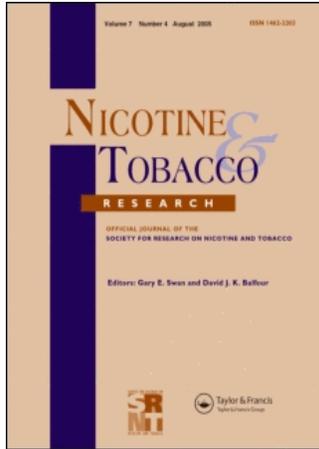


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Does smoking reduction increase future cessation and decrease disease risk? A qualitative review

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Does smoking reduction increase future cessation and decrease disease risk? A qualitative review

John R. Hughes, Matthew J. Carpenter

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This review examines whether reduction in smoking among smokers not currently interested in quitting (a) undermines or promotes future smoking cessation or (b) decreases the risks of developing smoking-related diseases. Systematic computer searches and other methods located 19 studies examining reduction and subsequent cessation and 10 studies examining reduction and disease risk. Because of the heterogeneity of methods and results, a meta-analysis could not be undertaken. None of 19 studies found that reduction undermined future cessation, and 16 found that reduction was associated with greater future cessation, including the two randomized trials of reduction versus nonreduction. The 10 trials of disease risk found conflicting results, and none was an adequate test. We conclude that (a) smoking reduction increases the probability of future cessation and (b) whether smoking reduction decreases the risks of smoking-related diseases has not been adequately tested.

Introduction

Although tobacco policies aimed at populations and interventions aimed at individuals increase cessation (U.S. Department of Health and Human Services [USDHHS], 2000), both have produced less than optimal results (Susser, 2002). In fact, even in countries with the most effective cessation activities, few smokers stop smoking within a given year. For example, in the United States and United Kingdom, less than 3% of smokers stop each year and many smokers never stop (Centers for Disease Control and Prevention, 2004; West, 2005). These disappointing results have increased interest in noncessation methods to decrease the morbidity and mortality from smoking among smokers not currently trying to stop smoking (Hatsukami, Henningfield, & Kotlyar, 2004; Hatsukami et al., 2002; Institute of Medicine, 2001; Warner, 2003).

Noncessation methods include use of less-risky tobacco products, substitution of pure nicotine products, early detection of disease, and chemoprevention (Shiffman et al., 2002). One noncessation

method is to reduce the number of cigarettes smoked per day (CPD) among smokers not currently interested in quitting (i.e., “smoking reduction”; Shiffman et al., 2002). Whether smokers can substantially reduce their CPD and maintain such reduction over time has been debated; however, a recent comprehensive review of 18 studies concluded “smokers make significant reductions in their smoking and maintain these reductions over time” (Hughes & Carpenter, 2005).

Two major public health questions about smoking reduction are whether reduction (a) will undermine motivation to quit smoking and (b) produce a clinically significant decrease in the risks of smoking-related diseases. Prior reviews have addressed these questions (Hatsukami, Henningfield et al., 2004; Hatsukami et al., 2002; Health Development Agency, 2001; Institute of Medicine, 2001; Warner, 2003); however, many new studies have appeared since these reviews. For example, the previously cited reviews reported on 5 or fewer studies on the effect of reduction on cessation, whereas the present review looked at 19 such studies.

Does reduced smoking undermine or promote smoking cessation?

One of the most common concerns about smoking reduction is that it may undermine motivation to

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stop smoking (Hatsukami, Henningfield et al., 2004; Hatsukami et al., 2002; Institute of Medicine, 2001; Warner, 2003) because smokers will see smoking reduction as an alternative to cessation. Many smokers have difficulty quitting (Colby, Tiffany, Shiffman, & Niaura, 2000; Shadel, Shiffman, Niaura, Nichter, & Abrams, 2000), and many do not believe they will ever be able to stop (Boyle et al., 2000). Thus, smokers who reduce may rationalize that achieving what they believe is risk reduction is all that they can or want to accomplish.

However, smoking reduction might increase future cessation for at least two reasons. First, reduction can be thought of as a step toward cessation, and a step taken toward finishing a task increases one's self-efficacy toward the ultimate task and thereby makes success more likely (Bandura, 1977). Second, since nicotine dependence may decrease as one reduces and since dependence is a barrier to smoking cessation (Colby et al., 2000; Shadel et al., 2000), reducing smoking may make it easier to quit smoking once a quit attempt is made.

Does reduced smoking decrease the health risks of smoking?

