Smoking has been associated with a number of common and severe ocular diseases, such as age-related macular degeneration,1-3 Graves ophthalmopathy,4 and ocular inflammation.5 There is evidence of a dose-response effect of smoking on ocular morbidity. Formation of free radicals and lower levels of circulating antioxidants may initiate the ocular pathogenesis by oxidative stress.6,7

Smoking is an established risk factor for cataract, which is the leading cause of visual impairment in the world, responsible for more than 50% of world blindness.8 The World Health Organization Prevention of Blindness and Deafness Program has estimated that 20 million people are blind from cataract and a further 82 million have low vision due to cataract.9

Surgery is the only effective treatment available. Despite high-volume operation rates, the number of people with cataract is predicted to increase because of the growing elderly population worldwide. Access to medical care is of importance and differs around the world. Preventing cataract has therefore a substantial economic and public health effect, with smoking being a major modifiable risk factor.
The effect of smoking cessation on the risk of cataract has been examined in 3 large prospective cohort studies in the United States among men and women and in 1 prospective cohort of Swedish women.

To further examine the effect of smoking cessation on risk of cataract among men, we prospectively examined the association between smoking habits and time since quitting smoking with the incidence of age-related cataract extraction in a prospective cohort of Swedish men aged 45 to 79 years.

Methods

The Cohort of Swedish Men
The Cohort of Swedish Men was established in late fall 1997 to study the association between lifestyle factors and major chronic diseases, including cataract. All men aged 45 to 79 years and living in central Sweden (Örebro and Västmanland counties) received by mail a self-administered questionnaire regarding diet and lifestyle-related factors. Answers were obtained from 48,645 men (48.5%). The study cohort is a sample from the general population in 2 counties in central Sweden, covering both countryside and cities. The cohort represents the Swedish population of middle-aged and elderly men according to distribution of age (45-59 years, 52% vs 56%; 60-69 years, 27% vs 24%; and 70-79 years, 21% vs 20%), smoking habits (25% vs 22%), prevalence of diabetes mellitus (6.5% vs 5.5%) and hypertension (23% vs 22%), body mass index (calculated as weight in kilograms divided by height in meters squared) of more than 25 (56% vs 56%), and educational level of more than 12 years (16% vs 12%).

We excluded men who turned in blank questionnaires (n = 92), had a diagnosis of cancer (other than nonmelanoma skin cancer) (n = 2592), or died before baseline (n = 55). For this study, we excluded men with cataract extraction (n = 857) before baseline and men with missing data on smoking status (n = 678), yielding a cohort of 44,371 men. The study was approved by the ethics committee at the Karolinska Institutet (Stockholm, Sweden), and completion of the questionnaire was considered to imply informed consent.

Assessment of Smoking Status
On the basis of the self-report in the questionnaire, we classified the men in the cohort as current, past, or never smokers. The number of cigarettes smoked per day was reported in the questionnaire for several periods: ages 15 to 20 years, each decade thereafter, and the present. Cumulative dose of cigarette smoking was calculated in pack-years by multiplying the mean number of cigarettes smoked per day by the total number of years of smoking.

Results

In this cohort of Swedish men, 24.9% were current smokers, 38.8% were past smokers, and 36.3% were never smokers at the start of follow-up in 1998. Alcohol consumption was higher among ever smokers than among never smokers (59 vs 22%; 70-79 years, 21% vs 20%), smoking habits (25% vs 22%), prevalence of diabetes mellitus (6.5% vs 5.5%) and hypertension (23% vs 22%), body mass index (calculated as weight in kilograms divided by height in meters squared) of more than 25 (56% vs 56%), and educational level of more than 12 years (16% vs 12%).

We estimated the risk of cataract extraction according to the mean number of cigarettes smoked per day during the period of smoking, cumulative dose of smoking, age at starting smoking, and duration of smoking (years). Risk estimates were calculated for past smokers who had quit smoking less than 10 years, 10 to 20 years, or more than 20 years before the start of follow-up in 1998. In the multivariate model, we adjusted for potential risk factors, including age, diabetes mellitus, hypertension, corticosteroid medication, alcohol consumption, use of vitamin supplements, body mass index, and educational level. All reported P values are 2-sided, and we tested for trends by using the median value of each category as a single continuous variable.

Identification of Incident Cases and Follow-up of the Cohort
Between January 1, 1998, and December 31, 2009, a total of 5713 incident cases of cataract extraction were identified by linking the study population, using personal identification numbers, with the Swedish National Day-Surgery Register and local registers of cataract extraction in the study area, including private and public clinics (International Classification of Diseases, 10th Revision code H25 for age-related cataract). Cataract considered congenital or secondary to ocular trauma or intraocular inflammation and previous intraocular surgery were excluded (International Classification of Diseases, 10th Revision code H26).

