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Review

Is there a health benefit of reduced tobacco consumption? A systematic review

Charlotta Pisinger, Nina S. Godtfredsen

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This review presents the available evidence on the health effects of reduced smoking. Smoking reduction was defined as reduction of the daily intake of tobacco without quitting. Only published papers were reviewed. Case reports and studies without a thorough definition of smoking reduction or health outcome were excluded. We searched in personal databases, BioMail Medline Search, Medline, the Cochrane Database of Systematic Reviews, and EMBASE. We followed the QUORUM standards for systematic reviews, and both authors read and discussed all publications. A total of 25 studies (31 publications) were identified: 8 articles reported on effects on the cardiovascular system; 11 on the airways; 7 on carcinogens, DNA damage, and lung cancer; 3 on birth weight; and 4 on other health effects. Some papers assessed more than one outcome. In most studies, reduction was defined as less than 50% of baseline tobacco consumption. Most of the studies were small, with the populations selected and short follow-up periods. The limited data suggest that a substantial reduction in smoking improves several cardiovascular risk factors and respiratory symptoms. In addition, smoking reduction is associated with a 25% decline in biomarkers and incidence of lung cancer and a small, mostly nonsignificant, increase in birth weight. There seem to be no substantial beneficial effects on lung function. The evidence on other health effects and mortality is too limited to draw conclusions. A substantial reduction in smoking seems to have a small health benefit, but more studies are needed to determine the long-term effects of smoking reduction.

Introduction

The health benefits of smoking cessation are well documented (Doll, Peto, Boreham, & Sutherland, 2004; Doll, Peto, Wheatley, Gray, & Sutherland, 1994). Yet many smokers ignore their doctor’s advice to quit smoking, because they do not want to quit or have relapsed so many times that they do not believe they are able to quit. In some countries, only 4%–11% of smokers are in the preparation stage, ready to quit in the near future (Etter, Perneger, & Ronchi, 1997; Pisinger, Vestbo, Borch-Johnsen, Thomsen, & Jorgensen, 2005). A dose-response relationship between smoking and mortality has been reported (American Thoracic Society 1996; Loeb, Ernster, Warner, Abbotts, & Laszlo, 1984), but heavy smokers, who are at the highest risk of smoking-related disease, are highly dependent and have low abstinence rates (Hymowitz et al., 1997).

Medical doctors compromise daily, accepting suboptimal control of cholesterol, blood pressure, weight, and asthma. In the past decade, professionals working with smoking control have introduced the concept of smoking reduction—that is, smoking fewer cigarettes daily without quitting—in an attempt to reduce the harm of smoking (Fagerström, Tejding, Westin, & Lunell, 1997; Hughes, 2000). From a public health perspective, smoking reduction could be a supplement to smoking cessation and a suboptimal goal for the reluctant
smoker if it can be documented that smoking reduction decreases the harm of smoking or increases the smoker’s motivation to quit. Previous reviews on tobacco harm reduction have focused primarily on feasibility, compensation, future cessation, and new tobacco products or biomarkers of harm (Fagerström, 2005; Hatsukami, Henningfield, & Kotlyar, 2004; Hughes & Carpenter, 2005; Tonnesen, 2002). This review aims to present and discuss the available evidence on the health consequences of reduced tobacco consumption, which to our knowledge has not been done previously.

Method

Definitions and inclusion criteria

We followed the QUORUM standards for systematic reviews (Turpin, 2005). We searched for peer-reviewed articles in Medline, the Cochrane Database of Systematic Reviews, and EMBASE using the following search terms: SR, reduced smoking, reducing smoking, modified smoking, modified tobacco consumption, modification of cig-, modification of smoking, cigarette reduction, reduced cig-, reduction in cig-, harm reduction, reduced tobacco consumption, and tobacco consumption, combined with a disease search term (e.g., cancer). All included articles were reviewed thoroughly for references, and we searched for other articles by the first authors of the included articles. The systematic search ended September 2005. Three additional studies were found after this date by the BioMail Medline Search.

Smoking reduction was defined as self-report of reduction of daily intake of tobacco, or reduction in cigarettes per day (CPD). Case reports, studies without a thorough definition of smoking reduction and health outcome, and studies with smoking cessation (reduction to 0 CPD), even if intermittent, were excluded. We included only studies that reported on individual, not population-based, health effects. Validation of smoking reduction by measurement of one or more biochemical markers of tobacco smoke exposure was assessed whenever possible. Most studies accepted any decrease in biomarkers as indicative of smoking reduction, although well-known difficulties exist in interpreting values for nicotine and cotinine if supplemental nicotine was administered.

We divided the literature into five areas, each describing the effect of reduction on a particular health outcome. All included articles are presented and discussed within these areas. Details of the studies (e.g., validation, average tobacco consumption, use of nicotine replacement therapy, $p$ values) are presented in Table 1.

Results

Effect of reduced tobacco consumption on the cardiovascular system

 Effect on cardiovascular risk factors. In Bolliger (2000), an intervention study, 70 smokers achieved reduction, defined as reducing the number of cigarettes per day by at least 50%. Reduction at the 4-month follow-up was associated with a significant decrease in white blood cell count (WBC) and low-density lipids (LDL) and a significant increase in high-density lipids (HDL). This study was evaluated after 2 years (Bolliger et al., 2002). At that time, 25 smokers had reduced successfully and continuously from week 6 to 2 years. Compared with those who did not reduce, reducers showed a significant decrease in hemoglobin concentrations, cholesterol/HDL ratio, and pulse rate.

In Eliasson, Hjalmarson, Kruse, Landfeldt, and Westin (2001), a case-control study, reduction was defined as reducing number of cigarettes per day by at least 50%. Smoking reduction was achieved by 26 smokers, but the risk factor analyses for the reduction group were carried out for the 33 who were abstinent at week 17. In smokers who had achieved successful reduction, fibrinogen, hemoglobin, hematocrit, red blood cell count (RBC), and WBC were significantly reduced at week 9, and the HDL/LDL ratio was increased significantly compared with baseline values of all smokers.

In Hatsukami et al. (2005), another case-control study, 64 smokers succeeded in reducing by at least 40%. Reduction at 3 months was significantly associated with improvement in hemoglobin, hematocrit, RBC and WBC, lipids, systolic blood pressure, and heart rate. Significant positive correlations between reduction and biomarkers were observed for WBC, total cholesterol/HDL ratio, and heart rate. In Haustein, Krause, Haustein, Rasmussen, and Cort (2004), an open intervention study with 26 weeks of follow-up, 29 smokers reduced smoking, defined as smoking less than 50% of baseline number of cigarettes per day. Smoking reduction improved the microcirculation by significantly increasing tissue oxygenation. Fibrinogen, hematocrit, WBC, systolic blood pressure, and heart rate were decreased in reducers.

In another intervention study (J. H. Stein et al., 2002), 15 smokers achieved reduction, defined as reducing by at least 50%, at the 3-month follow-up. The decrease in homocysteine (an independent risk factor for atherosclerotic vascular disease) in the reduction group was nonsignificant and smaller than in the group of continuous smokers.