Many studies have documented that the risks of disease, morbidity, and mortality are highly related to CPD, usually in a linear manner (USDHHS, 2004). However, the dose-response relationships in these studies are based on cross-sectional analysis of self-selected groups; that is, smokers who chose to smoke more cigarettes per day versus those who chose to smoke fewer cigarettes per day. Cross-sectional analyses typically used post-hoc corrections to minimize the possibility that associations were related to factors that differ between groups other than CPD; however, the completeness of such corrections is never certain (Gordis, 2004). As a result, the effect of dose is often larger in cross-sectional tests than in longitudinal (or cohort) or experimental studies (Gordis, 2004).

Method

For our analyses, reduced smoking was defined as reducing CPD in smokers not actively trying to quit. This definition excluded reductions in smoking topography (Glasgow, Murray, & Lichtenstein, 1989), cigarette length (McMorrow & Fox, 1983), or tar/nicotine yield (National Cancer Institute, 2001), as well as reduction as a method to quit among smokers actively trying to quit (Cinciripini, Lapitsky, Seay, Wallfisch, & Kitchens, 1995). Our analyses focused on population and clinical studies of adult daily smokers and excluded studies of adolescents (USDHHS, 1994; Wetter et al., 2004),

pregnant smokers (USDHHS, 2001), or smokers with a current psychiatric disorder (Dalack & Meador-Woodruff, 1999; George et al., 2002; Weiner, Ball, Summerfelt, Gold, & Buchanan, 2001), as well as laboratory studies of smokers not trying to reduce (Benowitz, Jacob, Kozlowski, & Yu, 1986).

We attempted to follow the QUOROM standards for systematic reviews (Egger, Smith, & Altman, 2001; Moher et al., 1999). We began with a search of the first author's files of articles on smoking reduction compiled from the last 5 years of the Institute for Scientific Information *Personal Alerts* database (http://alerting.isinet.com/pa_home.html) tailored for the first author. We then searched Medline, EMBASE, and PsychAbstracts databases. We found the most productive search method for these databases was to search titles and abstracts for the stems "harm reduc-," "smoking reduc-," "cigarette reduc-," "reducing smok-," "reduced cig-," "reduction in cig-," and "reducing cig-." We used a similar strategy to search the Computer Retrieval of Information on Scientific Projects (CRISP) database of U.S. National Institutes of Health grants (www.crisp.cit.nih.gov) and sent a request for publications to the principal investigators of the relevant grants. We examined abstracts of the 2001–2004 annual meetings of the Society for Research on Nicotine and Tobacco (www.srnt.org) and the U.S. National and World Conferences on Tobacco or Health (www.nctoh2003.org and www.wctoh2003.org). We searched the Cochrane Registry (www.cochrane.org). We queried the SRNT listserve (srntlist@tmahq.com) and relevant pharmaceutical companies for studies. When articles from these searches cited references that might be relevant, we sought out these. Our search terminated in November 2004.

The inclusion criteria were a report of a change in CPD in smokers and a report either of future cessation or of disease outcomes. Studies that reported on self-reported motivation to quit but not cessation outcomes were not included. Similarly, studies that reported on biomarkers but not disease outcomes were not included. Whether unpublished studies should be included in systematic reviews is debatable (Cook et al., 1993). However, because many of the studies we located were funded by pharmaceutical companies, and publication bias (i.e., failure to publish studies with negative results) by such companies has been documented (Bhandari et al., 2004), we decided to include unpublished studies. When the source was unpublished, we asked the authors for a full paper. This was usually not successful. We did not exclude or rank studies using methodological rigor scales because recent work questions the validity of such measures and suggests

that using such scales produces no benefits (Jüni, Witschi, Bloch, & Egger, 1999). We did not locate any foreign language articles that met our inclusion criteria.

The information from the articles was abstracted by the first author and verified by the second author. Disagreements were resolved by discussion and sometimes by contacting the study author. We intended to use meta-analytic methods but did not do so for three reasons: (a) Studies varied widely in their methods (e.g., randomized, controlled trials [RCTs] vs. pre-post comparisons of a single group, (b) to convert all the data to a common standard often required recalculation of data from study reports, and (c) combining results failed tests for statistical homogeneity (Egger et al., 2001; Rosenthal, 1995). Thus we had to use a subjective rating of the consistency and magnitude of results to make decisions.

Results

Does reduced smoking undermine or promote smoking cessation?