The dates of death in the cohort were ascertained from the Swedish Death Register, and the date when participants moved out of the study area was obtained by linking the cohort with the Swedish Population Register. These registers are almost 100% complete.
increased risk (RR, 1.19; 95% CI 1.11-1.28) and past smokers had an 18% increased risk (RR, 1.18; 95% CI, 1.11-1.25) of cataract extraction in the multivariate adjusted analysis.

Smoking intensity, measured as the mean number of cigarettes smoked per day during a lifetime, as well as cumulative exposure of cigarette smoking was associated with a higher risk (P for trend <.001) (Table 2). Among current smokers of more than 15 cigarettes per day, the relative risk of cataract extraction was 1.42 (95% CI, 1.28-1.58) compared with never smokers. We found no significant association between age at starting smoking and risk of cataract extraction after adjustment for smoking intensity (data not shown).

After smoking cessation, the risk of cataract extraction decreased with time (P for trend <.001) (Table 3). In an analysis of the effect of smoking cessation on the risk of cataract extraction, we also stratified by categories of amount smoked. Among men who had smoked more than 15 cigarettes per day, the risk decreased with time since stopping smoking compared with never smokers (P for trend <.001). More than 20 years after quitting smoking, the multivariate adjusted relative risk for cataract extraction was 1.21 (95% CI, 1.06-1.39). Among men who had smoked 15 cigarettes or less per day, the risk of cataract extraction more than 2 decades after smoking cessation had declined to a statistically significant level but did not reach that of never smokers (RR, 1.13; 95% CI, 1.04-1.24).

### Discussion

We observed a positive association between cigarette smoking and cataract extraction in this population-based prospective cohort of men, with a significant dose response for both intensity and the cumulative effect of smoking compared with never smokers. Smoking cessation was associated with a statistically significant decrease in risk with increasing time from stopping smoking. Even heavy smokers had some benefit from quitting smoking, indicating that the lens has some capability to recover, although more than 2 decades after quitting smoking, the risk did not reach the level of never smokers.
Our results add to numerous previous epidemiologic studies on the association between smoking and cataract. Although the relative risk estimates vary, most studies have reported a positive association between smoking and cataract.8 To our knowledge, the effect of smoking cessation on the risk of cataract has been considered in only a few studies.10,11,13,15 Depending on whether the reference group is current or never smokers, the risk estimates differ among studies. In a prospective study of 19,698 men, Christen et al11 indicated a 25% decreased risk of cataract surgery among past smokers within 10 years since quitting smoking compared with current smokers, with little additional reduction more than 20 years after stopping smoking. In a prospective study of women in the Nurses’ Health Study and among men in the Health Professionals Follow-up Study, Weintraub et al10 observed that past smokers 25 years or more after quitting smoking had a 20% decreased risk of cataract extraction compared with current smokers, but the risk did not decrease to the level of never smokers. In a prospective cohort of 34,595 women in Sweden, we observed a decreased risk of cataract extraction according to smoking cessation with time. Women smoking 10 cigarettes or less per day more than 10 years after smoking cessation no longer had an increased risk for cataract extraction compared with never smokers. Among women smoking more than 10 cigarettes per day, the risk was not significantly increased more than 20 years after smoking cessation. In the City Eye Study, the risk of cataract among past light smokers (<15 cigarettes/d) was equal to never smokers, and no statistically significant increased risk was observed among moderate past smokers (15-24 cigarettes/d) compared with never smokers. No reduction in risk was noted among past heavy smokers (>25 cigarettes/d); however, time since quitting smoking was not taken in account.13 A cross-sectional study of 838 watermen in Maryland found a 33% decreased risk of nuclear opacity in past smokers 10 years after quitting smoking compared with current smokers.15

The strengths of our study are the population-based cohort design, the large study size, information on potential confounders, and a long follow-up, which is virtually complete. The prospective design with information on presumed risk factors before cataract extraction minimizes the risk for recall bias. Nonrandom misclassification is reduced since we performed a follow-up of the cohort using computerized registers of cataract extraction from eye clinics in the study without knowing exposure status. We were able to conduct a subgroup analysis with reasonable statistical power due to the large number of men with cataract extractions.

Some potential limitations exist in our study. We had no information on cataract subtype in our cohort. In our study, we focused on the degree of cataract severe enough to cause visual impairment that affected activities of daily living, thus requiring lens extraction and therefore having the greatest clinical and public health importance. According to the Swedish National Cataract Register, the mean preoperative best-corrected visual acuity in the cataract eye during the study period was 20/60 Snellen equivalents (corresponding to difficulty in reading) compared with 20/32 Snellen equivalents in the nonoperated-on eye.16 Access to cataract surgery is high in Sweden, with a mean waiting time for surgery in the study area of 5 months at the beginning of the time period.16 The patient charge is less than $50 per operation. However, we cannot exclude a possibility for potential bias due to underestimation of cataract extractions, but under-ascertainment of cases would lead to a diluted risk estimation. Random misclassification could occur if smoking men with cataract were less likely to have a cataract extraction compared with never smokers. Failed quitters (eg, men who in the questionnaire said they had quit smoking but may have started again) could have been improperly included with past smokers. This would lead to a reduced benefit of smoking cessation. The questionnaire did not assess sunlight exposure, which did not allow us to control for the UV effect on cataract development. The men in the cohort were, however, residing in northern Europe, where exposure status. We were able to conduct a subgroup analysis with reasonable statistical power due to the large number of men with cataract extractions.