Effect on myocardial infarction. A large prospective cohort study (Godtfredsen, Osler, Vestbo, Andersen,
### Table 1. Studies included in the review.

<table>
<thead>
<tr>
<th>Study and aim</th>
<th>Study design</th>
<th>Randomized to smoking reduction</th>
<th>Use of nicotine replacement therapy</th>
<th>Number and characteristics of smokers</th>
<th>Definition of successful reduction</th>
<th>Number of successful reducers and duration of follow-up</th>
<th>Data analysis and effect on health in smokers who achieved reduction</th>
<th>Validation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bolliger (2000): to determine the short-term effect of smoking reduction on cardiovascular risk factors</td>
<td>Intervention study (smoking reduction)</td>
<td>Yes</td>
<td>Yes</td>
<td>400 healthy smokers, without a wish to quit, &gt;15 CPD; controlled intervention study on smoking reduction</td>
<td>Reducing the number of cigarettes by at least 50%, validated by decrease in CO</td>
<td>52 (26%) of the smokers in the NRT group and 18 (9%) in the placebo group achieved successful reduction at 4 months</td>
<td>Compared with baseline (within smoking reduction group); significant decrease in WBC (10%) and LDL (8%); significant increase in HDL (17%); fibrinogen unchanged</td>
<td>Expired CO; intergroup comparison not made because CO was included in definition of success</td>
</tr>
<tr>
<td>Bolliger et al. (2002): 2-year evaluation of Bolliger (2000) study, to determine the long-term effect of smoking reduction on cardiovascular risk factors, lung function, and self-reported general health</td>
<td>Intervention study (smoking reduction)</td>
<td>Yes</td>
<td>Yes</td>
<td>310 subjects could be evaluated at 2-year follow-up</td>
<td>Reducing the number of cigarettes by at least 50%, validated by decrease in CO</td>
<td>25 smokers had sustained reduction from week 6 to 2 years</td>
<td>Compared with nonreducers: decrease in hemoglobin concentrations (−5.7 ± 9.4 g/L), p = .023, cholesterol/HDL ratio (−2.4 ± 1.7, p = .024), and pulse rate (−3.7 ± 10.4 bpm, p = .043); no differences in cholesterol, HDL, LDL, WBC, fibrinogen, hematocrit, or blood pressure; no difference in FEV1 and FVC; improved self-reported general health score (9.4, p = .049)</td>
<td>Expired CO; intergroup comparison not made because CO was included in definition of success</td>
</tr>
<tr>
<td>Eliasson et al. (2001), to determine the short-term effect of smoking reduction on cardiovascular risk factors</td>
<td>Open intervention study (smoking cessation and smoking reduction)</td>
<td>Yes</td>
<td>Yes</td>
<td>58 healthy smokers, &gt;15 CPD; assisted in (a) smoking reduction and (b) smoking cessation</td>
<td>Primary goal during the first 8 weeks was reducing daily tobacco consumption by at least 50%</td>
<td>Achieved by 45% (26 subjects) at week 9; average cigarette consumption was reduced by 50.2% (21.5 ± 0.6 CPD to 10.8 ± 0.6 CPD)</td>
<td>Compared with baseline values (all participants): reduced fibrinogen (p = .011), hemoglobin (p &lt; .001), hematocrit (p &lt; .001), RBC (p = .005), and WBC (p = .005); increased HDL/LDL ratio (p = .005); no significant changes observed in thrombocytes, HDL, or LDL</td>
<td>Plasma thiocyanate (reduced by 21%) and expired CO (reduced by 17%)</td>
</tr>
<tr>
<td>Hatsukami et al. (2005): to determine the short-term effect of smoking reduction on cardiovascular risk factors and respiratory symptoms</td>
<td>Intervention study (smoking reduction)</td>
<td>Yes</td>
<td>Yes</td>
<td>151 healthy smokers, &gt;15 CPD; randomized to (a) waitlist or (b) smoking reduction; following a scheduled reduction, asked to reduce to 50% or quit after 6 weeks</td>
<td>Reducing the number of cigarettes by at least 40% but not abstinent</td>
<td>64 smokers reduced from weeks 4 to 12</td>
<td>Reducers compared with all smokers at baseline (based on the time point for analyses), week 12: (p for all: &lt; .0167); reduced hemoglobin (−1.91%), hematocrit (−1.58%), WBC (−7.45%), LDL (−3.53%), total cholesterol/HDL ratio (−7.77%), apolipoprotein B (−4.18%), systolic blood pressure (−2.98%), and heart rate (−5.50%); increased HDL (10.08%) and HDL/LDL ratio (16.91%); significant positive correlations observed for WBC, total cholesterol/HDL ratio, and heart rate; improved self-reported respiratory score (cough, phlegm, shortness of breath, and other respiratory symptoms; −12.87%, p &lt; .001)</td>
<td>Urinary cotinine and anatabine (no change with reduction); CO measured but not compared with reduction in CPD</td>
</tr>
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<td>Haustein et al. (2004): to determine the short-term effect of smoking reduction on cardiovascular risk factors</td>
<td>Open, parallel-group intervention trial (smoking cessation)</td>
<td>Within-group comparison</td>
<td>No</td>
<td>Yes</td>
<td>197 males, aged 25–45 years, smoking &gt;20 CPD; 164 subjects were instructed to stop smoking and received NRT for 12 weeks; 33 acted as controls</td>
<td>Reducing by at least 50%</td>
<td>29 smokers reduced at end of study; follow-up: 26 weeks</td>
<td>Changes from baseline within reducer-group compared with changes in smokers: improved transcutaneous partial oxygen tension ($p&lt;.0001$); decreased plasma fibrinogen, hematocrit (week 8, $p=.0002$), WBC (week 26, $p=.015$), systolic blood pressure (week 26, $p=.008$), heart rate (week 26, $p=.02$); no significant change in erythrocyte deformability, reactive capillary blood flow, or number of platelets</td>
</tr>
<tr>
<td>J. H. Stein et al. (2002): to determine the short-term effects of smoking reduction on plasma homocysteine levels</td>
<td>Intervention study (smoking reduction) Case-control</td>
<td>51 healthy heavy smokers, 35.9 ± 6.4 CPD</td>
<td>Yes</td>
<td>Yes</td>
<td>Reducing by at least 50%</td>
<td>Reduction achieved by 15 smokers; follow-up: 12 weeks</td>
<td>Compared with usual smokers (randomized group): decrease in homocysteine levels was nonsignificant ($-0.22 ± 0.12$, $p=.41$)</td>
<td>Plasma cotinine; no significant changes in serum cotinine or nicotine levels</td>
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<tr>
<td>Godtfredsen et al. (2003): to determine the effect of smoking reduction on risk of myocardial infarction</td>
<td>Prospective cohort study</td>
<td>No</td>
<td>No</td>
<td>10,956 men and 8,467 women, record linkage to mortality and hospital registers; Cox proportional hazard analyses with continuous heavy smokers as reference</td>
<td>Heavy smokers ($&gt;15$ CPD) at baseline who reduced their daily tobacco consumption by at least 50% without quitting</td>
<td>Reduction achieved by 643 smokers; mean follow-up: 13.8 years</td>
<td>Compared with persistent heavy smokers: no association with reduced risk of myocardial infarction, $HR=1.15$ (95% CI=0.94–1.40), adjusted for cardiovascular risk factors</td>
<td>No</td>
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<tr>
<td>Hughson et al. (1978): to determine if smoking reduction has any influence on the natural history of intermittent claudication</td>
<td>Clinical trial Case-control</td>
<td>No</td>
<td>No</td>
<td>60 patients were followed up for 4–5 years after first referral or admission to hospital for intermittent claudication</td>
<td>No definition, but reduced from average &gt;20 to average &lt;10 CPD</td>
<td>9 smokers; follow-up: 4–5 years</td>
