UPDATE/REVIEW

Smoking and cataract: Review of causal association

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Several risk factors for the development of cataract have been identified. This review evaluates epidemiologic literature that has examined tobacco smoking as a risk factor for cataract formation using established causality criteria. Twenty-seven studies were included in this review. Evidence suggests that smoking has a 3-fold increase on the risk for incident nuclear cataract development. There was also evidence of dose response, temporal relationship, and reversibility of effect. There was limited evidence of an association between smoking and posterior subcapsular cataract, but little or no association with cortical cataract. Thus, the literature review indicated a strong association between smoking and the development of cataract, particularly nuclear cataract. The association fulfills the established criteria for causality. The association between smoking and other types of cataract is less distinct and requires further evaluation.

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Age-related cataract is usually a gradual, progressive opacification of the crystalline lens resulting in impaired visual function. The 1998 World Health Report estimated that there were over 19 million people blind from cataract, which represented 43% of global blindness.[1] The definitive management for cataract is surgical extraction with intraocular lens implantation. As yet, no medical treatment has been proven to prevent, delay, or reverse the development of cataract in otherwise healthy human eyes. Cataract causes major visual impairment among affected individuals and results in significant health resource consumption for populations and society. Identifying modifiable risk factors for cataract is thus important and may help establish preventative measures.

Increasing age is the most important risk factor for cataract, possibly because of the accumulation of lens damage with age together with an age-related decline in protection against oxidative damage in the eye.[2] Other risks for cataract include environmental factors, for example exposure to ultraviolet radiation.[3] Systemic diseases have an important role in cataract formation.[3] In some studies, high alcohol consumption was associated with increased risk for cataract,[4–8] but no association was found in other studies.[9–11] There has been considerable interest in the possible protective role of dietary antioxidants and supplements in age-related cataract, but evidence of effectiveness to date is equivocal.[3] In 2 clinical trials, high-dose antioxidant supplementation did not delay cataract formation,[12,13] but in a third study, supplementation did delay progression.[14]

Tobacco smoking is a major modifiable risk factor for many chronic diseases. This article reviews epidemiologic studies that investigated the association between smoking and cataract.

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MATERIALS AND METHODS

Medline (1966 to July 2003) and Embase (1980 to July 2003) bibliographic databases were searched using the key words *smoking* and *cataract*. Bibliographies of identified original research and review papers were checked for further relevant studies.

Studies were included in the review if they were epidemiologic studies, published in English, assessed the relationship between tobacco smoking and cataract, and included an estimate of the degree of association (usually odds ratio [OR] or relative risk [RR]).

Data were extracted on the number of patients, study design, methods of defining and measuring exposure (tobacco smoking) and outcome, and degree of adjustment for potential confounding factors. Data on outcomes included the type(s) and classification of cataract and whether cataract was defined as the presence of cataract (incidence or surgical extraction) or progression of established cataract. The definition of cataract was that used by study investigators.

The evidence of association was reviewed against a framework for assessing causality using criteria for attribution derived from Hill[15] and subsequently modified by Susser[16] (Table 1).

RESULTS

Design of Studies

Thirty-two studies that examined the association between smoking and cataract were identified from the literature search. Three studies were excluded because they did not report a measure of association such as an OR or RR for the risk of smoking and cataract.[10,17,18] The Chesapeake Bay Watermen Study did not report an OR or RR at baseline[19] but did report an OR[20] at 5-year follow-up and, therefore, both reports from this study were included.

Three study designs were used: 11 cross-sectional studies (Table 2), 9 prospective cohort studies (Table 3), and 7 case-control (Table 4). Two of the cohort studies were extensions of cross-sectional studies reporting results after 5 years of follow-up.[8,20] Another 2 of the cohort studies were analyses at different time points from the same study.[21,22] Studies originated mainly from North America (12 studies) or Europe (7 studies) or Australia (2 studies).

Table 1. Criteria for causal attribution.[15,16]

- Consistency of findings: between study types, settings, populations, and time
- Strength of association
- Evidence of dose response: greater intensity and/or duration of smoking associated with greater effect
- Evidence of reversibility: reduced risk with removal of exposure; that is, among ex-smokers compared with current smokers
- Temporal relationship: evidence that exposure preceded effect
- Biological plausibility: evidence of supporting biological evidence from animal and tissue models and other sources

The outcome measure was the presence of cataracts as defined by the investigators of each study. Most study designs consisted of patients having an ophthalmologic examination to assess the presence of cataract and completing a questionnaire or interview about their smoking status and history. The Physicians' Health Study[21] and Nurses' Health Study[23] relied on initial self-reporting of the diagnosis of cataract among patients followed by confirmation of the reported diagnosis from the patients' ophthalmologists.

Characteristics of Patients

All studies except 3[24–26] recruited patients older than 30 years; patients were mostly in their sixth and seventh decade. Some studies also included patients up to their 90s. Where reported, most studies recruited both men and women; some occupational studies recruited only men[19–22] or women.[23]

Strength and Consistency of Association Between Smoking and Cataract

For current smokers compared with never smokers or nonsmokers, 19 of the 27 publications found a positive association between smoking and 1 or more types of cataract: risk estimates for developing cataract in current smokers compared with never smokers or nonsmokers were 1.08 to 3.31.

