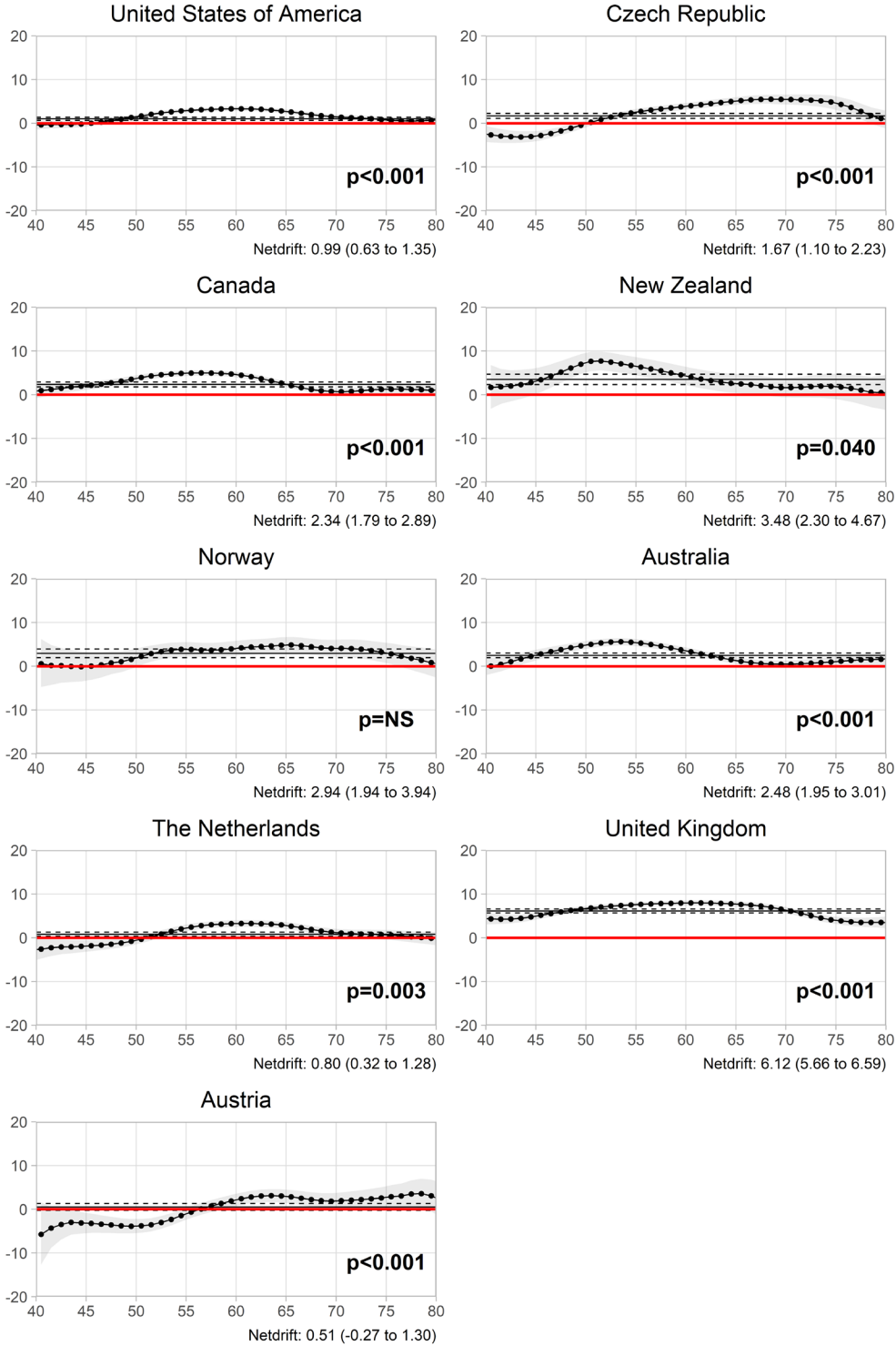
SUPPLEMENTARY FIGURE 5. Cont'd.



