

Does use of flue-cured rather than blended cigarettes affect international variation in mortality from lung cancer and COPD?

Relative risk estimates for current and ex smoking
for lung cancer and for COPD

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The paper by Lee *et al* on flue-cured and blended cigarettes presents summary relative risk estimates for current smoking and for ex smoking, but does not give the individual study estimates. These are presented in Table 1 (lung cancer) and Table 2 (COPD).

As described in the paper, the relative risks for current and ex-smoking for lung cancer were taken from the International Evidence on Smoking and Lung Cancer (IESLC) database^{1,2} which was based on data for all epidemiological lung cancer studies with over 100 cases published by the year 2000. All the estimates selected related to the relevant period, were for all lung cancer types and all ages combined, were sex-specific, and were not by amount smoked. There were a total of 80 estimates for the current smoking relative risk and 80 for the ex-smoking relative risk. Summary relative risks by period were used in the paper and Table 1 therefore separates the data by period.

Also as described in the paper, relative risks for COPD were derived from a literature search. Attention was limited to age-adjusted estimates for COPD mortality based on prospective studies, as preliminary work showed that results from cross-sectional or case-control studies led to extremely variable estimates. Although this preliminary work used data from earlier studies, only six studies³⁻⁸ were found which related to the relevant countries and period, these providing 11 sex-specific relative risk estimates for current smoking and 10 for ex-smoking. Here summary relative risks were not separately calculated by period.