Studies suggested a stronger association between smoking and nuclear cataract than between smoking and cortical or posterior subcapsular cataract. Fourteen of 17 studies that investigated the link between smoking and the development of nuclear cataract found a positive association: 7 cross-sectional studies with RR/OR 1.09–4.40,[7,9,19,27–30] 5 cohort studies with OR/RR 1.05–2.41,[8,21,31–33] and 2 case-control studies, OR/RR 1.68–1.99.[11,34]

Thirteen studies investigated the association between smoking and posterior subcapsular cataracts. Three cohort studies found an association between smoking and posterior subcapsular cataract at follow-up, but this association was for heavy smokers only.[21,23,33] Two studies found an association for men only[28] or for ex-smokers only.[35] The remaining 8 studies found no association. None of the 12 studies that investigated smoking and the development of cortical cataracts found a positive association.

Most studies considered only cigarette smoking. Flaye et al.[9] found too few pipe smokers and cigar smokers to warrant a separate analysis and classified these patients as nonsmokers. Two studies included pipe and cigar smokers and calculated separate values for the association with cataract.[7,35] In the Blue Mountains Eye Study,[35] pipe smoking was more strongly associated with nuclear cataract than cigarette smoking. In the Reykjavik Eye Study,[7] the OR for development of cataract in pipe and cigar smokers compared with

nonsmokers was 2.48 (95% confidence interval [CI], 1.20 to 5.12, $P = .014$).

Of the 8 reports that find no association between smoking and cataract or were inconclusive, 4[24,29,35,36] were cross-sectional studies—the weakest of the study types included for establishing causality. Furthermore, 2 of these studies only assessed the association between cataract in ever smokers compared with never smokers or nonsmokers,[24,29] a crude method of exposure assessment with a high risk of misclassification, and hence of biasing estimates of association toward the null.

Of the 3 case-control studies[26,37,38] that did not find a positive association, 1 Nigerian study was both inconclusive and limited by very small numbers.[26] Another study apparently found a protective effect of being a current-smoker or ex-smoker (compared with a never smoker) in Japanese men and a null effect in women.[37] However, the approach was flawed by making comparisons with smokers and ex-smokers combined, making no adjustment for potential confounders, and having very small numbers in the never smoker group, making estimates unstable. In addition, there was no indication of how heavily or for how long smokers had smoked and duration (and probably intensity) of smoking are likely to be low among women smokers in a society where women smoking is rare (7.9% of female controls in this study) and until recently socially unacceptable. Furthermore, there was a paucity of nuclear cataracts (the cataract type most strongly associated with smoking) included in this study (2.4%). Finally the OR (calculated by the authors of this review) for current smokers compared with never and ex-smokers combined in men was 1.07 (95% CI, 0.54 to 2.12), showing a null rather than protective effect of current smoking.

No association with current smoking was found in a large case-control study from Scotland,[38] although a nonsignificant increase in risk for cataract among heavy smokers (>30/day, OR, 1.46; 95% CI, 0.89 to 2.39) was reported. The authors noted that the use of prevalent cases meant that the possibility of changes in smoking status after diagnosis obscuring associations could not be ruled out.

Only 1 prospective cohort study[25] restricted to diabetic patients attending hospital clinics in Nottingham, United Kingdom, did not report an association between cataract and smoking. It is possible an association could have been missed in this study as smoking was categorised into current/ex/never smokers at baseline only and so the effect of subsequent changes in smoking behavior could not be incorporated. Drop out in cohort studies like this one might also cause bias. This could occur if smokers at the highest risk for developing cataract (eg, the heaviest smokers and smokers with multiple risk factors for coronary heart and neoplastic disease) were also those at highest risk of drop out because of serious ill health or death. This would result in the selective loss to the study of smokers at highest risk for cataract, leading to a reduction in the observed association between cataract and smoking. Whether differential loss to follow-up because of death or illness was a cause of bias is not clear, particularly as the authors did not have data on intensity or duration of smoking. However, it is highly plausible, especially as other studies that did investigate for a dose response all found it to be present (see below). There is a mass of evidence in prospective studies that smokers have greatly increased mortality and morbidity, and this is greatest in heavy and prolonged smokers, so selective loss to follow-up is highly plausible.

Temporal Relationship

Prospective cohort studies are best placed to demonstrate that smoking preceded the development of cataract. Reports of analyses from 7 of 9 prospective cohort studies following patients for up to 16 years (Table 3) confirmed an association between smoking and cataract thus providing evidence of a temporal relationship.[8,20,21,23,31–33] The association was strongest for nuclear cataract. For example, the increased risk for nuclear cataract for smokers found at baseline was maintained at 5-year follow up in the Beaver Dam Eye Study.[8] The Physicians' Health Study[21] observed an association between smoking and any type of cataract (RR, 2.16; 95% CI, 1.46 to 3.20), nuclear cataract (RR, 2.41; 95% CI, 1.59 to 3.66) and posterior subcapsular cataract (RR, 3.31; 95% CI, 1.91 to 5.71) at 5-year follow-up in heavy smokers. Follow-up of patients in the Chesapeake Waterman Study found an association of smoking with the progression of cataracts but not with the incidence of cataracts.[20]