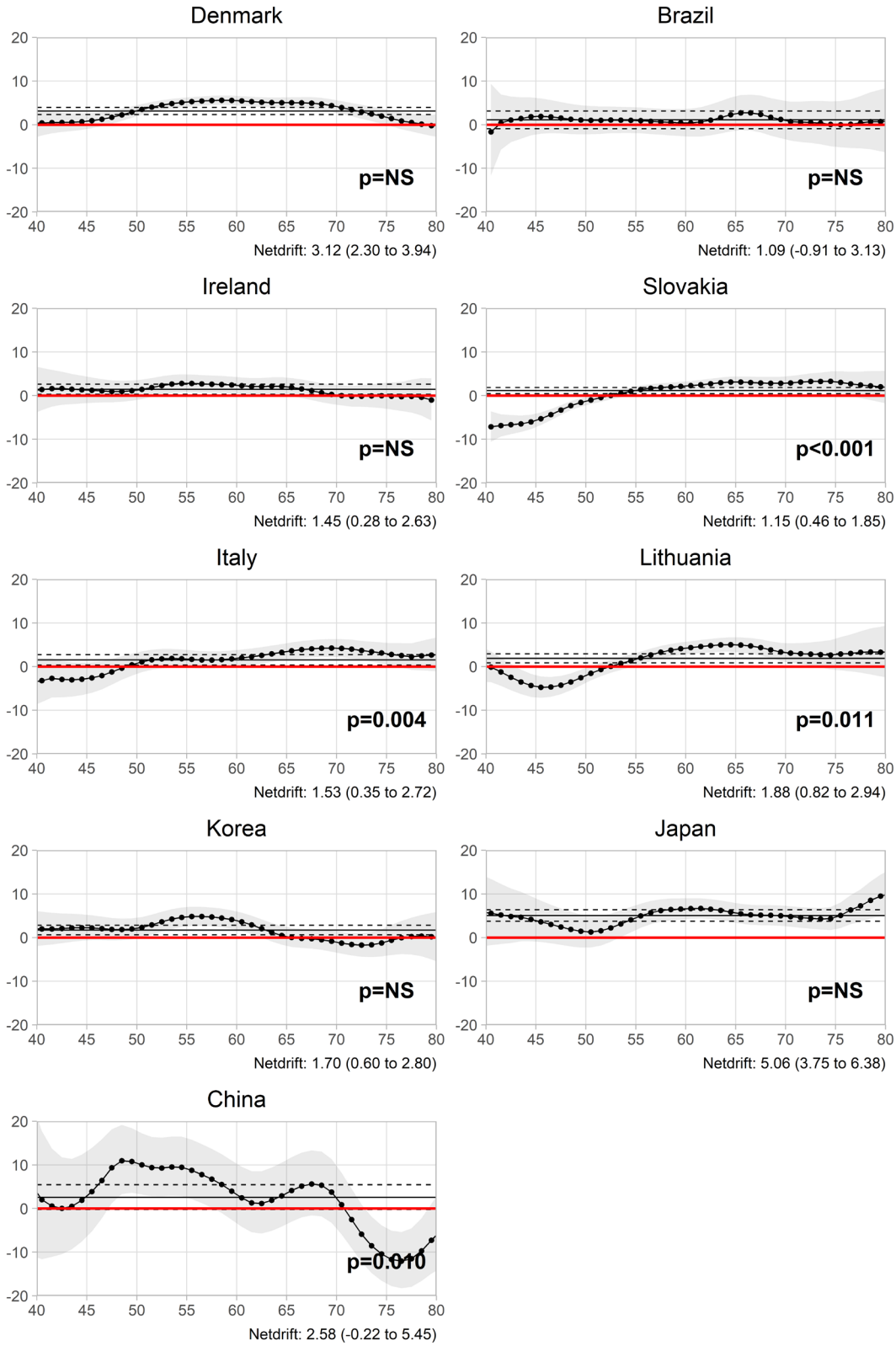
SUPPLEMENTARY FIGURE 6. Cohort rate ratios for oropharyngeal cancer (OPC) in men in countries with significant increases in OPC. P-values represent the heterogeneity in cohort rate ratios over time, with the year 1945 as a reference. NS, non-significant ($P>0.05$).



SUPPLEMENTARY FIGURE 7. Age-specific local drifts in oropharyngeal cancer incidence by age in men for countries with significant increases in oropharyngeal cancer incidence. P-values represent the heterogeneity in age-specific local drifts versus the overall net drift for a given country. NS, non-significant ($P>0.05$).

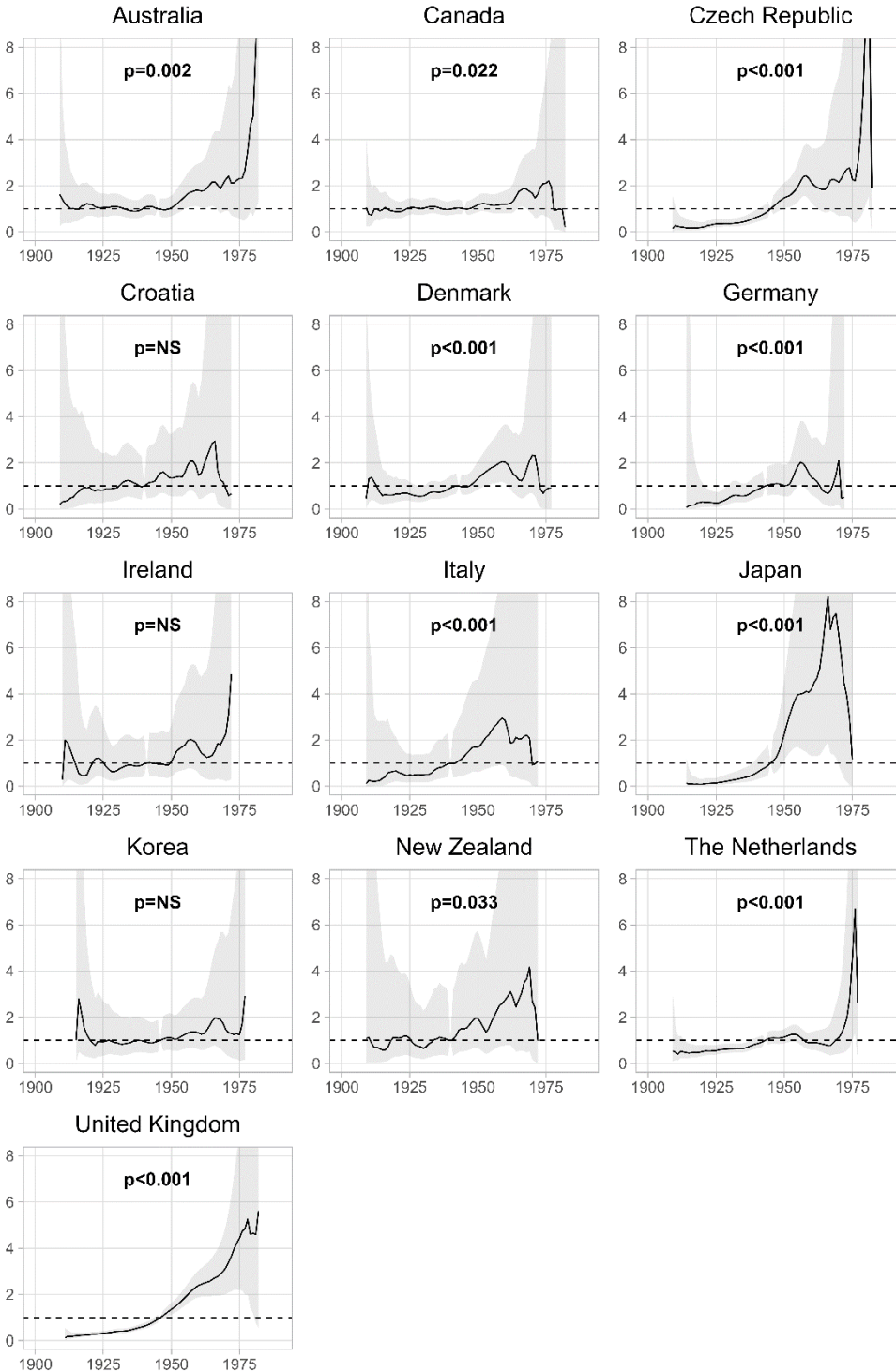


SUPPLEMENTARY FIGURE 7. Cont'd.