Two types of studies have provided indirect tests of the association between reduced smoking and future quitting among smokers not trying to quit: (a) Studies of those who spontaneously chose to reduce versus those who did not do so and (b) RCTs of active versus control interventions for reducing CPD among smokers, all of whom were trying to reduce. A third type of study—RCTs assigning smokers to either reduce or not reduce—provided a direct test of the causal association between reduction and future quitting.

Spontaneous reduction. The first type of study divided smokers into groups of those who did or did not reduce their smoking by at least 50% between time 1 and time 2 and then compared the incidence of abstinence between these two groups by time 3. We located six such analyses based on five studies that used similar methods (Table 1). Three of these studies

were nonintervention studies. In one such study, U.S. smokers aged 51–61 years who reduced by at least 50% had a greater probability of quitting a year later than did nonreducers (Falba, Jofre-Bonet, Busch, Duchovny, & Sindelar, 2004). In another study, U.S. smokers in a state with a successful tobacco control program who reduced by at least 67% or reduced to less than 15 CPD were more likely to go on to quit in the next 2 years (Farkas, 1999). In addition, the amount of reduction predicted the probability of future quitting in a dose-related manner across two different measures of reduction. In a third small, unpublished study, those in the U.S. Normative Aging Study who reduced by at least 50% did not have a greater chance of cessation at a 20-year follow-up (Nordstrom, Kinnunen, & Garvey, 2000).

Three analyses used data from RCTs. Two used data from the U.S./Canada Community Intervention Trial (COMMIT), which tested the effect of tobacco policies on cessation in heavy and light smokers (Hughes, Cummings, & Hyland, 1999; Hyland et al., 2005). The study did not encourage reduction. In both analyses, the data were aggregated across experimental groups. Both analyses found an adjusted odds ratio of 1.7 for increased cessation among those who reduced by at least 50%. This finding was statistically significant only in the latter analysis, which had a greater sample size and longer follow-ups (5 years; Hyland et al., 2005). Another analysis used data from the Lung Health Study, which tested a smoking cessation intervention combining nicotine gum and behavioral therapy in smokers with early pulmonary diseases (Hughes, Lindgren, Connett, & Nides, 2004). The study did not encourage reduction, but many reducers were allowed to continue to use nicotine gum. Reducers did not have a greater rate of abstinence than nonreducers by the end of the 5-year period.

Other studies provided less-rigorous tests of whether reducing leads to increased quitting. One study reported that those who attempted to reduce (amount and success unspecified) did not have more later quitting (Meyer, Rumpf, Schumann, Hapke, & Ulrich, 2003). Another study reported that those who

Table 1. Point-prevalence abstinence in self-selected reducers ($\geq 50\%$) vs. nonreducers.

Study	Number of reducers	Follow-up (months)	Abstinence		Adjusted odds ratio
			Reducers	Nonreducers	
<i>Nonintervention studies</i>					
Falba et al., 2003	680	12	32%	14%	1.4*
Farkas, 1999	245	24	21%	9%	2.2*
<i>Nordstrom et al., 2000</i>	35	240	45%	46%	1.0
<i>Intervention studies</i>					
Hughes et al., 1999	113	24	14%	10%	1.7
Hyland et al., 2005	522	60	35%	24%	1.7
Hughes et al., 2004	1022	60	3%	3%	1.0

Note. Unpublished studies in italics. * $p < .05$; otherwise, $p > .05$ or not reported.

planned to reduce (outcome unspecified) were later more likely to be abstinent than those who did not plan to reduce (Dijkstra & DeVries, 2000). Although several studies have shown that nondaily smokers are more likely to quit (Henrikus, Jeffery, & Lando, 1996; Lindstrom, Isacson, & The Malmö Shoulder-Neck Study Group, 2002; McCarthy, Zhou, & Hser, 2001), none has examined quitting specifically among daily smokers who have become nondaily smokers.

In summary, none of these nonexperimental studies suggests that reduction undermines future cessation and several suggest it increases cessation. However, these studies compared self-selected groups of reducers and nonreducers; thus, their interpretation is problematic. For example, those who choose to reduce might a priori be more motivated to stop smoking than those who do not choose to reduce. Thus, any association of reduction with improved quitting may have been related, not to reduction per se, but rather to the preexisting characteristics of reducers (i.e., related to selection bias). On the other hand, those who chose to reduce may be heavier, more dependent smokers who cannot quit; this would minimize any causal effect of reduction. Most of the preceding analyses attempted to correct for such confounds by adding covariates; however, no analysis controlled for all the possible differences between reducers and nonreducers that could be hypothesized.