TABLE 1 Relative risk estimates for lung cancer for current and ex smoking

<u>Study/Ref</u>	<u>Sex</u>	<u>Product</u>	<u>Denominator</u>	<u>Cig type</u>	<u>RR</u>	<u>RRL</u>	<u>RRU</u>
<u>Current smoking – study mid year 1970-79</u>							
ALDERS ⁹	m	Cigs +	never smoker	Flue cured	14.29	8.23	24.81
DEAN3 ¹⁰	m	Cigs +	never smoker	Flue cured	7.04	4.60	10.77
GILLIS ¹¹	m	Cigs +	never smoker	Flue cured	6.56	3.72	11.56
GREGOR ¹²	m	Cigs +	never cigarettes	Flue cured	1.29	0.53	3.18
MIGRAN ¹³	m	Cigs +	never smoker	Flue cured	7.89	2.92	21.31
WIGLE ¹⁴	m	Cigs only	never smoker	Flue cured	12.40	7.21	21.31
AMANDU ¹⁵	m	Cigs +	never cigarettes	Blended	6.54	2.52	16.98
ARCHER ¹⁶	m	Cigs +	never cigarettes	Blended	6.15	2.71	13.96
BUFFLE ¹⁷	m	Cigs +	never smoker	Blended	11.03	4.31	28.22
CPSI ¹⁸	m	Cigs only	never smoker	Blended	12.30	10.71	14.13
ALDERS ⁹	f	Cigs only	never smoker	Flue cured	5.80	4.27	7.87
DEAN3 ¹⁰	f	Cigs only	never smoker	Flue cured	5.77	3.75	8.86
GREGOR ¹²	f	Cigs +	never cigarettes	Flue cured	14.38	1.77	116.90
MIGRAN ¹³	f	Cigs +	never smoker	Flue cured	10.12	3.57	28.74
WIGLE ¹⁴	f	Cigs +	never smoker	Flue cured	5.20	3.34	8.09
BUFFLE ¹⁷	f	Cigs +	never smoker	Blended	8.26	5.63	12.11
CPSI ¹⁸	f	Cigs only	never smoker	Blended	3.58	3.12	4.10
VUTUC ¹⁹	f	Cigs +	never cigarettes	Blended	7.84	5.46	11.25
				Overall	6.74	5.41	8.39
<u>Current smoking – study mid year 1980-89</u>							
JAIN ²⁰	m	Cigs +	never cigarettes	Flue cured	12.40	6.45	26.60
KINLEN ²¹	m	Cigs +	never smoker	Flue cured	13.97	6.65	29.34
LIDDEL ²²	m	Cigs +	never cigarettes	Flue cured	4.41	2.77	7.01
PETO ²³	m	All	never smoker	Flue cured	7.17	1.78	28.92
BECHER ²⁴	m	All	never smoker	Blended	14.90	4.52	49.09
BLOHM ²⁵	m	All	never smoker	Blended	3.20	2.48	4.12
BROWN ²⁶	m	Cigs +	never cigarettes	Blended	11.30	10.20	12.40
CHOW ²⁷	m	Cigs +	never smoker	Blended	21.46	9.38	49.10
COMSTO ²⁸	m	Cigs +	never smoker	Blended	18.11	6.37	51.48
DORANT ²⁹	m	All	never smoker	Blended	10.82	5.02	23.32
DORGAN ³⁰	m	Cigs +	never smoker	Blended	16.92	9.54	30.01
					40.93	12.17	137.66
GARSHI ³¹	m	All	never smoker	Blended	7.70	5.48	10.83
GOODMA ³²	m	Cigs +	never smoker	Blended	17.43	8.90	34.14
HEIN ³³	m	Cigs only	never smoker	Blended	22.55	3.12	163.06
HUMBLE ³⁴	m	Cigs +	never cigarettes	Blended	19.96	8.27	48.21
					15.79	3.43	72.69
KAISER ³⁵	m	Cigs +	never cigarettes	Blended	19.61	13.32	28.87
KELLER ³⁶	m	All	never smoker	Blended	13.17	11.45	15.15
					15.29	10.31	22.69
KHUDER ³⁷	m	Cigs +	never cigarettes	Blended	8.10	5.20	12.70
LAUSSM ³⁸	m	All	never smoker	Blended	5.19	3.89	6.94
NAM ³⁹	m	Cigs +	never cigarettes	Blended	8.67	5.66	13.26
OSANN ⁴⁰	m	Cigs +	never cigarettes	Blended	26.50	19.20	36.50
SCHWAR ⁴¹	m	Cigs +	never cigarettes	Blended	14.96	11.81	18.94
					9.64	6.56	14.15
WYNDE ⁴²	m	Cigs +	never smoker	Blended	16.05	12.62	20.41
HOLE ⁴³	f	All	never smoker	Flue cured	1.53	0.64	3.70
JAIN ²⁰	f	Cigs +	never cigarettes	Flue cured	16.80	9.93	30.60
BECHER ²⁴	f	All	never smoker	Blended	6.60	2.82	15.44
BROWN ²⁶	f	Cigs +	never cigarettes	Blended	13.60	12.30	15.10
COMSTO ²⁸	f	Cigs +	never smoker	Blended	13.10	6.68	25.67
DORGAN ³⁰	f	Cigs +	never smoker	Blended	12.16	8.99	16.46
					11.43	4.16	31.43
GOODMA ³²	f	Cigs +	never smoker	Blended	9.65	5.30	17.56
HUMBLE ³⁴	f	Cigs +	never cigarettes	Blended	16.72	7.44	37.61
					23.50	6.79	81.36

KAISER ³⁵	f	Cigs +	never cigarettes	Blended	6.53	4.50	9.48
KELLER ³⁶	f	All	never smoker	Blended	14.54	12.79	16.53
					11.64	8.35	16.24
NAM ³⁹	f	Cigs +	never cigarettes	Blended	10.84	7.26	16.18
OSANN ⁴⁰	f	Cigs +	never cigarettes	Blended	19.60	15.20	25.20
SCHWAR ⁴¹	f	Cigs +	never cigarettes	Blended	15.64	12.75	19.19
					17.56	11.64	26.50
WYNDE ⁴²	f	Cigs +	never cigarettes	Blended	14.63	11.90	17.99
				Overall	12.39	11.00	13.96