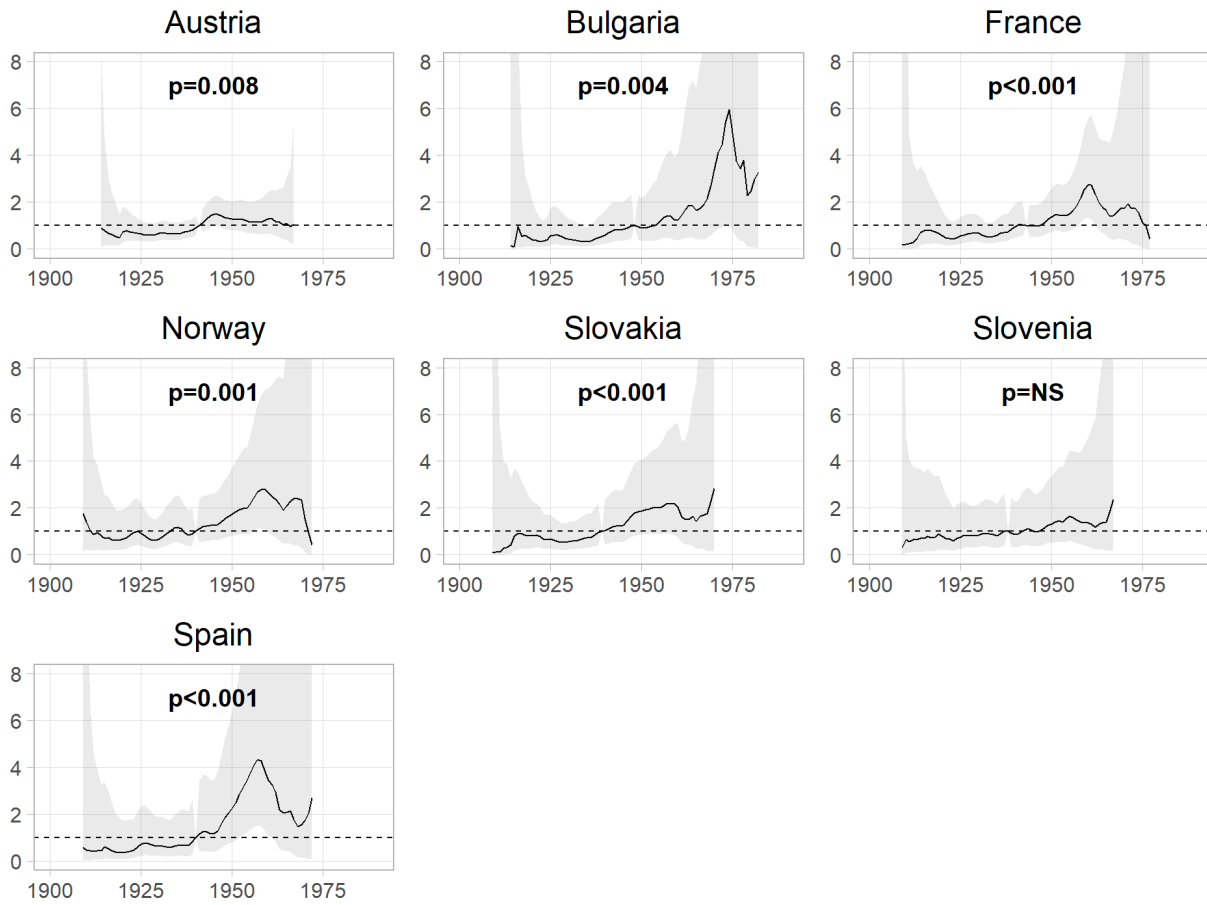
SUPPLEMENTARY FIGURE 8. Cohort rate ratios for oropharyngeal cancer (OPC) in women in countries with significant increases in OPC and A) stable or negative lung squamous cell carcinoma net drift or B) positive lung squamous cell carcinoma net drift. P-values represent the heterogeneity in cohort rate ratios over time, with the year 1945 as a reference. NS, non-significant ($P > 0.05$).

A)