<td>Reducers compared with usual smokers: probability of adverse events (death, amputation, onset of intermittent claudication in the other limb, myocardial infarction, and operation for deterioration of peripheral vascular disease) was significantly lower ($p=.036$)</td>
<td>No</td>
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<td>McCarthy et al. (1976): to assess measures of lung function before and after smoking reduction</td>
<td>Intervention study (smoking cessation)</td>
<td>No</td>
<td>No</td>
<td>131 smokers, 17–66 years old; smoking history: 91 smoked &lt;25 pack-years, 31 smoked 25–50 pack-years, and 9 smoked &gt;50 pack-years</td>
<td>Divided as more than or less than 25% reduction of baseline tobacco consumption without quitting</td>
<td>33 subjects reduced at 6–24 weeks; 38 subjects reduced at 24–48 weeks</td>
<td>Compared with baseline values: weeks 24–48, significant improvement in the slope of phase III of the N₂ washout curve, as well as closing volume/vital capacity, FVC, FEV₁, and peak flow; weeks 6–24, slope of phase III of the N₂ washout curve was significantly improved; lung function was improved more by smoking reduction than by smoking cessation at weeks 24–48 (could not be explained; there was no difference in distribution of age, sex, or smoking history in the two groups)</td>
<td>Unscheduled random carboxyhemoglobin estimations</td>
</tr>
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<td>Burchfiel et al. (1995): to examine the effects of smoking reduction on lung function</td>
<td>Prospective cohort study (identification of cardiovascular risk factors)</td>
<td>No</td>
<td>No</td>
<td>8,006 Japanese American men examined in 1965–1968; reexamined 6 years later in 1971–75; 4,451 men had three acceptable lung function measurements; age at baseline 45–68 years</td>
<td>Self-reported decrease of CPD, but not cessation</td>
<td>415 men who spontaneously reduced the number of CPD (mean CPD = 9.6); follow-up: 6 years</td>
<td>Compared with no change and increased smoking: average annual rate of FEV₁ decline (~32.6 ml) was similar (p = .86); test for linear trend was not significant; not adjusted for number of cigarettes smoked at baseline or duration of smoking</td>
<td>No</td>
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<tr>
<td>Rennard et al. (1990): to assess measures of lower respiratory inflammation before and after smoking reduction</td>
<td>Intervention study (smoking reduction) Case-control and within-subject comparison</td>
<td>Yes</td>
<td>Yes</td>
<td>15 healthy heavy smokers and a control group of 15 healthy never-smokers; average of 50 CPD at enrollment; bronchoscopy with bronchoalveolar lavage (BAL)</td>
<td>Self-reported decrease of CPD; reducing from approximately 51 to 19 CPD during the study</td>
<td>All smokers reduced; follow-up: 2 months</td>
<td>Reducers compared with baseline: significant reductions in measures of lower respiratory tract inflammation, significant improvement in subclinical bronchitis severity (p &lt; .01) and in total number of neutrophils in the BAL fluid (p &lt; .05); significant improvement in neutrophil elastase (p &lt; .01)</td>
<td>Expired CO (decreased from 48.5 ppm to 27.3 ppm)</td>
</tr>
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<td>Lange et al. (1989): to assess the effect of smoking reduction on lung function</td>
<td>Prospective cohort study</td>
<td>No</td>
<td>No</td>
<td>Smoking habits and decline of FEV₁ were examined in 7,764 men and women with a 5-year interval in the Copenhagen City Heart Study</td>
<td>Self-reported heavy smoking (≥15 CPD) at baseline and light smoking (1–14 CPD) at follow-up</td>
<td>326 participants met the reduction criterion; follow-up: 5 years</td>
<td>Less pronounced annual decline in FEV₁ among men younger than 55 years; not statistically significant when subjected to a regression analysis</td>
<td>No</td>
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<td>Waage et al. (1996): to assess the effect of smoking reduction on lung function and respiratory symptoms</td>
<td>Intervention study (smoking cessation)</td>
<td>Case-control</td>
<td>No</td>
<td>Not known</td>
<td>231 smoking, formerly asbestos-exposed men (average 15 CPD)</td>
<td>Self-reported decrease in tobacco consumption</td>
<td>52 smokers reduced on average 46.7 g tobacco per week (6.7 CPD); follow-up: 2 years</td>
<td>Compared with usual smokers: significantly lower prevalence of cough (56% vs. 68%, ( p = .05 )) and chronic cough (31% vs. 52%, ( p = .003 )) at follow-up; no change in prevalence of dyspnea</td>
</tr>
<tr>
<td>Simmons et al. (2005): to assess the effect of smoking reduction on lung function</td>
<td>Intervention study (smoking cessation)</td>
<td>Case-control</td>
<td>No</td>
<td>Yes</td>
<td>1,980 subjects who reduced smoking during the first study year were examined for changes in FEV1 and respiratory symptoms</td>
<td>Self-reported decrease in CPD; percentage reduction in smoking rate divided into categories (11%–25%, 26%–50%, 51%–75%, &gt;75%)</td>
<td>8% of study participants reduced by at least 50% of baseline consumption without quitting; follow-up: 1 year</td>
<td>Compared with usual smoking: adjusted analysis of covariance and linear regression analysis revealed no statistically significant relationship between percentage change in CPD and change in FEV1; only the 2% (39 persons) who reduced by 85% or more experienced an increase in FEV1; all other categories of reduction had decline in FEV1 similar to unchanged smokers</td>
</tr>
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<td>Bohadana et al. (2005): to examine whether smoking reduction improves airway hyperresponsiveness and thereby slows down the decline in lung function</td>
<td>Intervention study (smoking cessation or smoking reduction)</td>
<td>Case-control and within-group comparison</td>
<td>No</td>
<td>Yes</td>
<td>165 occupationally exposed (dusty work: bakers, hairdressers, woodworkers, painters, etc.) healthy smokers</td>
<td>Reducing by at least 50%, validated by decrease in CO</td>
<td>17 smokers at 1-year follow-up; participation rate at follow-up was 41%, no differences in baseline respiratory symptoms, lung function tests, and airway responsiveness (participants and nonparticipants)</td>
<td>Compared with baseline (within group): significantly improved cough (( p = .046 )), bronchitis symptoms (( p = .027 )), and shortness of breath (( p = .027 )); no significant improvement in phlegm (( p = .163 )); reducers compared with usual smokers: no significant improvement in airway responsiveness (( p = .057 )) or in FEV1 (( p = .55 ))</td>
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<td>Stein et al. (2005): to determine the short-term effects of smoking reduction on respiratory symptoms</td>
<td>Intervention study (smoking cessation)</td>
<td>Case-control</td>
<td>No</td>
<td>Yes</td>
<td>383 smokers from methadone maintenance programs; smoking-related respiratory symptom severity (SRRSS) was assessed with a seven-item summated rating index (coughing, phlegm, wheezing, sinus congestion, fatigue, pain/tightness in chest, and shortness of breath during exercise)</td>
<td>Self-reported decrease of CPD; percentage reduction in smoking rate divided into categories (25% or more, 50% or more, 75% or more); absolute reductions of CPD registered in categories (5+, 10+, 20+, 30+, 40+)</td>