Controlled trials. The second type of indirect test is a RCT of an intervention to reduce smoking in smokers who are not planning on quitting in the near future. In these studies, *all* smokers were encouraged to reduce and randomized to active treatment to reduce or a control group. Even though cessation was not the goal of the intervention or of the smokers, several of these studies reported the incidence of quitting in the active versus control groups. The rationale for examining these trials is that if the active treatment reduced smoking more

than the control, and if reduction leads to increased cessation, then the rates of cessation should be higher in the active than the control group.

We located eight such trials (Table 2) that provided nine active versus control comparisons (one trial had two control groups). All of these studies were placebo-controlled RCTs of medication treatments (Batra et al., 2005; Bolliger et al., 2000; Etter, Laszlo, & Perneger, 2004; Haustein, Batra, Landfeldt, & Westin, 2003; Joseph, Bliss, Zhao, & Lando, 2005; Kralikova, Kozak, & Rasmussen, 2002; Rennard et al., 2002; Wennike, Danielsson, Landfeldt, Westin, & Tonnesen, 2003). Five of the trials were available only via abstracts or posters. Because these eight studies examined the prompting of new quit attempts, they reported point-prevalence abstinence rates (Hughes et al., 2003).

In all eight studies, active medication produced more reduction than in the control group; thus the premise of the rationale for examining these studies is valid. In none of the studies was there less cessation in the active than the control group—i.e., there was no evidence that reduction undermined cessation. In eight of the nine comparisons, the incidence of cessation was numerically higher in the active group, and in two of the trials, this difference was statistically significant. In five comparisons, the increase in quitting in the active group was either nonexistent or small ($OR=1.0-1.4$), and in four, it was substantial ($OR=2.4-4.3$). The odds ratios for the three published trials were 1.0–1.1, 1.3, and 2.9. For the five unpublished studies, the odds ratios ranged from 1.4 to 4.3.

One other reduction study used a somewhat different design (Hatsukami, Rennard et al., 2004). In this RCT of bupropion for reduction in smokers not initially interested in quitting, those smokers who during the trial chose to quit in either the bupropion reduction or placebo reduction arm were transferred to a third arm in which they received only bupropion for cessation. Although smoking reduction was

Table 2. Point-prevalence abstinence in studies testing a reduction intervention.^a

Study	Sample size	Follow-up (months)	Point-prevalence abstinence		Odds ratio for increased cessation in active group
			Active	Control	
<i>Nicotine gum</i>					
Batra et al., 2005	364	13	12%	5%	2.6 ^{a*}
Haustein et al., 2003	192	12	11%	8%	1.4 ^a
Wennike et al., 2003	411	24	9%	3%	2.9 ^{b*}
<i>Nicotine inhaler</i>					
Bolliger et al., 2000	400	24	11%	9%	1.3 ^c
Rennard et al., 2002	429	15	8%	2%	4.3 ^a
<i>Multiple NRTs</i>					
Etter et al., 2004	923	26	12%	12% ^d	1.0 ^a
Joseph et al., 2005	152	6	8%	7%	1.2 ^a
Kralikova et al., 2002	314	12	19% ^d	9% ^d	2.4 ^a

Note. Unpublished studies in italics. NRT, nicotine replacement therapy. ^aCalculated from abstinence rates. ^bAdjusted odds ratio from text. ^cSustained abstinence, not point-prevalence abstinence. ^dTwo control groups. * $p \leq .05$; otherwise, $p > .05$ or not reported.

greater in the bupropion arm, abstinence rates at 6 months did not differ between bupropion reduction versus placebo reduction arms (7% vs. 5%).

In summary, none of these RCTs suggests reduction undermined future cessation and many suggested reduction substantially increased cessation. However, this increase was very small or nonexistent in two of the three published trials. These RCTs avoid the problems of self-selected groups; however, participants in the active groups in these trials received both instructions to reduce and the medication to use in the period prior to a quit date. Thus, whether it was the reduction per se or the receipt of nicotine replacement therapy (NRT) that caused the future abstinence is unclear. No studies have examined whether simply giving NRT to smokers not interested in quitting would increase abstinence. The results of three studies indicate that among smokers preparing to make a quit attempt, making NRT available prior to the quit date without instructions to reduce increases quit rates, perhaps because this increases compliance with NRT or reduces the reinforcing efficacy of cigarettes (Herrera et al., 1995; Rose et al., 1994; Schuurmans, Diacon, van Biljon, & Bolliger, 2004). Thus, it is unclear whether reduction per se or the use of NRT is increasing future abstinence in the RCTs reviewed here.

