Mentholated cigarettes and non-lung smoking related cancers in California, USA

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We sought to discover if the higher risk among men of lung cancer associated with mentholated than with plain cigarettes¹ applied as well to other smoking related cancers (upper aerodigestive: mouth, pharynx, larynx, oesophagus; pancreas, renal adenocarcinoma, other urinary tract (urothelium), cervix). In 1979–1985, 79 946 subscribers of the Kaiser Permanente Medical Care Program in northern California, age 30–89 years, completed a detailed questionnaire about smoking habits² and were followed up through 1994. We here focus on 5770 men and 5990 women (58 438 and 63 775 person years, respectively) who reported cigarette smoking currently and for at least 20 years at the time of completing the questionnaires and who were free of smoking related cancers at entry and who had recorded whether their current cigarette was mentholated.¹ Compared with never smokers (14 409 men and 25 402 women) the rate ratio (95% confidence intervals (CIs)) for all of these long term smokers, of developing any of these non-lung cancers was 3.22 (2.55, 4.08) among men, and 2.23 (1.80, 2.76) among women. These and the mentholated/plain rate ratios and confidence intervals were calculated by the Mantel-Haenszel method adjusting for age. The numbers of mentholated cigarette smokers and plain cigarette smokers were, men: 1579 and 4191, women: 2075 and 3915, respectively.

Risk was not increased among persons who currently smoked mentholated compared with plain cigarettes for all of the non-lung smoking related cancers combined or for most sites studied. Two modestly increased rate ratios had 95% confidence intervals that widely overlapped 1.0 (table 1). Results were similar when current smokers of mentholated and plain cigarettes were restricted, respectively, to persons who reported smoking mentholated ciga-

rettes for at least 10 years and for less than six months. We also looked at prostate cancer because of its higher risk among African Americans, who also select mentholated cigarettes more than the white population³ and found no statistically significant excess risk associated with mentholation, both in these analyses not controlled for race (rate ratio 1.15, CIs 0.82, 1.62) and in Cox proportional hazards regression controlling for age and race (rate ratio 1.12, CIs 0.80, 1.58).

Possible mechanisms for an increased risk of lung cancer associated with mentholation include greater inhalation of smoke because of menthol's subjective cooling or anaesthetising effects and increased absorption of carcinogens.¹ Jarvik *et al*⁴ found no greater inhalation but did observe increased absorption of carbon monoxide from mentholated cigarettes. If absorption of carcinogens were also greater, risk of smoking induced cancers at non-lung sites might be expected to increase.

Why did these findings differ from those for lung cancer?¹ Although statistical power was low for individual sites, the total number of smoking related cancers among men, 163, approximated their 160 lung cancers.¹ Cancers in more distant organs may be less influenced by the effects of mentholation on smoking topography or on the absorption of smoke components than are lung cancers. Mentholation may have cancer promoting effects on tissue of the lungs but not of other organs. This would not be simply a matter of direct versus indirect contact because direct contact also occurs with the mucosa of the mouth, pharynx and larynx, the sites of most of the upper aerodigestive cancers, which showed no association with mentholation here, or in a study of oral and pharyngeal cancer, looking at these two sites combined.⁵ Finally, the association of mentholation with lung cancer in this study population may be merely a chance finding, particularly as it was absent in women¹ and has not been replicated elsewhere.

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Table 1 Mentholated/plain rate ratios for non-lung smoking related cancers among men and women who reported smoking cigarettes for at least 20 years, based on the presence or absence of mentholation in their currently smoked cigarette. Persons with the cancer of interest at or before entry were excluded

Site	Men		Women	
	Number of cases (mentholated/plain)	Rate ratio (95% confidence intervals)	Number of cases (mentholated/plain)	Rate ratio (95% confidence intervals)
Upper aerodigestive	12/48	0.68 (0.36, 1.28)	7/20	0.70 (0.30, 1.67)
Pancreas	6/28	0.60 (0.25, 1.44)	7/19	0.76 (0.32, 1.81)
Renal adenocarcinoma	4/9	1.28 (0.39, 4.15)	1/3	0.73 (0.08, 7.00)
Other urinary tract	13/44	0.83 (0.45, 1.55)	7/21	0.71 (0.30, 1.68)
Uterine cervix	—	—	13/21	1.06 (0.53, 2.12)
All smoking related	35/128	0.76 (0.52, 1.11)	34/84	0.79 (0.53, 1.18)