Dose-Response Effect of Smoking

The association between degree or quantity of smoking and the development of cataract was assessed in 9 publications.[7,9,19,21,23,27,30,31,33,39] All these studies observed a dose-response effect. The Physicians' Health Study[21] observed an association between smoking and any type of cataract, nuclear cataract, and posterior subcapsular cataract at 5-year follow-up in heavy smokers (≥20 cigarettes/day) but there was no association for lighter smokers (<20 cigarettes/day). In the 8-year follow-up of the Nurses' Health Study,[23] associations between smoking and any type of cataract and posterior subcapsular cataract were observed in heavy smokers (≥65 pack-years) but not in lighter smokers. Weintraub et al.[33] noted a highly significant trend in the risk for nuclear cataract, posterior subcapsular cataract, and any type of cataract with pack years smoking after 16 years follow-up. Further analysis

Table 2. Cross-sectional studies examining the association between smoking and cataract.

Study	Patients	Cataract Type	Relative Risk or Odds Ratio (95% CI)
City Eye Study,[9] UK	1029	Nuclear	Light current smokers vs nonsmokers RR = 2.54 (1.63 to 3.97) Moderate current smokers vs nonsmokers RR = 2.66 (1.63 to 4.33) Heavy current smokers vs nonsmokers RR = 2.88 (1.4 to 5.85)
Chesapeake Bay Watermen Study,[19] USA	838	Nuclear	Cumulative dose of smoking Regression coefficient = 0.009, $P<.004$
		Cortical	Cumulative dose of smoking Regression coefficient = 0.002, NS
		Posterior subcapsular	Cumulative dose of smoking Regression coefficient = 0.012, $P = .063$
Beaver Dam Eye Study,[28] USA	4926	Nuclear	Current smokers per 10 pack years M OR = 1.09 (1.05 to 1.14) F OR = 1.09 (1.04 to 1.16)
		Cortical	Current smokers per 10 pack years M OR = 1.00 (0.97 to 1.05) F OR = 1.02 (0.96 to 1.07)
		Posterior subcapsular	Current smokers 10 pack years M OR = 1.05 (1.01 to 1.11) F OR = 1.06 (0.98 to 1.14)
		Surgery	Current smokers 10 pack years F OR = 1.12 (1.03 to 1.20) M OR = 1.08 (1.04 to 1.14)
Polynesia[24]	4056	Any cataract	Ever smokers vs nonsmokers OR = 1.24 (0.79 to 1.92)
Finland[29]	500	Nuclear	Ever smokers vs never smokers 70 to 74 y M RR = 4.40, F RR = 0.76 75 to 79 y M RR = 0.71, F RR = 0.9 80 to 84 y M RR = 1.65, F RR = 0.7
		Cortical	Ever smokers vs never smokers 70 to 74 y M RR = 1.79, F RR = 0.33 75 to 79 y M RR = 0.44, F RR = 1.60 80 to 84 y M RR = 0.68, F RR = 0.69
Blue Mountains Study, Australia[35]	3654	Nuclear	Current smokers vs never smokers OR = 1.3 (0.9 to 2.0)
		Cortical	Current smokers vs never smokers OR = 1.0 (0.8 to 1.4)
		Posterior subcapsular	Current smokers vs never smokers OR = 1.2 (0.7 to 2.0)
		Cataract surgery	Current smokers vs never smokers OR = 1.1 (0.6 to 2.0)
Visual Impairment Project, Australia[27,39]	4744	Nuclear	Current smokers >30 pack years OR = 1.87 (1.43 to 2.44)
POLA Study, France[40]	2468	Nuclear	Current smokers vs nonsmokers OR = 1.91 (0.98 to 3.71)
		Surgery	Current smokers vs nonsmokers OR = 2.34 (1.07 to 5.15)
Taiwan[36]	2038	Nuclear	Current smokers vs nonsmokers OR = 1.32 (0.99 to 1.77), $P = .055$
		Cortical	Current smokers vs nonsmokers OR = 0.95 (0.59 to 1.54), $P = .846$
		Posterior subcapsular	Current smokers vs nonsmokers OR = 0.98 (0.68 to 1.43), $P = .932$

Table 2 (cont.)

Study	Patients	Cataract Type	Relative Risk or Odds Ratio (95% CI)
Reykjavik Eye Study, Iceland[7,56]	1045	Nuclear	<20 pack years: RR = 1.41 (0.83 to 2.38), P = .199 >20 pack years: RR = 2.52 (1.52 to 4.13), P<.001
Tanjong Pagar Study, Singapore[30]	1206	Nuclear	Current smokers >10/day vs nonsmokers: OR = 2.3 (1.4 to 3.7), P = .001 Current smokers ≤10/day vs nonsmokers: OR = 1.5 (0.6 to 3.7), P = .36
		Cortical	Current smokers >10/day vs nonsmokers: OR = 1.5 (0.9 to 2.3), P = .08 Current smokers ≤10/day vs nonsmokers: OR = 0.9 (0.4 to 1.9), P = .71
		Posterior subcapsular	Current smokers >10/day vs nonsmokers: OR = 1.3 (0.7 to 2.3), P = .42 Current smokers ≤10/day vs nonsmokers: OR = 0.6 (0.2 to 1.7), P = .33
		Any cataract	Current smokers >10/day vs nonsmokers: OR = 1.8 (1.1 to 3.0), P = .02 Current smokers ≤10/day vs nonsmokers: OR = 1.6 (0.6 to 4.4), P = .36
		Surgery	Current smokers >10/day vs nonsmokers: OR = 0.7 (0.3 to 1.4), P = .30 Current smokers ≤10/day vs nonsmokers: OR = 1.6 (0.8 to 3.4)