<td>287 (90%) had any reduction: 6% reduced by 1–5 CPD, 19% by 5–10, 34% by 10–20, 28% by 20–40, and 4% by ≥40; follow-up: 3 months</td>
<td>Reduced SRRSS in smokers with reduction in average daily smoking. (correlation 0.26, p &lt; .001); correlation between percentage reduction and reduced SRRSS (0.20, p &lt; .001); largest improvements in symptom severity among those with largest absolute reductions; a reduction in cigarette use was significantly associated with a reduction in SRRSS after adjusting for sociodemographic factors, respiratory disease, and nicotine dependency (B = 0.29, t = 5.16, p &lt; .01)</td>
</tr>
<tr>
<td>Tonnesen et al. (2005): to assess asthma regulation after smoking reduction</td>
<td>Intervention study (smoking cessation or smoking reduction)</td>
<td>Case-control</td>
<td>Yes</td>
<td>Yes</td>
<td>220 smokers aged 18–60 years with stable asthma; average 20 CPD</td>
<td>Smoking fewer than 7 CPD without smoking cessation</td>
<td>33 study participants achieved reduction goal (23% of the cessation group, 15% of the reduction group, 2% of controls); follow-up: 4 months</td>
<td>Compared with usual smoking, smoking reduction did not improve general health score; of 10 asthma regulation items, 3 were improved after smoking reduction (night-time use of β2-agonists, p &lt; .05; dose of inhaled corticosteroids, p &lt; .05; and bronchial hyper reactivity, p &lt; .05)</td>
</tr>
<tr>
<td>Godtfredsen et al. (2002): to determine the effect of smoking reduction on risk of first hospitalization for COPD</td>
<td>Prospective cohort study</td>
<td>No</td>
<td>No</td>
<td>19,709 men and women followed for a mean of 14 years for a first hospitalization for COPD</td>
<td>Heavy smokers (&gt;15 CPD) at baseline who reduced daily tobacco consumption by at least 50% without quitting</td>
<td>Reduction achieved by 832 smokers (11% of baseline heavy smokers); from average 20 CPD to 9 CPD at follow-up; followed for mean of 14 years</td>
<td>Compared with persistent heavy smokers: no reduction in risk of hospital admission for COPD after smoking reduction, adjusted HR = 0.93, 95% CI = 0.73–1.18</td>
<td>No</td>
</tr>
<tr>
<td>Hecht, Murphy et al. (2004): to assess the short-term effect of smoking reduction on biomarkers associated with harm</td>
<td>Intervention study (smoking reduction)</td>
<td>Within-group comparison</td>
<td>Yes</td>
<td>Yes</td>
<td>151 smokers assigned to a control or a reduction group; measures of levels of the lung carcinogen metabolites NNAL and NNAL-Gluc in urine</td>
<td>Subgroups that reduced CPD by at least 40% were defined</td>
<td>21 of the smokers; followed up to 26 weeks</td>
<td>Compared with baseline: statistically significant reductions in NNAL + NNAL-Gluc at week 12 (p &lt; .001); reductions in NNAL were best in those who reduced by ≥70%; however, the observed decreases were less than the reductions in CPD</td>
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<td>Use of nicotine replacement therapy</td>
<td>Number and characteristics of smokers</td>
<td>Definition of successful reduction</td>
<td>Number of successful reducers and duration of follow-up</td>
<td>Data analysis and effect on health in smokers who achieved reduction</td>
<td>Validation</td>
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<tr>
<td>Hecht, Carmella et al. (2004): to assess the short-term effect of smoking reduction on biomarkers associated with harm</td>
<td>Intervention study (smoking reduction)</td>
<td>Yes</td>
<td>Yes</td>
<td>151 smokers assigned to a control or a reduction group; measures of urinary levels of 1-HOP, a biomarker of PAH uptake</td>
<td>Subgroups that reduced CPD by at least 40% were defined</td>
<td>21 of the smokers; followed up to 26 weeks</td>
<td>Compared with baseline: statistically significant reductions in 1-HOP at most time points (ranging from 14% to 35% in all groups and time points examined); however, the observed decreases were less than the reductions in CPD, and the relationship between 1-HOP and CPD was not consistent</td>
<td>Expired CO; urinary cotinine and urinary anatabine (reduced by 30%–70% of baseline values)</td>
</tr>
<tr>
<td>Hurt et al. (2000): to assess the short-term effect of smoking reduction on biomarkers associated with harm</td>
<td>Intervention study (smoking reduction)</td>
<td>Yes</td>
<td>Yes</td>
<td>23 heavy smokers (&gt;40 CPD)</td>
<td>Goal: 10 CPD at week 9; on average the subjects reduced CPD by &gt;50% at week 12, but only two reduced to 10 CPD</td>
<td>15 smokers completed the study; followed up to 24 weeks</td>
<td>Compared with baseline: no reduction in the carcinogen-derived biomarkers urinary NNAL or plasma 4-ABP-Hb adducts; significant reduction of NNAL-Gluc, and the sum of NNAL and NNAL-Gluc, but only at week 24</td>
<td>Expired CO (no reduction); serum cotinine (no reduction); serum thiocyanate (increased)</td>
</tr>
<tr>
<td>Pulera et al. (1997): to assess the short-term effect of smoking reduction on biomarkers associated with harm</td>
<td>Within-group comparative open-label study (smoking reduction)</td>
<td>Yes</td>
<td>Yes or placebo</td>
<td>50 healthy heavy smokers (15–50 CPD); presence of antibodies against BPDE-DNA adducts, a biomarker of DNA damage; sera tested blindly</td>
<td>Self-reported decrease in CPD</td>
<td>22 smokers reduced from 28 CPD to 7 CPD at week 6, and 9 CPD at week 12</td>
<td>Antibody positivity was low at baseline (8%); a paradoxical rise in prevalence of antibody positivity with both smoking reduction (41%) and smoking cessation (21%) was observed at week 12; stimulation of the immune system after smoking reduction/cessation is suggested</td>
<td>Expired CO (decreased); plasma cotinine and nicotine (no change)</td>
</tr>
<tr>
<td>Benhamou et al. (1989): to evaluate how changes in smoking habits influence lung cancer risk</td>
<td>Matched case-control study</td>
<td>No</td>
<td>No</td>
<td>1,027 histologically confirmed lung cancers in men and 1,481 matched controls; smokers or ex-smokers only</td>
<td>Self-reported decrease in CPD</td>
<td>29 smokers who reduced 1%–25% CPD; 42 smokers who reduced 26%–50% CPD; 30 smokers who reduced &gt;50%; follow-up: 20 years</td>
<td>Compared with matched controls: nonsignificantly reduced risk of lung cancer (26%–50% reduction, RR = 0.8, 95% CI = 0.5–1.2; &gt;50% reduction, RR = 0.8, 95% CI = 0.4–1.3)</td>
<td>No</td>
</tr>
<tr>
<td>Lubin et al. (1984): to determine the effect of smoking reduction on risk of lung cancer</td>
<td>Matched hospital-based case-control study</td>
<td>No</td>
<td>No</td>
<td>7,181 lung cancer patients and 11,006 controls were analyzed by years since smoking cessation or reduction</td>
<td>Divided as more than or less than 50% reduction of baseline tobacco consumption without quitting</td>
<td>45 (11%) of the cases and 1,083 (11%) of the controls; duration of reduction was noted (1 to &gt;25 years)</td>
<td>Compared with unchanged smoking: No RRs for lung cancer were 0.84 (95% CI = 0.7–1.0) for &lt;50% reduction and 1.01 (95% CI = 0.9–1.2) for &gt;50% reduction; there was a trend toward lower risk with increasing number of years after &gt;50% smoking reduction</td>
<td>No</td>
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<tr>
<td>Study and aim</td>
<td>Study design</td>
<td>Randomized to smoking reduction</td>