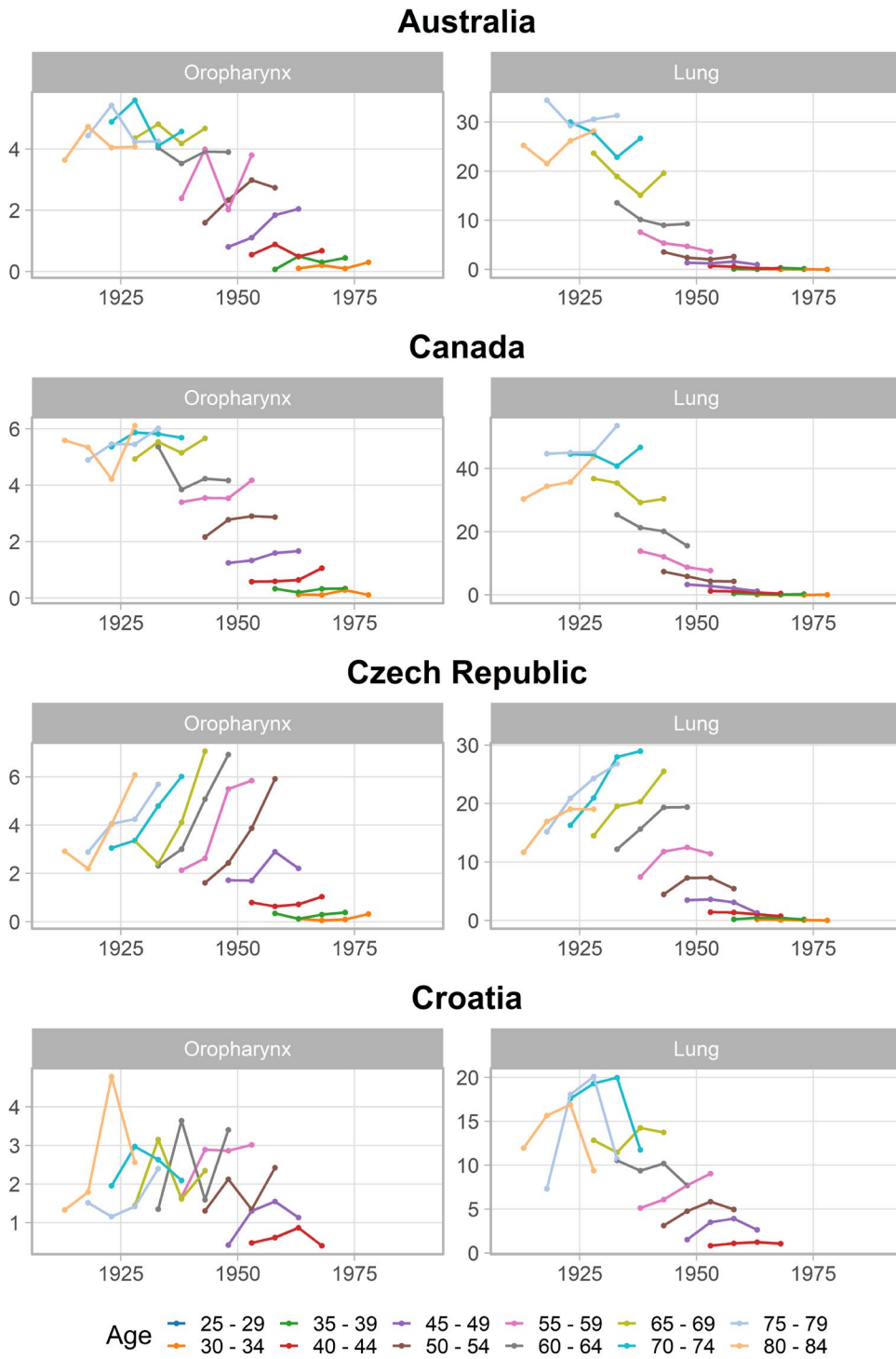
SUPPLEMENTARY FIGURE 8. Cont'd.

B)



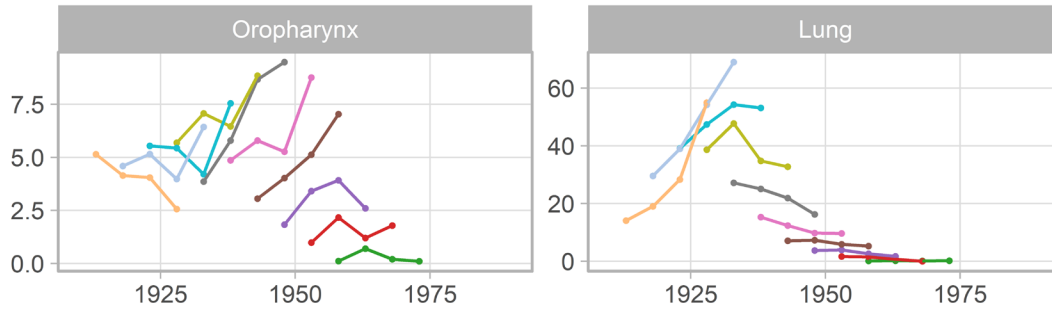
SUPPLEMENTARY FIGURE 9. Birth cohort and age effects in oropharyngeal cancer incidence in women for countries with significant increases in oropharyngeal cancer incidence and A) negative or not significantly positive and B) positive net drifts for lung squamous cell carcinoma.

A)

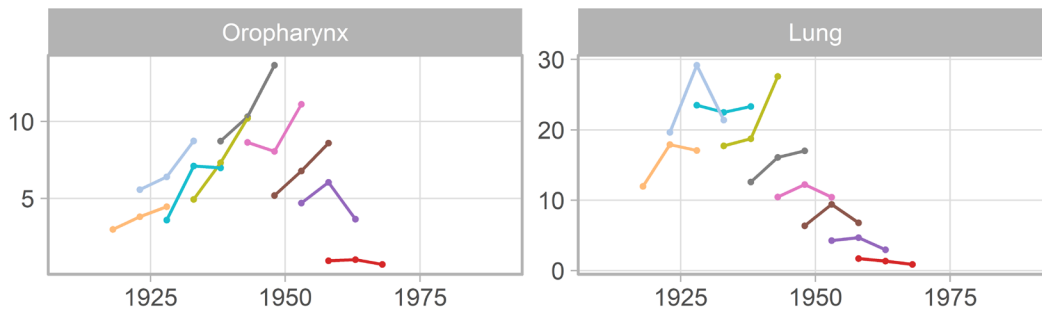


SUPPLEMENTARY FIGURE 9A. Cont'd.