CI = confidence interval; OR = odds ratio; RR = risk ratio

suggested that significantly increased risk for cataract was confined to heavier smokers (≥15 cigarettes/day). In the Chesapeake Bay Waterman study,[19] the age-adjusted prevalence of nuclear opacities was highest in those who had begun smoking before 16 years of age. In addition, the severity of nuclear opacification was found to increase with increasing cigarette consumption (P<.001).

Reversibility: What Is the Effect of Stopping Smoking?

Twelve studies assessed the risk for developing cataract in ex-smokers.[9,19–23,25,26,33,35,37,40] Compared with never smokers, ex-smokers generally also had an increased risk for cataract. The effects of smoking cessation on the incidence of cataract were specifically examined in 2 large U.S. prospective cohort studies. In the Physicians Health Study,[22] ex-smokers had a reduced risk for developing cataract compared with current smokers, and this risk was greater than for never smokers. Thus, compared with current smokers, relative risks in patients who stopped smoking <10 years, 10 to 20 years, and ≥20 years before the study were 0.79 (95% CI, 0.64 to 0.98), 0.73 (95% CI, 0.61 to 0.88), and 0.74 (95% CI, 0.63 to 0.87), respectively. In comparison, the relative risk for never smokers compared with current smokers was 0.64 (95% CI, 0.54 to 0.76). Weintraub et al.[33] pooled results from the Nurses' Health Study and the Health Professionals' Follow-up Study and observed that compared with current smokers, ex-smokers who had stopped smoking >25 years previously had a 20% lower risk for extraction of all types of cataract (RR, 0.80, 95% CI, 0.71 to 0.91). The risk in past smokers did not decrease to the levels seen among never smokers (RR, 0.64 95% CI, 0.52 to 0.79). These 2 studies suggest that smoking cessation reduces the risk for cataract; the effect of cessation takes some time and may only be partial.

Using regression analysis, West et al.[19] observed that there was a lower prevalence of cataracts in ex-smokers who had stopped more than 10 years previously (OR, 0.67; 95% CI, 0.49 to 0.92) compared with those who stopped fewer than 10 years previously (OR, 0.76; 95% CI, 0.51 to 1.13) suggesting that the damage to the lens caused by smoking may be partially reversible. The Nurses' Health Study[23] examined the effect of intensity of past smoking on cataract extraction. For current smokers compared with nonsmokers the RR was 1.16 (95% CI, 0.94 to 1.42). Compared with nonsmokers, the RR was 0.95 (95% CI, 0.70 to 1.29) for ex-smokers of 1 to 14 cigarettes per day, 0.82 (95% CI, 0.56 to 1.19) for 15 to 24 cigarettes per day, 1.12 (95% CI, 0.64 to 1.97) for 25 to 34 cigarettes per day, and 1.68 (95% CI,

Table 3. Prospective cohort studies examining the association between smoking and cataract.

Study	Patients	Follow-up	Cataract Type	Relative Risk or Odds Ratio (95% CI)
Physicians' Health Study,[21] USA	17 824	5 years	All cataract	Current smokers <20/day vs never smokers: RR = 0.94 (0.48 to 1.86) Currentsmokers ≥20/day vs never smokers: RR = 2.05 (1.38 to 3.05)
			Nuclear	Current smokers ≥20/day vs never smokers: RR = 2.24 (1.47 to 3.41)
			Posterior subcapsular	Current smokers ≥20/day vs never smokers: RR = 3.17 (1.81 to 5.53)
Nurses' Health Study,[23] USA	98 462	8 years	All cataract	Current smokers ≥65 pack-years vs nonsmokers: RR = 1.58 (1.13 to 2.19), P = .03
			Nuclear	Current smokers ≥65 pack-years vs nonsmokers: RR = 1.79 (0.83 to 3.88), P = .72
			Posterior subcapsular	Current smokers ≥65 pack-years vs nonsmokers: RR = 2.59 (1.49 to 4.50), P = .005
Chesapeake Bay Watermen Study,[20] USA	442	5 years	Incidence	Current smokers vs nonsmokers OR = 1.26 (0.26 to 6.09)
			Progression	Current smokers vs non- and ex-smokers OR = 2.45 (1.00 to 6.04)
Framingham Eye Study,[31] USA	660	12.5 years	Nuclear	Light smoker vs never smoker OR = 1.57 (1.07 to 2.31), P<0.05 Heavy smoker vs never smoker OR = 2.14 (1.31 to 3.50), P<0.05
			Cortical	Light smokers vs never smokers OR = 1.20 (0.80 to 1.80) Heavy smokers vs never smokers OR = 0.95 (0.55 to 1.64)
			Posterior subcapsular	Light smokers vs never smokers OR = 0.88 (0.52 to 1.51) Heavy smokers vs never smokers OR = 1.13 (0.58 to 2.2)
Longitudinal Study of Cataract,[32] USA	764	Median 4.8 years	Nuclear	Current smokers vs nonsmokers RR = 1.58 (1.06 to 2.35), P<.05
Beaver Dam Eye Study,[8] USA	3684	5 years	Nuclear	Smoking/10 pack years OR = 1.05 (1.01 to 1.09), P = .02
			Cortical	Smoking/10 pack years OR = 1.03 (0.99 to 1.07), P = .14
			Posterior capsular	Smoking/10 pack years OR = 1.04 (0.99 to 1.10), P = .15
Nottingham, UK[25]	3606 patients with diabetes	Mean 5 years	Any cataract	Current smokers vs never smokers RR = 1.06 (0.83 to 1.35)
Physicians' Health Study,[22] USA	20 907 M	Mean 13.6 years	Any cataract	Never smokers vs current smokers OR = 0.64 (0.54 to 0.76)
			Surgery	Never smokers vs current smokers OR = 0.65 (0.53 to 0.79)
Nurses Health Study and Health Professionals Follow-up study,[33] USA	124 690	F 16 years M 10 years	Any cataract	Current smokers 1–14/day vs never smokers RR = 1.12 (0.75 to 1.68) Current smokers ≥15/day vs never smokers RR = 1.53 (1.39 to 1.69)