Current smoking – study mid year 1990-99

DARBY ⁴⁴	m	Cigs +	never smoker	Flue cured	90.98	28.96	285.90
DEKLER ⁴⁵	m	Cigs +	never smoker	Flue cured	23.79	3.32	170.45
DOLL ²⁴⁶	m	Cigs +	never smoker	Flue cured	12.20	5.77	25.82
CHANG ⁴⁷	m	Cigs +	never cigarettes	Blended	8.39	3.32	21.21
CHYOU ⁴⁸	m	Cigs +	never cigarettes	Blended	11.40	6.50	20.10
CPSII ⁴⁹	m	Cigs only	never smoker	Blended	20.25	16.37	25.05
ENSTRO ⁵⁰	m	Cigs only	never smoker	Blended	12.99	10.46	16.13
HENNEK ⁵¹	m	All	never smoker	Blended	15.38	9.69	24.42
JAHN ⁵²	m	Cigs +	never smoker	Blended	6.03	3.46	10.54
TOUSEY ⁵³	m	Cigs +	never smoker	Blended	59.20	21.00	167.30
DARBY ⁴⁴	f	Cigs +	never smoker	Flue cured	20.67	13.05	32.74
DOLL ²⁵⁴	f	Cigs only	never smoker	Flue cured	8.65	2.93	25.55
CHANG ⁴⁷	f	Cigs +	never cigarettes	Blended	5.15	2.60	10.21
CPSII ⁴⁹	f	Cigs +	never cigarettes	Blended	11.78	10.14	13.68
ENSTRO ⁵⁰	f	Cigs only	never smoker	Blended	6.95	6.01	8.04
SPEIZE ⁵⁵	f	Cigs +	never cigarettes	Blended	12.69	9.97	16.16
TOUSEY ⁵³	f	Cigs +	never smoker	Blended	30.20	16.00	57.40
				Overall	11.47	9.29	14.16

Ex smoking – study mid year 1970-79

DEAN ³¹⁰	m	Cigs only	never smoker	Flue cured	3.21	1.96	5.25
GILLIS ¹¹	m	Cigs +	never smoker	Flue cured	4.46	2.45	8.13
GREGOR ¹²	m	Cigs +	never cigarettes	Flue cured	0.72	0.28	1.86
MIGRAN ¹³	m	Cigs +	never smoker	Flue cured	2.94	1.00	8.65
WIGLE ¹⁴	m	Cigs only	never smoker	Flue cured	8.02	4.55	14.16
AMANDU ¹⁵	m	Cigs +	never cigarettes	Blended	2.13	0.62	7.29
ARCHER ¹⁶	m	Cigs +	never cigarettes	Blended	7.89	3.14	19.87
BUFFLE ¹⁷	m	Cigs +	never smoker	Blended	12.45	4.84	32.05
CPSI ¹⁸	m	Cigs only	never smoker	Blended	3.74	3.14	4.46
DEAN ³¹⁰	f	Cigs only	never smoker	Flue cured	1.17	0.51	2.69
GREGOR ¹²	f	Cigs +	never cigarettes	Flue cured	5.50	0.56	53.99
MIGRAN ¹³	f	Cigs +	never smoker	Flue cured	1.59	0.18	14.22
WIGLE ¹⁴	f	Cigs only	never smoker	Flue cured	2.03	0.99	4.19
BUFFLE ¹⁷	f	Cigs +	never smoker	Blended	5.07	3.29	7.81
CPSI ¹⁸	f	Cigs only	never smoker	Blended	1.04	0.69	1.58
VUTUC ¹⁹	f	Cigs +	never cigarettes	Blended	5.14	3.36	7.87
				Overall	3.47	2.51	4.81