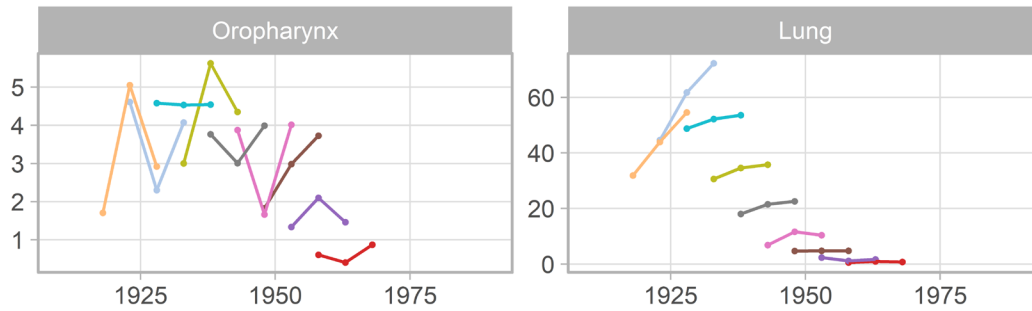
Denmark



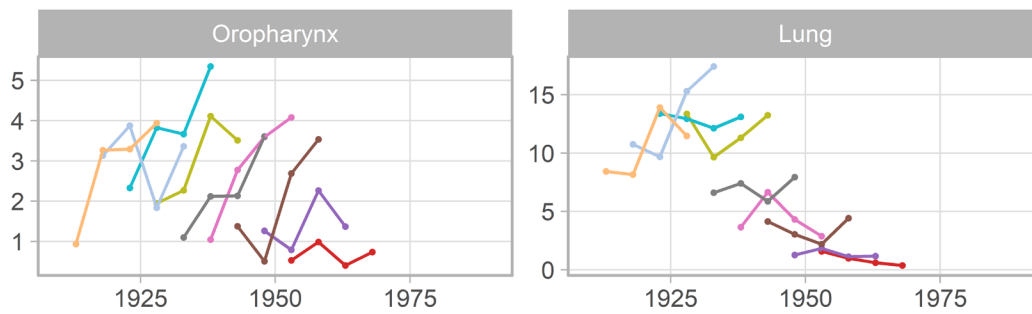
Germany



Ireland



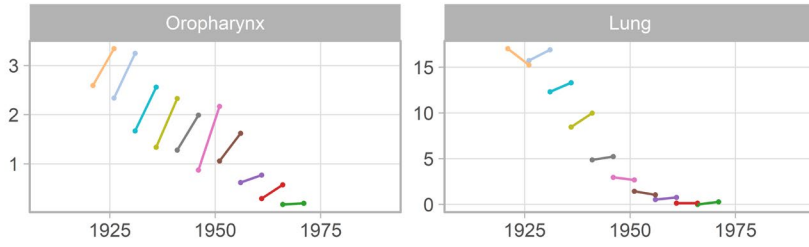
Italy



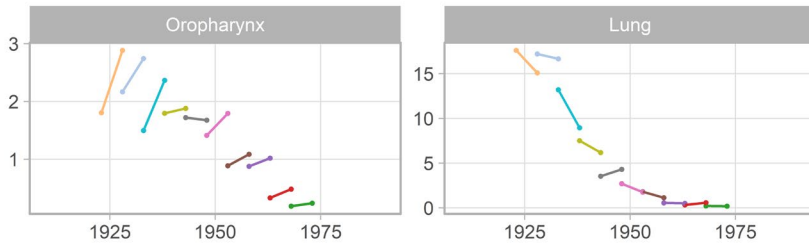
Age — 25 - 29 — 35 - 39 — 45 - 49 — 55 - 59 — 65 - 69 — 75 - 79
 — 30 - 34 — 40 - 44 — 50 - 54 — 60 - 64 — 70 - 74 — 80 - 84

SUPPLEMENTARY FIGURE 9A. Cont'd.

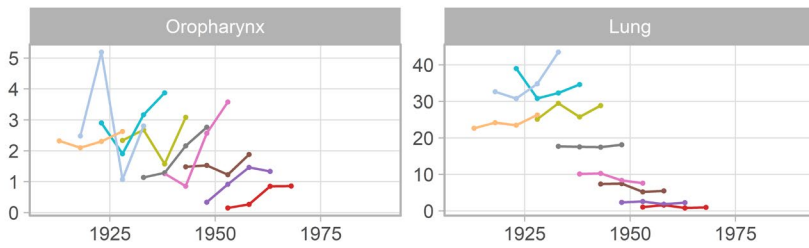
Japan



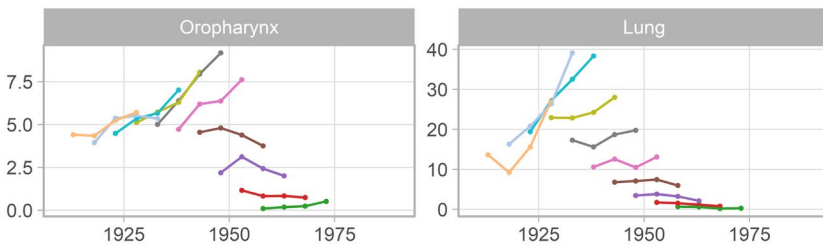
Korea



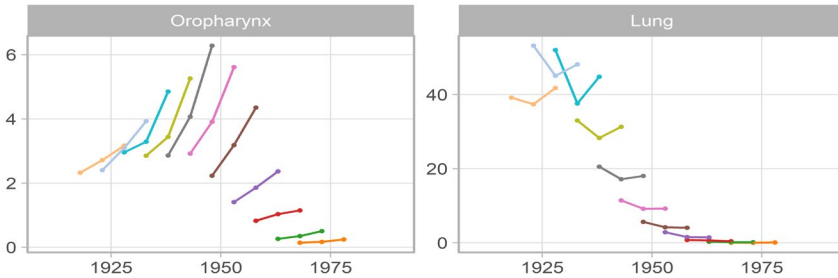
New Zealand



The Netherlands



United Kingdom

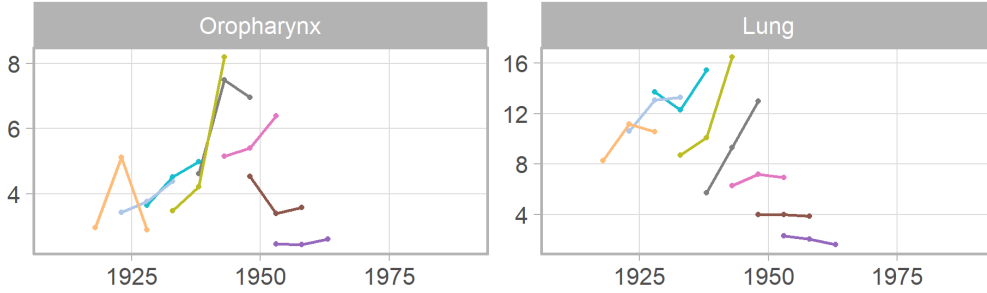


Age — 25 - 29 — 35 - 39 — 45 - 49 — 55 - 59 — 65 - 69 — 75 - 79
 — 30 - 34 — 40 - 44 — 50 - 54 — 60 - 64 — 70 - 74 — 80 - 84