<td>Use of nicotine replacement therapy</td>
<td>Number and characteristics of smokers</td>
<td>Definition of successful reduction</td>
<td>Number of successful reducers and duration of follow-up</td>
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<tr>
<td>Godtfredsen et al. (2005): to determine the effect of smoking reduction on risk of lung cancer</td>
<td>Prospective cohort study</td>
<td>No</td>
<td>No</td>
<td>11,151 men and 8,563 women; Cox proportional hazard analyses with continuous heavy smokers as reference</td>
<td>Heavy smokers who reduced their daily tobacco consumption by at least 50% without quitting between first and second examination</td>
<td>Reduction achieved by 832 smokers; mean follow-up was 18 years</td>
<td>Compared with unchanged heavy smoking: adjusted HR for lung cancer was 0.73 (95% CI=0.54–0.98), and a linear dose-response relationship existed between amount smoked and lung cancer risk</td>
<td>No</td>
</tr>
<tr>
<td>Secker-Walker &amp; Vacek (2002): to determine whether smoking reduction during pregnancy has an effect on the birth weight of term infants</td>
<td>Intervention study (smoking cessation)</td>
<td>Case-control</td>
<td>No</td>
<td>No</td>
<td>240 smoking pregnant women with singleton births with available urinary cotinine at baseline and last visit; average 16 CPD baseline and 6 CPD at end of pregnancy</td>
<td>Achieved by at least 50%</td>
<td>Compared with nonreducers: nonsignificantly higher birth weight (36 g, p&gt;.05); infants in the &gt;=50% urinary cotinine reduction group had nonsignificantly higher weight (21 g, p&gt;.05); birth weight was not significantly higher in infants of women who quit</td>
<td>No</td>
</tr>
<tr>
<td>England et al. (2001): to determine whether smoking reduction during pregnancy has an effect on the birth weight of term infants</td>
<td>Intervention study (smoking cessation)</td>
<td>Case-control</td>
<td>No</td>
<td>No</td>
<td>1,583 pregnant smokers; only singleton term and infants of birth weight 900–5,300 grams included; registered CPD and measured urinary cotinine at first prenatal visit and at endpoint; average 18 CPD at baseline</td>
<td>Reducing by at least 50%</td>
<td>277 had reduced; average 5 CPD at end of pregnancy; 176 women had reduced urinary cotinine by &gt;=50%</td>
<td>Compared with nonreducers: increase in mean adjusted birth weight of 32 g after smoking reduction, which was not significant (p=.33); reduced urinary cotinine was associated with a nonsignificant (p=.57) increase in birth weight (21 g); significant increase (201 g) in birth weight among the 29 reducers with very low (&lt;5 CPD) baseline consumption; birth weight was significantly higher in infants of women who quit</td>
</tr>
<tr>
<td>Li et al. (1993): to determine whether smoking reduction during pregnancy has an effect on the birth weight of term infants</td>
<td>Intervention study (smoking cessation)</td>
<td>Case-control</td>
<td>No</td>
<td>No</td>
<td>803 pregnant women; only singleton live births included; salivary cotinine measured at first prenatal visit and at endpoint (&gt;=32 weeks’ gestational age)</td>
<td>(a) &gt;=60 ng/ml reduction for patients with baseline cotinine levels &gt;100 ng/ml or (b) &gt;=20 ng/ml reduction for patients with a baseline cotinine level of &lt;100 ng/ml</td>
<td>144 women had reduced</td>
<td>Compared with no-changers: higher adjusted mean infant birth weight of infants born to the reducers (74 g; not significant, p=.17); higher birth weight (241 g) for Whites with cotinine levels &gt;100 ng/ml (p=.01); birth weight was significantly higher in infants of women who quit</td>
</tr>
<tr>
<td>Study and aim</td>
<td>Study design</td>
<td>Randomized to smoking reduction</td>
<td>Use of nicotine replacement therapy</td>
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<td>Moller et al. (2002): to determine whether smoking reduction before surgery has an effect on postoperative complications</td>
<td>Intervention study (smoking cessation)</td>
<td>No</td>
<td>Yes</td>
<td>120 heavy smokers (&gt;15 CPD) randomized to smoking cessation intervention or control 6–8 weeks before planned surgery</td>
<td>Reducing by at least 50%</td>
<td>14 smokers; follow-up: 6–8 weeks</td>
<td>Compared with unchanged smoking: no significant difference in prevalence of wound complications or other postoperative complications compared with controls; smoking cessation associated with fewer peri- and postoperative complications</td>
<td>CO (not compared with CPD for validation purpose)</td>
</tr>
<tr>
<td>Bluman et al. (1998): to determine whether preoperative smoking reduction decreases the risk for postoperative pulmonary complications</td>
<td>Prospective cohort study</td>
<td>No</td>
<td>No</td>
<td>410 patients, including 141 current smokers (smoked within 2 weeks); patients scheduled for noncardiac elective surgery; baseline CPD missing</td>
<td>Subjects who reported to smoke less than at baseline from knowledge of surgery (&gt;1 week prior to surgery)</td>
<td>36 smokers reduced; average reduction =34%; follow-up: within 1 week to &gt;1 month</td>
<td>Compared with nonreducers, but not adjusted for baseline CPD: no trend in duration of reduction before surgery; increased risk for postoperative pulmonary complications (OR = 7.1, 95% CI = 3.0–17.0), not controlled for CPD or cumulative tobacco exposure</td>
<td>No</td>
</tr>
<tr>
<td>Godtfredsen et al. (2002): to determine the effect of smoking reduction on risk of all-cause mortality, mortality from COPD/respiratory infections, or due to cardiovascular disease</td>
<td>Prospective cohort study</td>
<td>No</td>
<td>No</td>
<td>11,159 men and 8,573 women; Cox proportional hazard analyses with continuous heavy smokers as reference</td>
<td>Heavy smokers at baseline who reduced their daily tobacco consumption by at least 50% without quitting between first and second examination</td>
<td>Reduction achieved by 858 smokers; mean follow-up: 15.5 years</td>
<td>Compared with persistent heavy smokers: no reduction in risk of all-cause mortality, mortality from COPD/respiratory infections, or mortality due to cardiovascular disease after long-term smoking reduction; borderline significant decline in risk of tobacco-related cancer mortality</td>
<td>No</td>
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Note. Studies are organized by disease and are in the same order as mentioned in the text. Some studies are mentioned more than once. Abbreviations: BPDE: benzo(a)pyrene diolepoxide; bpm: beats per minute; CI: confidence interval; CO: carbon monoxide; CPD: cigarettes per day; FEV₁: forced expiratory volume in 1 s; FVC: forced vital capacity; HDL: high-density lipids; 1-HOP: 1-hydroxypyrene; HR: hazard ratio; LDL: low-density lipids; NNAL: 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol; NNAL-Gluc: glucuronide of NNAL; NRT: nicotine replacement therapy; OR: odds ratio; PAH: polycyclic aromatic hydrocarbon; RBC: red blood cell count; RR: relative risk; WBC: white blood cell count.
& Prescott, 2003), with a mean follow-up of 15 years, linked information on smoking reduction with data on first hospital admission with the discharge diagnosis of myocardial infarction. Compared with continuous heavy smoking, self-reported reduction of at least 50% of baseline smoking was not associated with a decreased risk of hospitalization for myocardial infarction.