Table 3 (cont.)

Study	Patients	Follow-up	Cataract Type	Relative Risk or Odds Ratio (95% CI)
			Nuclear	Current smokers 1–14/day vs never smokers RR = 1.09 (0.50 to 2.36) Current smokers ≥15/day vs never smokers RR = 1.61 (1.40 to 1.84)
			Posterior subcapsular	Current smokers 1–14/day vs never smokers RR = 0.85 (0.56 to 1.29) Current smokers ≥15/day vs never smokers RR = 1.58 (1.33 to 1.87)

CI = confidence interval; OR = odds ratio; RR = risk ratio

1.04 to 2.72) for ≥35 cigarettes per day. This suggests that the greater the intensity of previous smoking, the longer it takes for the increased risk to decline.

DISCUSSION

This review provides evidence that cigarette smoking is associated with cataract formation and that this association fulfils 5 of the 6 criteria for the attribution of causality.[15,16] There is also additional evidence to fulfil the sixth criteria; that is, a plausible biological mechanism of action of smoking and cataract. Oxidative damage appears to play a major role in cataract formation,[2,41] and smoking causes oxidative stress through reducing endogenous levels of antioxidants.[42] Smoking may indirectly impose additional oxidative stress on the lens through reducing the levels of systemic antioxidants. Furthermore, tobacco smoke contains heavy metals such as cadmium, lead and copper, which both accumulate in the lens and cause direct toxicity.[43–46] In an in vitro study,[47] cigarette smoke was found to be directly toxic to the lens.

The epidemiologic evidence is strongest for nuclear cataract, with current smokers being up to 2.9 times more likely to develop this condition. As increasing numbers of cigarettes are smoked, the risk for cataract increases, suggesting a dose response between smoking and cataract. Prospective cohort studies demonstrate that exposure to smoking precedes the development of cataract. Importantly, ex-smokers generally have a lower risk for cataract, particularly after prolonged quitting, demonstrating partial reversibility of effect.

The evidence of an association of smoking with other types of cataract is less convincing. The weaker association with both cortical and posterior subcapsular cataract may be a result of different pathophysiologic processes in these situations, suggesting that risk factors for different types of cataract should be investigated separately.

There are several limitations to this review. A crucial issue in assessing evidence for an association between an exposure and outcome is to examine the possible influence of confounding factors. Problems arise if other known, or

Table 4. Case-control studies examining the association between smoking and cataract.

Study	Cases	Controls	Cataract Type	Relative Risk or Odds Ratio (95% CI)
UK[5]	124	266	Any cataract	Heavy smokers vs nonsmokers RR = 1.97 (1.05 to 3.67), $P = .032$
Lens Opacities Case–Control Study, USA[11]	945	435	Nuclear	Current smokers vs nonsmokers OR = 1.68 (1.03 to 2.75), $.01 < P < .05$
Japan[37]	212	212	Any cataract	Current smokers vs never smokers M: OR = 0.29 (0.07 to 1.16) F: OR = 0.84 (0.34 to 2.10)
UK[38]	990	858	Any cataract:	Current smokers vs nonsmokers OR = 1.11 (0.91 to 1.35), $P = 0.3$
India[49]	262	262	Any cataract	Current smokers (heavy) vs nonsmokers OR = 2.27 (1.27 to 4.07), $P = .006$
Nigeria[26]	31	31	Any cataract	Ex-smokers vs nonsmokers OR = 2.14 (0.57 to 8.30)
AREDS,[34] USA	Nuclear: 615, moderate 2044 mild	1818	Nuclear	Current smokers vs never smokers moderate: OR = 1.96 (1.35 to 2.83), $P \leq .01$ mild: OR = 1.44 (1.10 to 1.89), $P \leq .01$

CI = confidence interval; OR = odds ratio; RR = risk ratio

unknown, risk factors vary with smoking status and hence have a potentially confounding effect on the association observed between smoking and cataract.