Ex smoking – study mid year 1980-89

BENSHL ⁵⁶	m	Cigs +	never smoker	Flue cured	3.07	1.57	6.03
HOLE ⁴³	m	All	never smoker	Flue cured	2.69	1.16	6.23
JAIN ²⁰	m	Cigs +	never cigarettes	Flue cured	4.16	2.04	8.46
KINLEN ²¹	m	Cigs +	never smoker	Flue cured	4.88	2.26	10.56
LIDDEL ²²	m	Cigs +	never cigarettes	Flue cured	1.40	0.79	2.51
PETO ²³	m	All	never smoker	Flue cured	0.76	0.11	5.38
BECHER ²⁴	m	All	never smoker	Blended	6.52	1.93	21.96
BLOHMK ²⁵	m	All	never smoker	Blended	2.99	2.30	3.88
BROWN ²⁶	m	Cigs +	never cigarettes	Blended	7.20	6.50	7.90
CHOW ²⁷	m	Cigs +	never smoker	Blended	5.79	2.48	13.51
COMSTO ²⁸	m	Cigs +	never smoker	Blended	6.15	2.13	17.80

DORANT ²⁹	m	All	never smoker	Blended	4.30	1.98	9.36
DORGAN ³⁰	m	Cigs +	never smoker	Blended	6.36	3.58	11.30
					10.21	2.95	35.27
GARSHI ³¹	m	All	never smoker	Blended	4.04	2.84	5.74
GOODMA ³²	m	Cigs +	never smoker	Blended	5.91	2.96	11.79
HEIN ³³	m	Cigs only	never smoker	Blended	5.13	0.66	39.65
HUMBLE ³⁴	m	Cigs +	never cigarettes	Blended	7.20	3.00	17.60
					8.00	1.90	42.20
KAISER ³⁵	m	Cigs +	never cigarettes	Blended	4.65	2.84	7.64
KELLER ³⁶	m	All	never smoker	Blended	7.23	6.28	8.33
					10.58	6.99	16.04
KHUDER ³⁷	m	Cigs +	never cigarettes	Blended	7.50	4.80	11.90
LANGE ⁸	m	All	never smoker	Blended	2.10	0.70	6.00
LAUSSM ³⁸	m	All	never smoker	Blended	6.54	3.47	12.35
NAM ³⁹	m	Cigs +	never cigarettes	Blended	9.17	6.12	13.74
OSANN ⁴⁰	m	Cigs +	never cigarettes	Blended	12.20	8.80	17.00
SCHWAR ⁴¹	m	Cigs +	never cigarettes	Blended	4.70	3.74	5.90
					3.35	2.25	4.99
WYNDE ⁴²	m	Cigs +	never smoker	Blended	7.31	5.75	9.29
JAIN ²⁰	f	Cigs +	never cigarettes	Flue cured	3.54	2.04	6.13
BECHER ²⁴	f	All	never smoker	Blended	1.44	0.44	4.80
BROWN ²⁶	f	Cigs +	never cigarettes	Blended	11.60	10.40	13.00
BROWN ⁵⁷	f	All	never smoker	Blended	2.20	1.80	2.70
COMSTO ²⁸	f	Cigs +	never smoker	Blended	2.78	1.14	6.75
DORGAN ³⁰	f	Cigs +	never smoker	Blended	3.14	2.24	4.41
					3.14	0.93	10.58
GOODMA ³²	f	Cigs +	never smoker	Blended	6.12	3.02	12.42
HUMBLE ³⁴	f	Cigs +	never cigarettes	Blended	6.50	2.80	15.40
					6.30	1.50	27.80
KAISER ³⁵	f	Cigs +	never cigarettes	Blended	3.02	1.83	4.99
KELLER ³⁶	f	All	never smoker	Blended	9.10	7.85	10.54
					5.70	3.86	8.42
LANGE ⁸	f	All	never smoker	Blended	3.40	1.10	11.00
NAM ³⁹	f	Cigs +	never cigarettes	Blended	8.27	5.76	11.87
OSANN ⁴⁰	f	Cigs +	never cigarettes	Blended	8.10	6.00	11.00
SCHWAR ⁴¹	f	Cigs +	never cigarettes	Blended	4.61	3.69	5.76
					5.48	3.49	8.60
WYNDE ⁴²	f	Cigs +	never cigarettes	Blended	5.50	4.38	6.91
				Overall	6.56	5.83	7.38