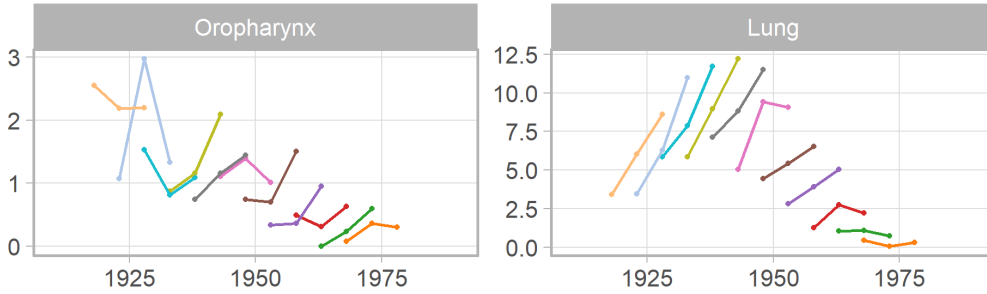
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B)

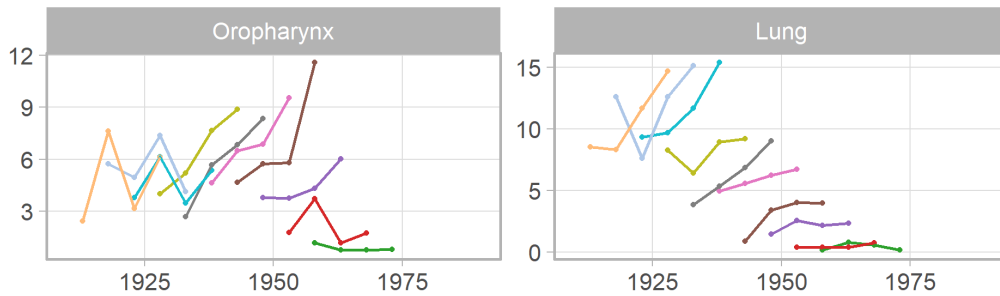
Austria



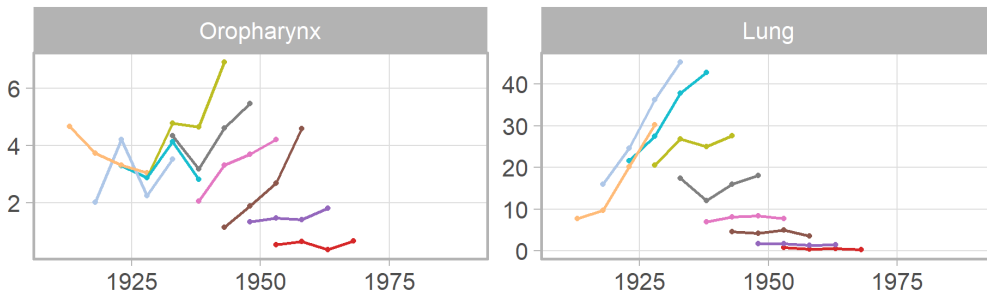
Bulgaria



France



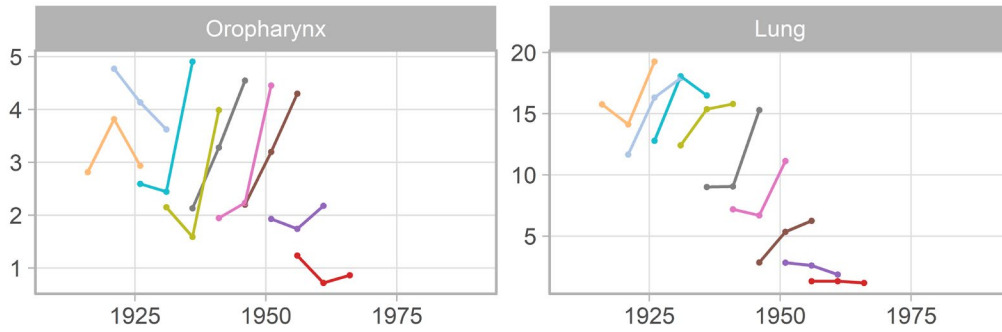
Norway



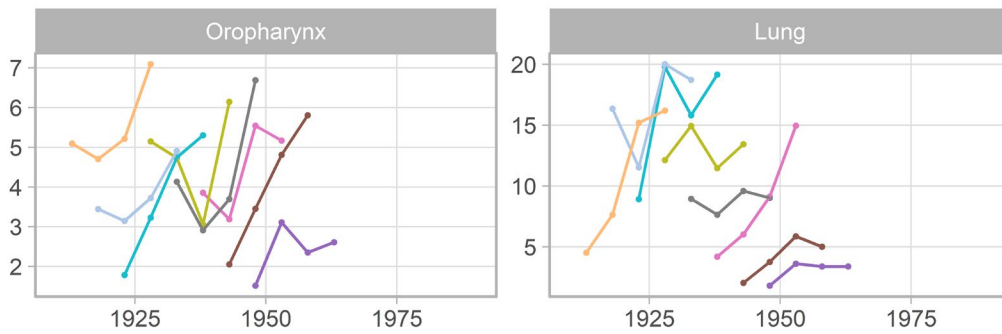
Age — 25 - 29 — 35 - 39 — 45 - 49 — 55 - 59 — 65 - 69 — 75 - 79
 — 30 - 34 — 40 - 44 — 50 - 54 — 60 - 64 — 70 - 74 — 80 - 84

SUPPLEMENTARY FIGURE 9B. Cont'd.