### Table 3. Relative Risk of Cataract Extraction Among Past Smokers by Time Since Quitting Smoking in the Cohort of Swedish Men, 1998 Through 2009

<table>
<thead>
<tr>
<th>Smoking Status</th>
<th>Time Since Quitting Smoking, y</th>
<th>Never Smokers (n = 16,083)</th>
<th>&lt;10 (n = 3785)</th>
<th>10-20 (n = 6486)</th>
<th>&gt;20 (n = 6877)</th>
<th>P Value for Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Past smokers</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of cases</td>
<td>1953</td>
<td>1953</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age-adjusted RR (95% CI)</td>
<td>1.0</td>
<td>1.32 (1.19-1.46)</td>
<td>1.25 (1.16-1.36)</td>
<td>1.14 (1.06-1.23)</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Multiadjusted RR (95% CI)</td>
<td>1.0</td>
<td>1.27 (1.15-1.41)</td>
<td>1.22 (1.12-1.32)</td>
<td>1.13 (1.04-1.22)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoked ≤15 cigarettes/d</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of cases</td>
<td>1953</td>
<td>1953</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age-adjusted RR (95% CI)</td>
<td>1.0</td>
<td>1.25 (1.09-1.44)</td>
<td>1.19 (1.07-1.31)</td>
<td>1.13 (1.04-1.23)</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Multiadjusted RR (95% CI)</td>
<td>1.0</td>
<td>1.22 (1.07-1.41)</td>
<td>1.17 (1.05-1.30)</td>
<td>1.13 (1.04-1.24)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoked &gt;15 cigarettes/d</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of cases</td>
<td>1953</td>
<td>1953</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age-adjusted RR (95% CI)</td>
<td>1.0</td>
<td>1.51 (1.31-1.75)</td>
<td>1.36 (1.20-1.54)</td>
<td>1.25 (1.10-1.43)</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Multiadjusted RR (95% CI)</td>
<td>1.0</td>
<td>1.44 (1.24-1.67)</td>
<td>1.31 (1.15-1.50)</td>
<td>1.21 (1.06-1.39)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: RR, rate ratio.
* Numbers do not add up to the total because of missing values.
+ Adjusted for age (5-year age groups: 45-49, 50-54, 55-59, 60-64, 65-69, 70-74, and 75-79 years), diabetes mellitus, hypertension, corticosteroid medication, alcohol consumption (in quartiles), vitamin supplement use, body mass index (<20, 20-<25, 25-30, and >30 [calculated as weight in kilograms divided by height in meters squared]), and education.
the risk of sunlight exposure is not likely to be large, although we cannot rule this out. There might be unknown factors that were not controlled for in the analysis, which could hypothetically influence the ability to detect an association.

Smoking increases the oxidative stress in the lens by generating free radicals and reduces the plasma concentration of several antioxidants, such as ascorbic acid. The amount of proteolytic enzymes and their capacity of removing damaged lens proteins is impaired. Long-time exposure of oxidative stress leads to accumulation of damaged lens proteins, thus promoting cataract development. Cigarette smoke also contains toxic metal ions, and cadmium can accumulate in cataractous lenses of smokers. Cadmium may affect anti-oxidative lens enzymes such as superoxide dismutase and glutathione peroxidase, thereby weakening the defense against oxidative damage and hastening cataract development.

Our study confirms previous studies showing that cigarette smoking is associated with cataract. Smoking cessation decreased the risk with time, indicating that the lens has some ability to repair protein damage with time, probably by halting oxidative stress, although it takes longer for the lens to recover with higher smoking intensity.

Although the prevalence of smokers in Sweden has decreased over the past 20 years and is among the lowest in the world (today around 13% of the population in Sweden are smokers; 12.5% among men), more people are currently smoking, and tobacco use is a major health problem worldwide. According to World Health Organization estimates, about one-third of the global population 15 years or older are smokers, and smoking intensity is rising. The increase is highest in the developing countries where cataract surgery is not always readily available and blinding from cataract is of great socioeconomic importance. A recent study of tobacco use among 3 billion individuals from 16 countries reported that almost 50% of men in low- and middle-income countries were smoking, and the quit ratio was low.

Smoking cessation may decrease the risk of cataract, but the risk among former smokers persists for decades. Since smoking is also related to other ocular diseases, strategies to prevent smoking and promote smoking cessation are important, and eye care professionals should encourage people to stop smoking.

REFERENCES