Ex smoking – study mid year 1990-99

DARBY ⁴⁴	m	All	never smoker	Flue cured	32.98	10.51	103.49
DEKLER ⁴⁵	m	All	never smoker	Flue cured	10.70	1.40	81.90
DOLL ²⁵⁸	m	Cigs +	never smoker	Flue cured	4.22	1.23	14.48
CHANG ⁴⁷	m	Cigs +	never cigarettes	Blended	3.97	1.58	9.97
CHYOU ⁴⁸	m	Cigs +	never cigarettes	Blended	3.10	1.60	5.80
HENNEK ⁵¹	m	All	never smoker	Blended	3.67	2.29	5.88
JAHN ⁵²	m	Cigs +	never smoker	Blended	5.93	3.43	10.25
TOUSEY ⁵³	m	Cigs +	never smoker	Blended	13.20	4.80	36.60
DARBY ⁴⁴	f	All	never smoker	Flue cured	6.82	4.23	10.99
DOLL ²⁵⁴	f	Cigs only	never smoker	Flue cured	3.29	0.88	12.24
CHANG ⁴⁷	f	Cigs +	never cigarettes	Blended	2.14	0.95	4.83
CPSII ⁵⁹	f	Cigs +	never cigarettes	Blended	4.84	4.00	5.86
JAHN ⁶⁰	f	Cigs +	never smoker	Blended	0.30	0.06	1.53
SPEIZE ⁵⁵	f	Cigs +	never cigarettes	Blended	3.69	2.72	5.01
TOUSEY ⁵³	f	Cigs +	never smoker	Blended	9.10	4.80	17.10
				Overall	4.71	3.34	6.63

Notes

Study/Ref The six letter code is that used in IESLC. The attached reference number links to the reference of the publication from which the relative risk and 95% confidence intervals were extracted directly or were derived from data presented. For four studies, results are shown separately by race. For studies DORGAN and SCHWAR the first set of results is for whites and the second for blacks, for study KELLER the first set is for whites and the

second for non-whites, while for study HUMBLE the first set is for whites excluding hispanics and the second for hispanic whites.

Product All = smoked any product or unspecified, Cigs only = smoked cigarettes and not other products, Cigs + = smoked cigarettes and may or may not have smoked other products.

Study mid-year For case-control studies this was taken as the mid-point of the interviewing period. For cohort studies this was taken as the final follow-up date. If no information on the study period was provided, then the year of the principal publication was used.

Overall For current smoking and separately for ex smoking, inverse-variance weighted regression analysis of the logarithms of the relative risk was carried out with separate mean values fitted for the three study periods. The deviance of the models (611.2 on 77 df for current smoking and 554.7 on 77 df for ex smoking) demonstrates considerable extra-binomial variability, and the widths of the 95% CI reflect this.