**Effect on intermittent claudication.** In a case-control study (Hughson, Mann, Tibbs, Woods, & Walton, 1978), nine smokers spontaneously reduced from more than 20 CPD to less than 10 CPD between baseline and 4–5 years. The prognosis of intermittent claudication was significantly better in reducers than in continuous smokers.

**Effect of reduced tobacco consumption on the airways (except lung cancer)**

**Effect on lung function, respiratory symptoms, and lower respiratory tract inflammation.** In an intervention study (McCarthy, Craig, & Cherniack, 1976), 38 subjects reduced the daily number of cigarettes smoked by more than 25%. Reduction resulted in significant improvement in the slope of phase III of the N2 washout curve, as well as closing volume/vital capacity, forced vital capacity (FVC), 1-s forced expiratory volume (FEV1), and peak flow at weeks 24–48. The finding that lung function was improved more by smoking reduction than by smoking cessation could not be explained. No differences were found between the two groups in the distribution of age, sex, or smoking history.

In a prospective cohort study (Burchfiel et al., 1995), more than 4,000 middle-aged/elderly men had their lung function examined three times over 6 years. The average annual rate of FEV1 decline was nonsignificantly smaller in the 415 men who spontaneously reduced the number of cigarettes smoked per day, but the analyses were not adjusted for cigarettes per day at baseline or duration of smoking.

Rennard et al. (1990) conducted an intervention study, in which the study population was highly selected and consisted of 15 healthy heavy smokers and a control group of healthy never-smokers. Subclinical bronchitis, as assessed visually by two physicians; number of neutrophils in the bronchoalveolar fluid; and neutrophil elastase measured as elastase-antigen complex improved significantly after 2 months of smoking reduction.

In an observational study (Lange, Groth, & Nyboe, 1989), reduced smoking was defined as self-reported heavy smoking at baseline and self-reported light smoking at 5-year follow-up. Results showed that the annual decline in FEV1 was less pronounced among men younger than 55 years of age who reported smoking reduction, compared with continuing heavy smokers. However, this finding was not statistically significant when subjected to a regression analysis.

Only 25 of the 400 enrolled study participants in an intervention study (Bolliger et al., 2002) had reduced successfully and continuously from week 6 to 2 years. After 24 months of follow-up, smoking reduction had no effect on lung function (FEV1 and FVC), compared with the control group.

A total of 52 smokers in a smoking cessation program that targeted asbestos-exposed workers reported a reduced tobacco intake by an average of 7 CPD (Waage, Vatten, Opedal, & Hilt, 1996). Subjects who had reduced reported significantly lower prevalence of cough and chronic cough at the 2-year follow-up, but the prevalence of dyspnea was unaffected. Data were not controlled for change in asbestos exposure/working conditions.

The Lung Health Study (Simmons et al., 2005) reported that only the 39 persons who reduced tobacco consumption by 85% or more achieved an improvement in lung function at the 1-year follow-up. Except for a borderline statistically significant decrease in phlegm production, there was no effect of smoking reduction on chronic lung symptoms.

At the 1-year follow-up of an intervention study (Bohadana, Nilsson, Westin, Martinet, & Martinet, 2005), 17 of the enrolled occupationally exposed healthy smokers had reduced smoking by at least 50%. Reduction was associated with significant improvement in cough, bronchitis symptoms, and shortness of breath when compared with group baseline values. FEV1 and airway responsiveness were not improved by reduction, compared with unchanged smoking.

A total of 207 smokers from methadone maintenance programs who participated in a randomized smoking cessation trial had reduced smoking at 3 months of follow-up (M. D. Stein, Weinstock, Herman, & Anderson, 2005). The mean reduction was 17 CPD; 66% had reduced by 10 CPD or more. A significant correlation was found between reduced smoking and reduction in respiratory symptom severity. Those with the largest absolute reductions achieved the largest improvements. A reduction in cigarette use was positively and significantly associated with smoking-related symptoms after adjusting for sociodemographic factors and nicotine dependence.

**Effect on asthma control.** At 4 months of follow-up, 33 asthma patients enrolled in an intervention study (Tonnesen et al., 2005) had reduced to less than 7 CPD. Reduction was associated with significantly decreased levels of biomarkers. Those who reduced smoking had less nighttime use of rescue medication,
reduced bronchial hyperreactivity, and a decrease in the amount of inhaled corticosteroids.