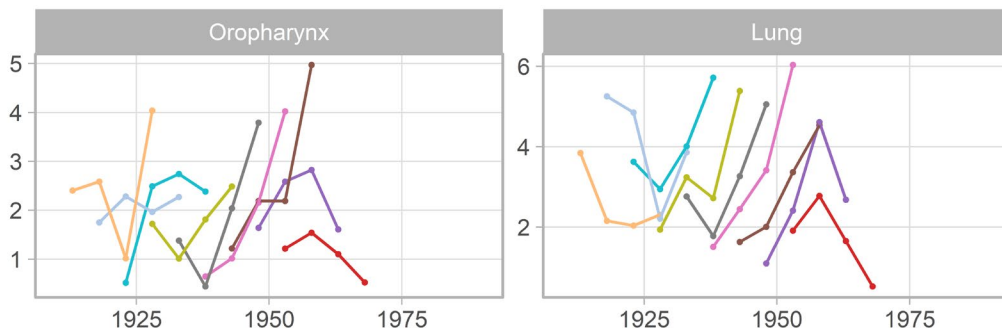
Slovakia



Slovenia

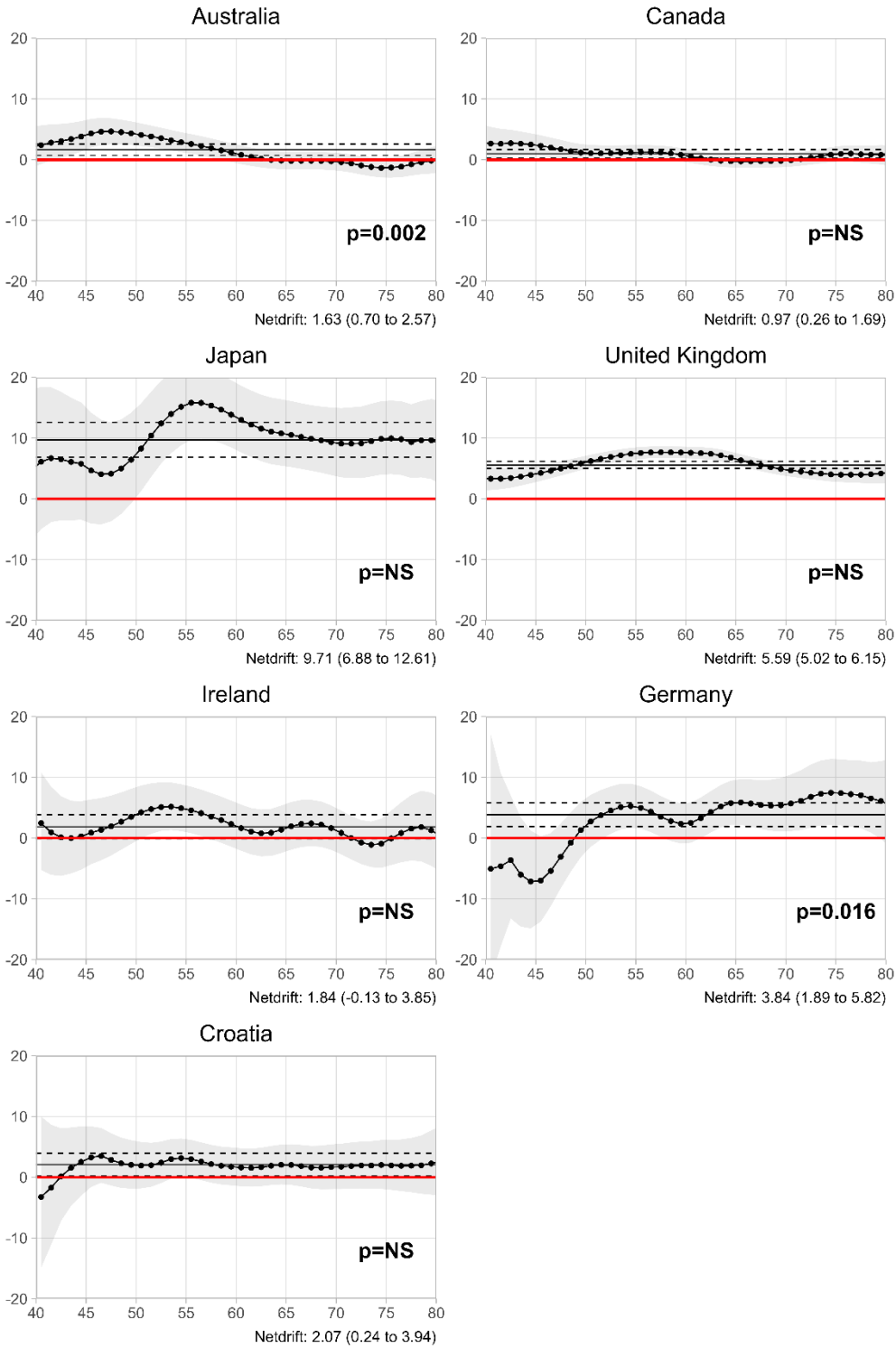


Spain

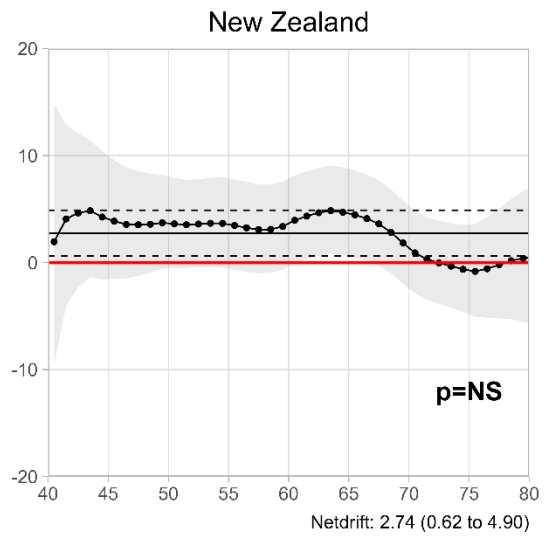
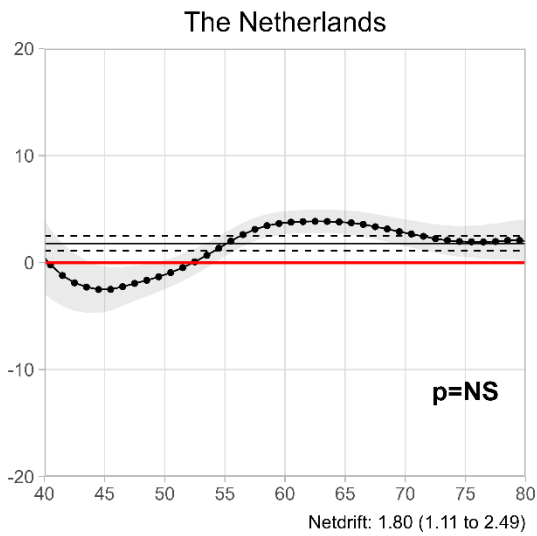
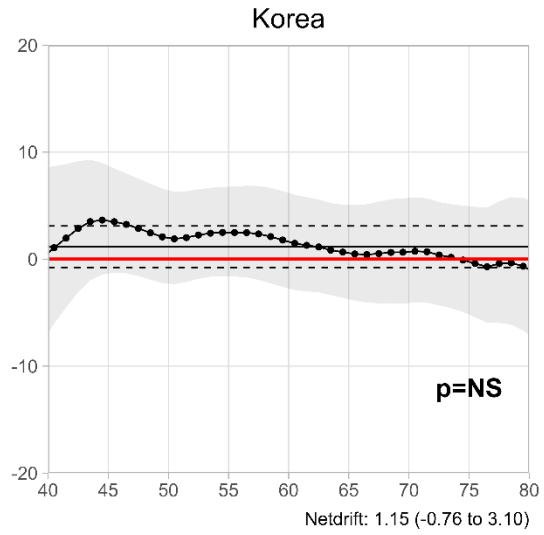
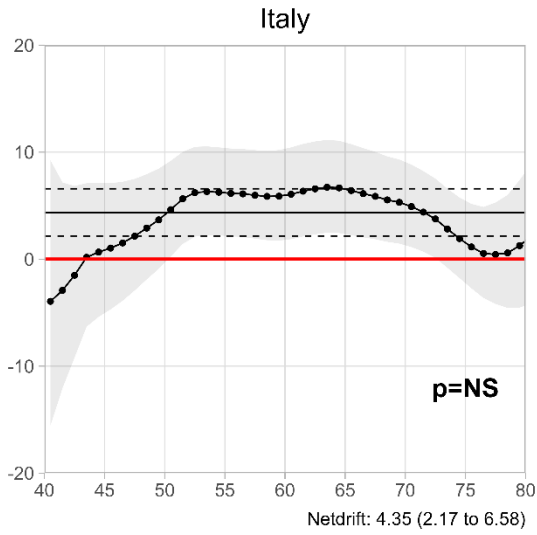
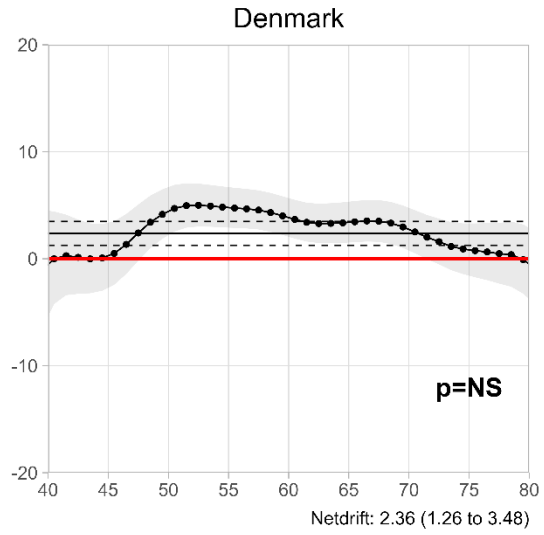
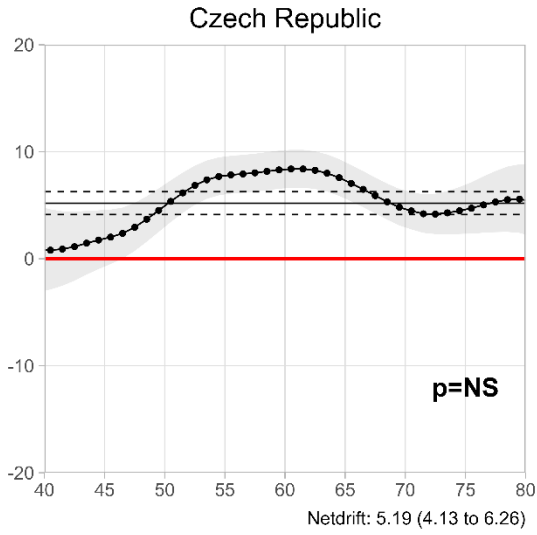


Age 25 - 29 35 - 39 45 - 49 55 - 59 65 - 69 75 - 79
 30 - 34 40 - 44 50 - 54 60 - 64 70 - 74 80 - 84

SUPPLEMENTARY FIGURE 10. Age-specific local drifts in oropharyngeal cancer incidence by age in women for countries with significant increases in oropharyngeal cancer incidence. NS, non-significant ($P>0.05$). P-values represent the heterogeneity in age-specific local drifts versus the overall net drift for a given country.



SUPPLEMENTARY FIGURE 10. Cont'd.



SUPPLEMENTARY FIGURE 10. Cont'd.