Age is an accepted risk factor for cataract, and 12 studies accounted or controlled for age or for age and sex in their analyses. Nine studies found an association between smoking and cataract,[11,20–23,31,34,35,40] and only 3 studies[25,36,38] found no association after adjustment for age.

Smokers have a higher prevalence of other health-threatening habits such as poor diet and high alcohol consumption.[48] These may also be risk factors for cataract formation, and hence potential confounding factors. The degree to which studies attempted to adjust for the range of such potential confounding factors was variable. However, of the 7 case-control and cohort studies with multiple adjustment for confounders,[11,21–23,33,34,49] 3 studies[11,34,49] found a significant positive association.

The methods used to define, measure, and categorize the extent of tobacco-smoking exposure is an important potential source of variation between studies. Thus, definitions of current and ex-smokers and the methods used to describe and categorize smoking exposure intensity (for example, numbers of cigarettes smoked, smoking duration, age of smoking onset, or time since quitting) varied greatly. For example, in categorizing smokers by intensity of smoking exposure, McCarty et al.[27,39] divided current smokers into those who smoked for less than or more than 30 pack-years, while Hankinson et al.[23] used 65 pack-years as the cut-off point. Other studies such as the Physician's Health Study[21] used the numbers of cigarettes currently smoked.

A potential weakness of all studies was that the smoking data were self-reported. Patients may underestimate or under report their smoking habits, resulting in misclassification of exposure status and inducing bias in estimates of association. A problem of prospective cohort studies is that many such studies assess smoking status only at baseline. Smoking status may change during follow-up, for example because of smokers quitting, particularly with prolonged follow-up. Such misclassification reduces the observed risk between smoking exposure and outcome, and bias the results toward no association. Of the 9 cohort studies, 6 studies reassessed smoking status during follow-up.[8,20–23,33]

All studies used cataract as an outcome measure. Many studies[5,22,23,40] used the prevalence or incidence of cataract, but some studies used cataract extraction as the measure of outcome and found an association between smoking and cataract extraction. However, cataract extraction rates depend on health care provision and access, which if different between smokers and nonsmokers would create bias and furthermore may be a poor marker for the true incidence of cataract in communities. Cataract extraction might be regarded as a combination measure of both cataract incidence severity and service provision and access. West et al.[20] used progression of nuclear cataract as an outcome measure in a prospective cohort study.

The lack of systematic diagnosis and grading of cataract in many studies is a limitation. Although most studies distinguished between nuclear, cortical, and posterior subcapsular cataract, some studies did not and grouped all types together for analysis.[5,9,22,25,26,37,38,49]

Standardized criteria for diagnosis of cataract were used in some studies. The Lens Opacities Classification System[50,51] or later updated versions of this system was used in 5 studies.[11,29,30,32,40] The Beaver Dam investigators developed the Wisconsin Cataract Grading system,[52] and this method was used by the Beaver Dam and Blue Mountains investigators.[8,28,35] The Age-Related Eye Disease Study[34] used an extension of this system.[53] Four studies[19,20,27,31,39] used the Wilmer cataract photograph grading system. Two studies used the criteria of the Japanese Co-operative Cataract Epidemiology Group.[7,37] Failure to use robust diagnostic or objective criteria might lead to some individuals without cataract being misclassified as having cataract and vice versa.

Although this review provides strong evidence for a link between cataract and active smoking, the evidence that passive smoking increases cataract development is limited. Only 1 study evaluated the association of passive smoking with cataract, finding no association.[35] However, the evidence is currently too limited to draw any conclusions about the role of passive smoking and cataract.

CONCLUSIONS

The epidemiologic evidence of a strong and consistent association between cataract and smoking across different populations, that smoking exposure precedes cataract outcome, and of a dose response effect, and some evidence of reversibility, together with evidence of biological plausibility, strongly support a causal relationship between smoking and cataractogenesis. In particular, there is good evidence for a causal relationship between tobacco smoking and the formation of nuclear cataract.

The reduced risk in ex-smokers suggests that stopping smoking will reduce the risk for developing nuclear cataract. Therefore, preventing smoking uptake and promoting smoking cessation should help reduce the incidence and burden of nuclear cataract. Evidence of the association of smoking with other types of cataract is less convincing.

This is the most comprehensive review of the causal association between smoking and cataract to date. However, this review has a number of limitations. Only a limited set of bibliographic databases were searched, non-English language articles were not included, there was no systematic

appraisal of the quality of included studies, and a quantitative summary of the studies was not attempted. We now intend to address these deficiencies by carrying out a formal systematic review of smoking and cataract and, if appropriate, a metaanalysis will be performed to address this gap in the evidence.

Our experience is that both the general population and many patients attending eye clinics are unaware of the significant link between smoking and eye disease. This is supported by a recent survey conducted among eye clinic and other out patient attenders in our department.[54] Eyecare professionals and cataract surgeons should highlight the availability and existence of smoking cessation services to their patients. To support smoking cessation activities for health professionals, the British Thoracic Society has produced guidance for hospital and community health professionals.[55] Smoking cessation support might also usefully be offered to people attending optometry or ophthalmology services. North West Action on Smoking and Health (http://www.nwash.co.uk) has launched a leaflet describing the ocular risks of smoking alongside user-friendly advice on smoking cessation.