Direct tests. The third type of study is the most important—a direct experimental test in which smokers who are not currently trying to quit are randomly assigned either to reduce or not to reduce. Thus, these trials differ from the RCTs described earlier in that the former instructed *all* smokers to reduce. Four direct RCTs of reduction versus nonreduction have been published and reported 6-month point-prevalence abstinence rates.

Two of these studies compared reduction to no treatment (Figure 1). One study randomized 616 smokers who had refused an offer of free cessation treatment to a reduction (reduction counseling+NRT) or a no intervention group; this study also had a third group, which received standard motivational intervention (Carpenter, Hughes, Solomon, & Callas, 2004). Treatment in this study was delivered via phone and mail. A second study randomized 220 asthmatic smokers to reduction (counseling+NRT) versus no treatment. It too had a third group, this time receiving cessation advice (Tonnesen et al., 2005). In the second study, smokers could have had plans to reduce or quit smoking and treatment assignment was not random; however, we have included it for the sake of completeness. In both studies, the rate of point-prevalence abstinence at the 6-month follow-up was significantly greater in the reduction than in the no

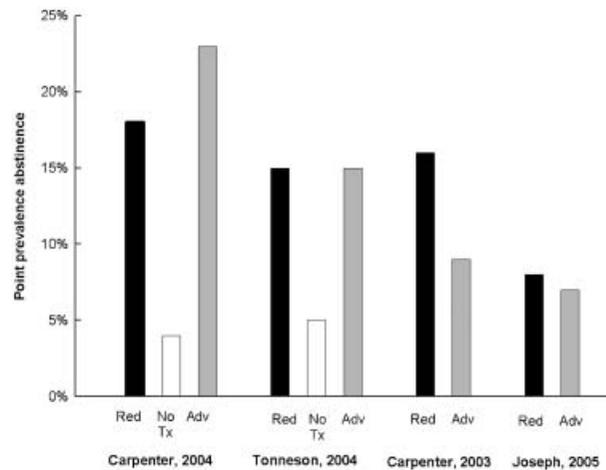


Figure 1. Long-term point-prevalence abstinence for randomized controlled trials of reducing vs. not reducing smoking. (Adv, cessation advice, No tx, no treatment; Red, reduction.) Studies are listed by first authors' last names and the year of publication.

treatment group (18% vs. 4% and 15% vs. 5%, respectively).

In these two studies, the abstinence rates in the reduction and motivational/cessation advice groups were not significantly different (18% vs. 23% and 15% vs. 15%, respectively). Two other studies also compared reduction versus motivational advice. One of these studies randomized smokers not interested in quitting ($n=67$) to either a reduction intervention (brief in-person counseling+NRT) or brief cessation advice alone (Carpenter, Hughes, & Keely, 2003). The other study randomized smokers with heart disease who were not interested in stopping smoking ($n=152$) to reduction (in-person counseling+NRT) or "usual care" (Joseph et al., 2004). This study has not been published. Both additional studies again found that the point-prevalence abstinence 6 months later did not differ significantly between groups; i.e., 16% versus 9% (Carpenter et al., 2003), and 8% versus 7% (Joseph et al., 2004).

These findings are the strongest evidence that reduction increases future cessation. Whether reduction increases future quitting by increasing quit attempts, by increasing the success of quit attempts, or both is unclear. In the only test of this question, one of the studies reported that reduction increased quit attempts by a factor of 4.2 and reported an almost identical increase in abstinence by a factor of 4.5 (Carpenter et al., 2004). Thus it appears that almost all of the beneficial effect of reduction in that study was related to its prompting quit attempts, not to its assisting in quitting once a quit attempt had been made. The previously mentioned caveat about whether reduction per se or the receipt of NRT is increasing cessation applies to these studies as well. However, two pieces of evidence suggest reduction per se may explain these increases. First, one of

the previously mentioned experimental studies (Carpenter et al., 2004) reported that smokers who reduced more had a greater probability of later quitting; however, whether this finding was independent of use of NRT was unclear (Carpenter et al., 2004). Another non-RCT study also found that the amount of reduction was correlated to the amount of cessation, again suggesting that reduction per se caused the increased cessation (Pisinger, Vestbo, Borch-Johnsen, & Jørgensen, 2005).