TABLE 2 Relative risk estimates for COPD for current and ex smoking

<u>Study/ref</u>	<u>Country</u>	<u>Sex</u>	<u>Product</u>	<u>Denominator</u>	<u>RR</u>	<u>RL</u>	<u>RU</u>	<u>Used</u>
<u>Current smoking</u>								
PETO ²³	UK	m	Cigs +	never smoked	22.62	1.41	363.2	No
DOLL ⁵⁸	UK	m	Cigs +	never smoked	12.70	7.13	22.62	No
WALD ³	UK	m	Cigs only	never smoked	29.50	3.96	220.0	Yes
CPSI ¹⁸	USA	m	Cigs +	never smoked	11.87	9.82	14.36	No
		f	Cigs +	never smoked	5.48	4.36	6.89	No
VETERANS ⁶¹	USA	m	Cigs +	never smoked	9.00	7.78	10.41	No
TOCKMAN ⁶²	USA	m	Cigs +	never smoked	7.18	3.13	14.65	No
		f	Cigs +	never smoked	3.45	1.66	7.17	No
MARCUS ⁶³	USA	m	Cigs +	never cigarettes	2.31	1.28	4.16	No
SPEIZE ⁴	USA	m	Cigs +	never cigarettes	12.18	0.73	204.62	Yes
		f	Cigs +	never cigarettes	4.28	1.50	12.20	Yes
FRIEDMAN ⁵	USA	m	Cigs only	never smoker	10.00	3.30	30.90	Yes
		f	Cigs only	never smoker	9.00	3.00	26.60	Yes
CPSII ⁶	USA	m	Cigs only	never smoker	11.70	9.10	15.00	Yes
		f	Cigs +	never smoker	12.80	10.40	15.90	Yes
STERLING ⁷	USA	m	Unspecified	never unspecified	7.32	4.13	12.97	Yes
		f	Unspecified	never unspecified	12.63	7.64	20.88	Yes
LANGE ⁸	Denmark	m	Cigs +	never smoker	6.70	2.14	21.00	Yes
		f	Cigs +	never smoker	15.61	3.62	67.34	Yes
Overall					11.59	10.05	13.37	
<u>Ex smoking</u>								
PETO ²³	UK	m	Cigs +	never smoked	12.58	0.75	211.6	No
DOLL ⁵⁸	UK	m	Cigs +	never smoked	5.70	3.18	10.23	No
CPSI ¹⁸	USA	m	Cigs +	never smoked	7.16	5.79	8.87	No
		f	Cigs +	never smoked	3.41	2.15	5.40	No
VETERANS ⁶⁴	USA	m	Cigs +	never smoked	4.10	3.60	4.80	No
TOCKMAN ⁶²	USA	m	Cigs +	never smoked	4.99	2.08	11.96	No
		f	Cigs +	never smoked	0.83	0.11	6.34	No
MARCUS ⁶³	USA	m	Cigs +	never cigarettes	2.34	1.21	4.53	No
SPEIZE ⁴	USA	m	Cigs +	never cigarettes	11.09	0.66	186.37	Yes
		f	Cigs +	never cigarettes	3.80	1.17	12.35	Yes
FRIEDMAN ⁵	USA	m	Cigs only	never smoker	4.66	1.50	14.45	Yes
		f	Cigs only	never smoker	3.29	0.92	11.83	Yes
CPSII ⁶⁵	USA	m	Cigs only	never smoker	8.75	6.48	11.80	Yes
		f	Cigs +	never smoker	7.04	5.33	9.30	Yes
STERLING ⁷	USA	m	Unspecified	never unspecified	6.77	4.24	10.82	Yes
		f	Unspecified	never unspecified	6.14	3.82	9.85	Yes
LANGE ⁸	Denmark	m	Cigs +	never smoker	3.00	0.90	10.00	Yes
		f	Cigs +	never smoker	11.00	2.50	53.0	Yes
Overall					7.05	5.97	8.32	

Notes

Study/Ref The study code identifies the study uniquely. The attached reference number links to the reference of the publication from which the relative risk and 95% confidence intervals were extracted directly or were derived from data presented.

Product All = smoked any product or unspecified, Cigs only = smoked cigarettes and not other products, Cigs + = smoked cigarettes and may or may not have smoked other products.

Used Indicates whether estimate used in summary relative risk (Yes), or was only used in the preliminary analyses (No).

Overall As there was no evidence of heterogeneity (deviance 9.06 on 10 df for current smoking and 7.65 on 9 df for ex smoking) the overall estimate was obtained by fixed-effects meta-analysis.

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