**Effect on the development of clinical chronic obstructive pulmonary disease (COPD)**

To our knowledge, the effect of smoking reduction on the risk of developing clinical COPD has been examined in only one study. This large prospective cohort study (Godtfredsen, Vestbo, Osler, & Prescott, 2002), with a mean follow-up of 15 years, linked information on smoking reduction with data on the first hospital admission with the discharge diagnosis of COPD. Compared with continuing heavy smoking, reducing smoking by at least 50% was not associated with a decreased risk of hospitalization for COPD.

**Effect of reduced tobacco consumption on reduction of lung carcinogens and lung cancer**

**Effect on tobacco-specific markers of lung carcinogens in urine or blood.** Subgroups that reduced number of cigarettes per day by 40% or more were defined, and reduction was achieved by 21 smokers in this intervention study (Hecht, Murphy et al., 2004). Urine samples were collected to assess the tobacco metabolite 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL) and its glucuronide (NNAL-Gluc), both important lung carcinogens. Statistically significant reductions in the lung carcinogen metabolites were observed at most intervals. However, the observed decreases were modest and smaller than the reductions in cigarettes smoked per day.

Hecht, Carmella et al. (2004) investigated the effects of smoking fewer cigarettes per day on another pulmonary carcinogen: the urinary levels of hydroxypyrene, a biomarker of carcinogenic polycyclic aromatic hydrocarbon uptake. Statistically significant reductions were observed at most time points in groups of smokers who reduced to different extents. The observed reductions in hydroxypyrene were modest and not fully consistent with reductions in cigarettes per day.

The subjects in one intervention study (Hurt et al., 2000) were able to reduce cigarettes per day by over 50% on average at week 12, but only two reduced to 10 CPD. Known biomarkers of harm, 4-aminobiphenyl hemoglobin (4-ABP-Hb) adducts, thiocyanate, carbon monoxide, and the urine metabolite NNAL and its glucuronide, NNAL-Gluc, were measured. Reduction was not associated with a decrease in NNAL, 4-ABP-Hb adducts, or expired carbon monoxide. There was a significant reduction in NNAL-Gluc, and in the sum of NNAL and NNAL-Gluc, but only at week 24.

A total of 22 smokers reduced from 28 CPD to 7 CPD at week 6, and 9 CPD at week 12 in an open-label study (Pulera et al., 1997). Sera were tested blindly for antibodies against benzo(a)pyrene diolepoxide-DNA adducts, indicators of DNA damage. A rise in antibody positivity with smoking cessation and smoking reduction was observed, indicating recovery of the immune response.

**Effect on lung cancer.** A matched case-control study included 1,027 histologically confirmed lung cancer cases and 1,481 matched control subjects (Benhamou, Benhamou, Auquier, & Flamant, 1989). Reducers were grouped according to the percentage reduction, which was not validated biochemically: 101 smokers had reduced by more than 1%, and 30 had reduced by 50% or more. The authors found a nonsignificantly reduced risk of lung cancer in those who reduced compared with those who sustained their smoking level.

A large case-control study included 7,181 lung cancer patients and 11,006 hospital-based control subjects (Lubin et al., 1984). A total of 11% of the patients and the controls reported smoking reduction, which was not validated biochemically. Overall, no differences were observed in lung cancer risk between persistent smoking and smoking reduction. After subjects were stratified by years since decrease in consumption, a trend toward lower risk was found, compared with unchanged smoking for 50% reduction or more only.

A paper from the Copenhagen Centre for Prospective Population Studies (CCPPS) shows that smoking reduction from heavy to light smoking was associated with a 27% reduction in the risk of lung cancer (Godtfredsen, Prescott, & Osler, 2005). These are observational data with up to 30 years of follow-up.

**Effect of reduced tobacco consumption on birth weight**

**Relationship between reduction of tobacco consumption in pregnancy and birth weight.** In one intervention study (Secker-Walker & Vacek, 2002), 44 women achieved smoking reduction, defined as a reduction of at least 50% in cigarettes per day. Urinary cotinine at baseline was almost twice as high in those who reduced in pregnancy as it was in those who quit. Infants born to reducers had nonsignificantly higher birth weights compared with those born to women who did not reduce. In 48 women, urinary cotinine was reduced by at least 50%. The infants in this group weighed more than infants of smoking women who did not reduce, but the difference was not significant. Yet birth weight was not significantly higher in infants of women who quit successfully.
In another intervention study (England et al., 2001), successful reduction was defined as reduction by 50%, which 277 women achieved. Reduced cigarette consumption was associated with a small nonsignificant increase in birth weight. A total of 176 women had reduced their urinary cotinine level by 50% or more, which was associated with a small nonsignificant increase in birth weight.

In the third trial including pregnant women (Li, Windsor, Perkins, Goldenberg, & Lowe, 1993), reduction was defined as (a) at least a 60 ng/ml reduction for patients with baseline cotinine levels of more than 100 ng/ml, or (b) at least a 20 ng/ml reduction for patients with a baseline cotinine level of 100 ng/ml or less. A total of 144 women reduced. The adjusted mean infant birth weight was higher among infants born to the reducers, compared with infants born to the no-changers, but this difference was not significant. In White women, those with a cotinine reduction of at least 100 ng/ml had infants with adjusted mean birth weights that were significantly higher compared with infants born to nonreducers.

Other health effects of smoking reduction

Effect of preoperative smoking reduction on postoperative complications after elective surgery. An intervention study (Moller, Villebro, Pedersen, & Tonnesen, 2002) found no significant difference in the prevalence of wound complications or other postoperative complications among control subjects or the 14 successful reducers, who reduced by 50% or more. A prospective cohort study (Bluman, Mosca, Newman, & Simon, 1998), in which smoking reduction was apparently defined as “able to reduce cigarette consumption since knowledge of surgery,” found an average reduction of 34%. Analyses were controlled for factors such as pulmonary function, cough, body mass index, and sociodemographic variables but not for number of cigarettes per day or cumulative tobacco exposure. The reducers also were included in other analyses as current smokers. Compared with unchanged smoking, smoking reduction was associated with an increased risk for postoperative complications; this association was explained by nicotine withdrawal.

Effect on self-reported general health. In Bolliger et al. (2002), self-reported general health score improved in the 25 smokers who had reduced successfully and continuously from week 6 to 2 years.

Effect on mortality. Analyses of total and cause-specific mortality following smoking reduction have been conducted in the large CCPPS (Godtfredsen, Holst, Prescott, Vestbo, & Osler, 2002). Compared with unchanged heavy smoking, no reduction was seen in risk of all-cause mortality, mortality from COPD/respiratory infections, or mortality due to cardiovascular disease after smoking reduction. A borderline significant decline was observed in risk of tobacco-related cancers in participants who reduced smoking, compared with continuous heavy smokers.

Discussion

This review identified 31 publications across 25 studies. Generally, data were limited, but smoking reduction appeared to have a small effect on several cardiovascular risk factors, biomarkers of harm, and pulmonary symptoms such as cough and phlegm. Furthermore, smoking reduction seemed to be associated with a consistent but very small and nonsignificant increase in birth weight. A discrepancy exists in the effect on lung cancer, but the more recent epidemiological and clinical data suggest a positive effect of smoking reduction in the magnitude of approximately 25% disease risk reduction with 50% reduction in number of cigarettes smoked per day (Hecht, Murphy et al., 2004; Godtfredsen et al., 2005). The data on asthma, COPD, postoperative complications, self-reported health, and mortality are too limited to draw any conclusions. However, results show consistently that the magnitude of health benefit following smoking reduction is smaller than the reported reductions in tobacco use.