One final study reported data relevant to cessation. This study randomized smokers not currently interested in quitting to receive a message that NRT could be used for reduction versus a message that NRT could be used only for cessation. Smokers who received the reduction message were slightly more, not less, likely to report increased motivation to quit than those who received the cessation message (Etter, LeHouezec, & Landfeldt, 2003).

Does reduced smoking decrease the health risks of smoking?

Two types of indirect tests of the association of smoking reduction and disease risk are case-control and cohort studies (Gordis, 2004). We located 13 articles reporting on 10 such studies (Table 3). The major additional criteria for inclusion in the disease risk analyses were (a) that the study must report on a disease outcome (i.e., not a biomarker) and (b) that it must not include abstainers in the reduction group (Stein, Weinstock, Herman, & Anderson, 2005).

Although we report the results of these 10 studies, we believe that none is an adequate test for several reasons. None of these studies was designed to examine reduction and, as a result, none had an adequate measure of smoking reduction. In these

studies, the measure of reduction was based on a single self-report of smoking at a particular time. The timing and duration of reduction was not reported; for example, in the one large study it was unclear whether reduction had been maintained for 1 week or 14 years (Godtfredsen, Hoist, Prescott, Vestbo, & Osler, 2002; Godtfredsen, Osler, Vestbo, Andersen, & Prescott, 2003; Godtfredsen, Vestbo, Osler, & Prescott, 2002). In addition, none of the studies biochemically verified that reduction had indeed occurred.

Case-control studies. Two case-control studies examined whether smokers who reduced their smoking in the past were less likely to develop lung cancer than smokers who did not reduce (Table 3). One small study found a relative risk of cancer of 0.8 in reducers compared to nonreducers, but this finding was not statistically significant (Benhamou, Benhamou, Auquier, & Flamant, 1989). In the other, much larger study, those who reduced by at least 50% did not have a reduced relative risk of lung cancer; however, paradoxically those who reduced by 1%–49% had a nonsignificant reduced relative risk of cancer of 0.84 (Lubin et al., 1984).

Cohort studies. Six cohort studies (that produced eight analyses) followed smokers who reduced versus those who did not reduce over time to examine their later disease risk (Table 1). Two small short-term studies reported that reducing smoking prior to surgery did not reduce surgery complications, length of stay, or the like (Bluman, Mosca, Newman, & Simon, 1998; Moller, Villebro, Pedersen, & Tonnesen, 2002).

Table 3. Studies of benefits of reduction on disease or symptom outcomes.^a

Study	Number of reducers	Reduction criteria	Follow-up	Outcome	Results
<i>Case-control studies</i>					
Benhamou et al., 1989	101	>0%	?	Lung cancer	Nonsignificant improvement
Lubin et al., 1984	745	>0%	1–25+ years	Lung cancer	Nonsignificant improvement
	358	≥50%			improvement
<i>Cohort studies</i>					
Bluman et al., 1998	36	>0%	1–4 weeks	Surgical complications	No effect
Moller et al., 2002	14	>0%	7–9 weeks	Surgical complications	No effect
Buist et al., 1976	23	≥25%	1 year	Pulmonary symptoms	Improved
Lange et al., 1989	326	<15 CPD	5 years	Pulmonary function and symptoms	Improved in subset
Simmons et al., 2005	1000	>10%	1 year	Pulmonary function and symptoms	Improved in subset
Hughson et al., 1978	33	≥50%	4 years	Claudication	Improved
<i>Nordstrom et al., 2000</i>	35	≥20%	20 years	Mortality	Improved
Godtfredsen, Hoist et al., 2002 ^a	858	≥50%	15.5 years	Mortality	No effect
Godtfredsen, Vestbo et al., 2002 ^a	832	≥50%	14 years	Hospitalization	No effect
Godtfredsen et al., 2003 ^a	643	≥50%	13.8 years	Myocardial infarction	No effect
Godtfredsen et al., 2005 ^a	832	≥50%	18 years	Lung cancer	Improved

Note. Unpublished studies in italics. CPD, cigarettes/day. ^aMultiple analyses from same study.