REFERENCES

1. World Health Organization. World Health Report. Life in the 21st Century: A Vision For All. Geneva, WHO, 1998
2. Taylor A, Jacques PF, Epstein EM. Relations among aging, antioxidant status, and cataract. Am J Clin Nutr 1995; 62(suppl):1439S–1447S
3. Taylor HR. Epidemiology of age-related cataract. Eye 1999; 13:445–448
4. Clayton RM, Cuthbert J, Duffy J, et al. Some risk factors associated with cataract in SE Scotland: a pilot study. Trans Ophthalmol Soc UK 1982; 102:331–336
5. Harding JJ, van Heyningen R. Drugs, including alcohol, that act as risk factors for cataract, and possible protection against cataract by aspirin-like analgesics and cyclopenthiazide. B J Ophthalmol 1988; 72: 809–814
6. Muñoz B, Tajchman U, Bochow T, West S. Alcohol use and risk of posterior subcapsular opacities. Arch Ophthalmol 1993; 111:110–112
7. Arnarsson A, Jonasson F, Sasaki H, et al. Risk factors for nuclear lens opacification: the Reykjavik Eye Study. Dev Ophthalmol 2002; 35: 12–20
8. Klein BEK, Klein R, Lee KE. Incident cataract after a five-year interval and lifestyle factors: the Beaver Dam Eye Study. Ophthalmic Epidemiol 1999; 6:247–255
9. Flaye DE, Sullivan KN, Cullinan TR, et al. Cataracts and cigarette smoking; the City Eye Study. Eye 1989; 3:379–384
10. Mohan M, Sperduto RD, Angra SK, et al. India-US case-control study of age-related cataracts; India–US Case-Control Study Group. Arch Ophthalmol 1989; 107:670–676
11. Leske MC, Chylack LT Jr, Wu S-Y. The lens opacities case-control study; risk factors for cataract; the Lens Opacities Case-Control Study Group. Arch Ophthalmol 1991; 109:244–251
12. Age-Related Eye Disease Study Research Group. A randomized, placebo-controlled, clinical trial of high-dose supplementation with vitamins C and E and beta-carotene for age-related cataract and vision loss; AREDS Report No 9. Arch Ophthalmol 2001; 119:1439–1452
13. Teikari JM, Rautalahti M, Haukka J, et al. Incidence of cataract operations in Finnish male smokers unaffected by alpha tocopherol or beta carotene supplements. J Epidemiol Community Health 1998; 52:468–472
14. Chylack LT Jr, Brown NP, Bron A, et al. The Roche European American Cataract Trial (REACT): a randomized clinical trial to investigate the efficacy of an oral antioxidant micronutrient mixture to slow progression of age-related cataract; the REACT Group. Ophthalmic Epidemiol 2002; 9:49–80
15. Hill AB. The environment and disease: association or causation? Proc R Soc Med 1965; 58:295–300
16. Susser M. What is a cause and how do we know one? A grammar for pragmatic epidemiology. Am J Epidemiol 1991; 133:635–648
17. Klein BEK, Klein R, Moss SE. Prevalence of cataracts in a population-based study of persons with diabetes mellitus. Ophthalmology 1985; 92:1191–1196
18. Angra SK, Pushker N, Sachdev MS, Jaffery NF. Risk factors for age-related posterior subcapsular cataract. Ann Ophthalmol 2000; 32: 101–106
19. West S, Munoz B, Emmett EA, Taylor HR. Cigarette smoking and risk of nuclear cataracts. Arch Ophthalmol 1989; 107:1166–1169
20. West S, Muñoz B, Schein OD, et al. Cigarette smoking and risk for progression of nuclear opacities. Arch Ophthalmol 1995; 113:1377–1380
21. Christen WG, Manson JE, Seddon JM, et al. A prospective study of cigarette smoking and risk of cataract in men. JAMA 1992; 268: 989–993
22. Christen WG, Glynn RJ, Ajani UA, et al. Smoking cessation and risk of age-related cataract in men. JAMA 2000; 284:713–716
23. Hankinson SE, Willett WC, Colditz GA, et al. A prospective study of cigarette smoking and risk of cataract surgery in women. JAMA 1992; 268:994–998
24. Newland HS, Woodward AJ, Taumoepeau LA, et al. Epidemiology of blindness and visual impairment in the kingdom of Tonga. Br J Ophthalmol 1994; 78:344–348
25. Janghorbani M, Jones RB, Allison SP. Incidence of and risk factors for cataract among diabetes clinic attenders. Ophthalmic Epidemiol 2000; 7:13–25
26. Ojofeitimi EO, Adelekan DA, Adeoye A, et al. Dietary and lifestyle patterns in the aetiology of cataracts in Nigerian patients. Nutr Health 1999; 13:61–68
27. McCarty CA, Nanjan MB, Taylor HR. Attributable risk estimates for cataract to prioritize medical and public health action. Invest Ophthalmol Vis Sci 2000; 41:3720–3725
28. Klein BEK, Klein R, Linton KLP, Franke T. Cigarette smoking and lens opacities; the Beaver Dam Eye Study. Am J Prevent Med 1993; 9:27–30
29. Hirvelä H, Luukinen H, Laatikainen L. Prevalence and risk factors of lens opacities in the elderly in Finland; a population-based study. Ophthalmology 1995; 102:108–117
30. Foster PJ, Wong TY, Machin D, et al. Risk factors for nuclear, cortical and posterior subcapsular cataracts in the Chinese population of Singapore: the Tanjong Pagar Survey. Br J Ophthalmol 2003; 87: 1112–1120
31. Hiller R, Sperduto RD, Podgor MJ, et al. Cigarette smoking and the risk of development of lens opacities; the Framingham Studies. Arch Ophthalmol 1997; 115:1113–1118
32. Leske MC, Chylack LT Jr, He Q, et al. Risk factors for nuclear opalescence in a longitudinal study; LSC Group. Longitudinal Study of Cataract. Am J Epidemiol 1998; 147:36–41
33. Weintraub JM, Willett WC, Rosner B, et al. Smoking cessation and risk of cataract extraction among US women and men. Am J Epidemiol 2002; 155:72–79
34. Age-Related Eye Disease Study Research Group. Risk factors associated with age-related nuclear and cortical cataract; a case-control