Evaluation of the presented evidence introduces several problems. First, the definition of a successful reduction in the studies was not the same, even though most studies defined successful reduction as smoking less than 50% of baseline consumption. Second, the duration of reduction was not always defined. Bolliger et al. (2002) measured continuous reduction from week 6 to year 2 verified by carbon monoxide, but most other studies were based on one baseline and one follow-up measurement, which is a problem especially in long-term cohort studies, as the duration of reduction might be between a few days and decades (Benhamou et al., 1989). Third, the average number of cigarettes smoked at baseline and after reduction differed from study to study. Some studies included very heavy smokers with a mean baseline consumption of 50 CPD (Rennard et al., 1990); other studies included smokers with a mean baseline consumption of 15 CPD (Waage et al., 1996). The health benefit might differ substantially when reducing by 25 CPD or 7 CPD. Fourth, smoking reduction was sometimes spontaneous and sometimes part of an intervention, assisted by the use of nicotine replacement therapy. Intervention studies have a tendency to include selected subjects, and a potentially beneficial effect of smoking reduction could be minimized by nicotine. Nicotine products were used in 14 of the studies, but it seems that use
did not negate eventual health improvements. Fifth, it might be questioned whether reducers are comparable with nonreducers. In several studies (England et al., 2001; Li et al., 1993), the baseline levels of tobacco consumption or cotinine were significantly higher in the reduction group than in the nonreduction group. Also, the groups might not be comparable in other risk factors (e.g., lifestyle factors such as diet or physical activity), which might influence the outcome. If we hypothesize that reducers generally have a higher tobacco consumption and unhealthier lifestyle at baseline and are compared with healthier smokers, a health benefit of reduction would be difficult to detect.

Generally, the number of studies in each of the five areas was small, and the number of smokers who reduced successfully was very low. We assume that a publication bias is probable, in which nonsignificant studies were published less frequently. Another limitation might be that, in many of the studies, outcome was reported on only those who reduced, and intention-to-treat analyses were not carried out. Furthermore, some studies were originally smoking cessation studies and not smoking reduction studies; hence, smoking reduction applied to only a subgroup of the study population. Statistical analyses may therefore be subject to type 2 errors, and a possible positive effect of smoking reduction may be underestimated.

We could not identify a consistent design bias given that a significant effect sometimes was found in epidemiological cohort studies but not in case-control studies (e.g., lung cancer), whereas the opposite was true in other areas (e.g., cardiovascular system). However, a positive effect of smoking reduction tended to appear more frequently in studies in which smokers were randomized to smoking reduction, compared with studies in which smoking reduction was self-selected or studies designed for another purpose.

Other major reasons for not detecting a health benefit of smoking reduction include compensatory smoking (Hughes & Carpenter, 2005), the low success rate of smoking reduction, and the biological time delays between smoking and harm, and subsequently between change in smoking habit and health benefit. Finally, those health outcomes that have been investigated in relation to smoking reduction exhibit very different dose-response relationships with tobacco exposure, which is highly likely to affect measures of the effect of smoking reduction.

Some biomarkers mentioned in the present review are biomarkers of exposure (e.g., carbon monoxide, cotinine); others are biomarkers of potential harm (e.g., indicators of DNA damage). We could have chosen to focus on disease risk only, and exclude biomarker/risk factor studies, given that there are several difficulties in interpreting the results. It can be argued that biomarkers do not predict disease onset accurately. However, we decided to include biomarker studies because they are a good supplement to case-control studies and epidemiological cohort studies. Also, such studies are the most rapid way to evaluate the effects. Conducting a randomized clinical trial requires a very large number of reducers, and a long follow-up would be needed to detect effects on disease and mortality. However, several previous reviews have highlighted both the lack of ideal biomarkers for assessing tobacco harm reduction and the problems in relating changes in biomarkers to changes in disease pathogenesis following smoking reduction (Hatsukami, Benowitz, Rennard, Oncken, & Hecht, 2006; Hecht, 2002; Shields, 2002). Clearly, this lack of understanding of the exact mechanisms involved in potential reversal of disease risk after reduced exposure to tobacco toxins is likely to influence study outcomes in the present review. For instance, although suitable and readily accessible biomarkers for lung cancer exist, this is not the case for tobacco-related lung diseases such as COPD. Many biomarkers are predictive of cardiovascular disease, but not all are tobacco related, and because the tobacco-attributable risk is much smaller for heart disease than for lung cancer and COPD, the interpretation of the role of biomarkers after smoking reduction is impeded. With respect to pregnancy, several promising biomarkers are currently under study, but only birth weight and cotinine as proxies of tobacco consumption have been used in smoking reduction studies. Furthermore, for many organ systems, it is still not known what extent of reduction in a given biomarker is needed to produce a reduction in subsequent disease risk. That is, the possible dose-response relationship between reduced exposure and reduced disease development is unclear.

Previously, smokers seeking assistance for smoking cessation were informed that smoking reduction was impossible and that smoking cessation was the only option. Data from the 1970s showed that smoking reduction was strongly associated with severely impaired lung function (Godtfredsen, Prescott, Osler, & Vestbo, 2001). Therefore, it is possible that studies on spontaneous smoking reduction some decades ago do not reflect the same smokers and health effects as today.

In conclusion, data are sparse, and more evidence is needed before we can tell if a substantial benefit on health can be achieved by reducing smoking. We suggest both more short-term risk factor studies combined with case-control and cohort studies focusing on target organs such as the heart and the lungs. For future studies we recommend biochemical validation to demonstrate verification of reduction...
and a 50% reduction to be the minimum percentage reduction in smoking. Optimally, the studies should be prospective, large, of longer duration, and with biochemical validation at multiple and more frequent intervals.

Studies have shown that smoking reduction is feasible and does not undermine smoking cessation (Fagerström, 2005; Hughes & Carpenter, 2005). Randomized controlled trials on smoking reduction show that smoking reduction seems to increase the smoker’s motivation to quit and to increase future cessation (Fagerström, 2005; Pisinger, Vestbo, Borch-Johnsen, & Jørgensen, 2005). Because it will take many years and be difficult to prove possible substantial health benefits of smoking reduction, the expression harm reduction should not be used. Instead smoking reduction could be introduced as an alternative way to approach the reluctant smoker and subsequently as “a first step toward smoking cessation.”

Finally, we must not forget that even if smoking reduction is associated with a small health benefit, consumption of as few as 1–4 CPD is still associated with a significantly increased health risk (Bjartveit & Tverdal, 2005), and no threshold exists below which it is considered safe to smoke voluntarily or involuntarily.

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References