Three cohort studies tested whether reduction improved respiratory function. One small study (23 reducers) found that reducing by at least 25% decreased respiratory symptoms over a year to a level halfway between that of continuing smokers and abstainers (Buist, Sexton, Nagy, & Ross, 1976; Hughson, Mann, Tibbs, Woods, & Walton, 1978). A second, larger study ($n=326$ reducers) found that CPD reduction of about 50% at a 5-year follow-up was associated with improved forced expiratory volume in one second (FEV_1) in younger (<55 years) smokers but not in older smokers (Lange et al., 1989), compared with continuing smokers. Finally, an analyses of the Lung Health Study ($n\sim 1,000$) found that the amount of reduction in continuing smokers was not related to changes in FEV_1 or to respiratory symptoms at the 1-year follow-up (Simmons et al., 2005). However, post-hoc tests based on examinations of the data suggested that reductions of at least 60% were associated with improved FEV_1 , and for 1 of the 10 respiratory symptoms (Simmons et al., 2005). Analyses of data for follow-up at years 2–5 were “unclear and difficult to interpret.” Another small study (33 reducers) found that reducing by at least 50% decreased intermittent claudication over a 4-year period (Hughson et al., 1978).

Two cohort studies directly examined morbidity and mortality. An analysis of the U.S. Normative Aging Study reported that at 20-year follow-up, younger men who reduced by at least 5 CPD had 50% less mortality; however, this study had a small sample size (35 reducers) and has been published as an abstract only (Nordstrom et al., 2000).

The only large generalizable study on the health benefits from reduction pooled data from three large cohorts in the Copenhagen Centre Study. These cohorts used medical records to measure disease outcomes and had smoking data only at wide intervals. In a series of three analyses that used 643–858 reducers followed over 14–15 years, smokers who had reduced by at least 50% did not have fewer myocardial infarctions (Godtfredsen et al., 2003), less obstructive lung disease (Godtfredsen, Vestbo et al., 2002), and less mortality (Godtfredsen, Hoist et al., 2002) than nonreducers. A fourth analysis reported that reducers had a 27% reduction in lung cancer diagnosis (Godtfredsen, Prescott, & Osler, 2005).

Experimental studies. Experimental studies would be the best direct tests for a causal effect of reduction (Gordis, 2004); however, no RCTs of reducing versus not reducing examined disease risks from smoking. Many RCTs have examined the effects of smoking reduction on biomarkers of cardiovascular disease (e.g., lipids), cancer (e.g., DNA adducts), and pulmonary disease (e.g., FEV_1). We did not include

these studies because they have been described in prior reviews and the interpretation of results from biomarker studies is problematic; e.g., a large overlap exists in biomarkers between reducers and nonreducers, and biomarkers often do not predict disease onset accurately (Hatsukami, Hecht, Hennrikus, Joseph, & Pentel, 2003; Hecht, 2002; Institute of Medicine, 2001; Shields, 2002).

Discussion

Smoking reduction and cessation

Across the 19 studies reviewed here, none found that reduction decrease later cessation in smokers not currently interested in quitting. The large majority of indirect evidence found that reduction was associated with an increased probability of future cessation. More important, the two direct experimental tests found that smoking reduction produces more subsequent cessation than no treatment. From these lines of evidence, we conclude that smoking reduction increases the probability of later quitting. This conclusion is consistent with that of our prior review (Hughes, 2000) and of more recent reviews (Fagerström, 2005; Tonnesen, 2002; Zellweger, 2001), all of which reviewed a much smaller set of earlier studies.

The studies reviewed here also consistently found that the effect of reduction on future cessation was similar to that of brief advice to stop smoking. Because cessation advice does not require NRT and its associated costs, one might question whether and when reduction should be used. One possible situation in which reduction could be indicated is when clinicians see smokers who have not responded to repeated cessation advice. Most clinicians treat many such smokers (Joseph et al., 2005), plus many smokers are interested in reducing (Hughes & Carpenter, 2005); thus, clinicians are often asked by smokers whether they should reduce.

If clinicians recommend reduction, they must tell smokers that it is unclear whether reduction itself improves health. Furthermore, clinicians should tell such smokers that they should see reduction as a step toward eventual cessation and that they should not see reduction itself as a positive outcome. This may be an acceptable message, given that surveys suggest smokers are more interested in reduction as a method of quitting than as a goal in itself (Meyer et al., 2003; Pillitteri et al., 2001).