study in the Age-Related Eye Disease Study, AREDS Report No 5. Ophthalmology 2001; 108:1400–1408
35. Cumming RG, Mitchell P. Alcohol, smoking, and cataracts; the Blue Mountains Eye Study. Arch Ophthalmol 1997; 115:1296–1303
36. Cheng CY, Liu JH, Chen SJ, Lee FL. Population-based study on prevalence and risk factors of age-related cataracts in Peitou, Taiwan. Chung Hua I Hsueh Tsa Chih 2000; 63:641–648
37. Katoh N, Sasaki K, Shibata T, et al. Case-control study of senile cataract in Japan: a preliminary report. Jpn J Ophthalmol 1993; 37:467–477
38. Phillips CI, Clayton RM, Cuthbert J, et al. Human cataract risk factors: significance of abstention from, and high consumption of, ethanol (U-curve) and non-significance of smoking. Ophthalmic Res 1996; 28:237–247
39. McCarty CA, Mukesh BN, Fu CL, Taylor HR. The epidemiology of cataract in Australia. Am J Ophthalmol 1999; 128:446–465
40. Delcourt C, Cristol JP, Tessier F, et al. Risk factors for cortical, nuclear, and posterior subcapsular cataracts: the POLA study; Pathologies Oculaires Liées à l'Age. Am J Epidemiol 2000; 151:497–504
41. Ottonello S, Foroni C, Carta A, et al. Oxidative stress and age-related cataract. Ophthalmologica 2000; 214:78–85
42. Chow CK, Thacker RR, Changchit C, et al. Lower levels of vitamin C and carotenes in plasma of cigarette smokers. J Am Coll Nutr 1986; 5:305–312
43. Rácz P, Erdöhelyi A. Cadmium, lead and copper concentrations in normal and senile cataractous human lenses. Ophthalmic Res 1998; 20:10–13
44. Ramakrishnan S, Sulochana KN, Selvaraj T, et al. Smoking of beedies and cataract: cadmium and vitamin C in the lens and blood. Br J Ophthalmol 1995; 79:202–206
45. Harding JJ. Cigarettes and cataract: cadmium or lack of vitamin C? [editorial] Br J Ophthalmol 1996; 79:199–200
46. Cekic O. Effect of cigarette smoking on copper, lead, and cadmium accumulation in human lens. Br J Ophthalmol 1998; 82:186–188
47. Shalini VK, Luthra M, Srinivas L, et al. Oxidative damage to the eye lens caused by cigarette smoke and fuel smoke condensates. Indian J Biochem Biophys 1994; 31:261–266
48. Department of Health. Survey for England 1998: Cardiovascular Disease. London, Department of Health, 1999
49. Ughade SN, Zodpey SP, Khanolkar VA. Risk factors for cataract: a case control study. Indian J Ophthalmol 1998; 46:221–227
50. Chylack LT Jr, Leske MC, Sperduto R, et al. Lens opacities classification system; the Lens Opacities Case-Control Study Group. Arch Ophthalmol 1988; 106:330–334
51. Leske MC, Chylack LT Jr, Sperduto R, et al. Evaluation of a lens opacities classification system; the Lens Opacities Case-Control Study Group. Arch Ophthalmol 1988; 106:327–329
52. Klein BEK, Klein R, Linton KLP, et al. Assessment of cataracts from photographs in the Beaver Dam Eye Study. Ophthalmology 1990; 97: 1428–1433
53. Age-Related Eye Disease Study Research Group. The Age-Related Eye Disease Study (AREDS) system for classifying cataracts from photographs: AREDS Report No 4. Am J Ophthalmol 2001; 131: 167–175
54. Bidwell G, Sahu A, Edwards R, et al. Perceptions of blindness related to smoking: a hospital-based cross-sectional study. Eye 2005; 19:945–948
55. Raw M, McNeill A, West R. Smoking cessation guidelines for health professionals—a guide to effective smoking cessation interventions for the health care system. Thorax 1998; 53(suppl 5):S1–S18
56. Katoh N, Jonasson F, Sasaki H, et al. Cortical lens opacification in Iceland; risk factor analysis—Reykjavik Eye Study. Acta Ophthalmol Scand 2001; 79:154–159