Despite these caveats, promotion of reduction might still produce harmful unintended consequences in populations other than smokers not trying to quit. For example, it could undermine resolve among smokers about to quit or send a message to teenagers that small amounts of smoking are safe. In the one

small trial in which reduction was offered as an alternative goal to those who were actively trying to stop (Glasgow et al., 1989), 66 such smokers were randomized to either a traditional abrupt cessation program or a program in which smokers reduced prior to quitting; however, when the quit date occurred, smokers in the reduction group were given the option of maintaining reduction as well as quitting. The 6-month abstinence outcomes were identical in the two groups. Although this study suggests that the existence of a reduction alternative does not undermine quitting, clearly larger and more rigorous studies are needed before a definitive conclusion can be reached. In terms of effects on teenagers, we could find no empirical studies of the effect of a reduction message on teenagers' beliefs about the safety of smoking.

The results of this review also suggest a possible behavioral mechanism for how tobacco control programs and policies work. When tobacco control policies or programs are introduced, cigarette sales typically decline prior to declines in smoking prevalence rates (Pierce et al., 1994; USDHHS, 2000). This finding suggests that policies first reduce CPD among ongoing smokers and then reduce prevalence. The results from this review support this explanation in that they indicate reducing smoking leads to future cessation. We suggest that evaluations of tobacco control evaluations conduct mediational analyses (Baron & Kenny, 1986) to more directly test the notion that reduction mediates the effect of policies on cessation.

Smoking reduction and the risk of smoking-related diseases

Whether reduced smoking reduces health risks is unclear because of the lack of adequate empirical tests and the existence of contradictory results among studies. For example, only one dataset had a large sample size (i.e., the Copenhagen Centre Study); however, measurement of reduction was poor in that study. Thus the mostly negative results from that study could be false negatives. Another possible explanation for the generally negative results is that the dose-responsivity between CPD and disease risk has a threshold such that smokers must reduce by a large amount before health risks are reduced. Although most of the cross-sectional studies on dose-responsivity show linear effects with no evidence of thresholds (USDHHS, 2004), some studies suggest the dose-response curve for the risk of cardiovascular disease is especially steep at very low rates of smoking (Bjartveit & Tverdal, 2005; Pechacek & Babb, 2004). Thus, it may be that smokers must reduce to very low levels (i.e., much more than the 50% or more threshold used in

the preceding studies) before health benefits are realized.

Another possible explanation is that when smokers reduce, they compensate for nicotine reduction by smoking remaining cigarettes more intensely (Scherer, 1999). This explanation appears to account for the absence of benefit in switching to low-tar cigarettes (National Cancer Institute, 2001); thus, it might be applicable to smoking reduction as well. A recent review of 15 smoking reduction studies did show that compensation occurred; however, the compensation was not complete and a reduction in smoke intake was still evident with reduction (Hughes & Carpenter, 2005).

A final possibility is that the reduction studies did not document how long smokers had reduced. It may be that reduction must persist for many months before a health benefit can occur.

Future studies

Several excellent review articles and texts have outlined the methodological problems in showing that reduction increases cessation or decreases health risks from reduced smoking (Hatsukami, Henningfield et al., 2004; Hatsukami et al., 2002; Health Development Agency, 2001; Institute of Medicine, 2001; Warner, 2003). Future studies need to address these problems.

As discussed earlier, one important question is whether the increase in quitting with NRT-assisted reduction is related to NRT availability or reduction per se. A study that induced reduction without using NRT could answer that question.

The most direct test of the health benefit of reduction would be an RCT of a reduction intervention versus no such intervention versus a cessation intervention among smokers not currently trying to quit. Such a trial would require a very large sample and long-term follow-up (comparable in size to community tobacco control trials) and has not been attempted. Given the difficulty of such a RCT, we believe that existing large prospective studies measuring health outcomes should collect data not just on smoking status but also on self-reported CPD over time. These questions should be asked on a repeated basis so that the duration, magnitude, and fidelity of smoking reduction can be ascertained. Such studies would provide important replication tests of the single large existing cohort study. One group that might be especially important to study is daily smokers who convert to nondaily smoking because this is often a large reduction and the incidence of nondaily smoking appears to be increasing (Hughes & Carpenter, 2005).

Three other important questions are whether promoting reduction would (a) undermine the

resolve of those about to quit by giving them a less-difficult alternative, (b) promote relapse among quitters by suggesting that low-rate smoking is relatively safe, or (c) increase initiation of smoking by suggesting that one can smoke in a somewhat safe manner. Whether these questions can be addressed adequately using laboratory studies, clinical studies, or analog studies and using self-reported intentions/resolve to quit or not start smoking is unclear. Thus, these questions may be able to be answered adequately only via monitoring after reduction is widely promoted. Since reduction has been approved as an indication in several countries, postmarketing studies could begin to answer these questions.

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