

## ONLINE FIRST

# Stopping Smoking Shortly Before Surgery and Postoperative Complications

## A Systematic Review and Meta-analysis

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**Objective:** To examine existing smoking studies that compare surgical patients who have recently quit smoking with those who continue to smoke to provide an evidence-based recommendation for front-line staff. Concerns have been expressed that stopping smoking within 8 weeks before surgery may be detrimental to postoperative outcomes. This has generated considerable uncertainty even in health care systems that consider smoking cessation advice in the hospital setting an important priority. Smokers who stop smoking shortly before surgery (recent quitters) have been reported to have worse surgical outcomes than early quitters, but this may indicate only that recent quitting is less beneficial than early quitting, not that it is risky.

**Design:** Systematic review with meta-analysis.

**Data Sources:** British Nursing Index (BNI), The Cochrane Library database, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Embase, Medline, PsycINFO to May 2010, and reference lists of included studies.

**Study Selection:** Studies were included that allow a comparison of postoperative complications in patients undergoing any type of surgery who stopped smoking within 8 weeks prior to surgery and those who continued to smoke.

**Data Extraction:** Two reviewers independently screened potential studies and assessed their methodologic quality. Data were entered into 3 separate meta-analyses that

considered all available studies, studies with a low risk of bias that validated self-reported abstinence (to assess possible benefits), and studies of pulmonary complications only (to assess possible risks). Results were combined by using a random-effects model, and heterogeneity was evaluated by using the  $I^2$  statistic.

**Results:** Nine studies met the inclusion criteria. One found a beneficial effect of recent quitting compared with continuing smoking, and none identified any detrimental effects. In meta-analyses, quitting smoking within 8 weeks before surgery was not associated with an increase or decrease in overall postoperative complications for all available studies (relative risk [RR], 0.78; 95% confidence interval [CI], 0.57-1.07), for a group of 3 studies with high-quality scores (RR, 0.57; 95% CI, 0.16-2.01), or for a group of 4 studies that specifically evaluated pulmonary complications (RR, 1.18; 95% CI, 0.95-1.46).

**Conclusions:** Existing data indicate that the concern that stopping smoking only a few weeks prior to surgery might worsen clinical outcomes is unfounded. Further larger studies would be useful to arrive at a more robust conclusion. Patients should be advised to stop smoking as early as possible, but there is no evidence to suggest that health professionals should not be advising smokers to quit at any time prior to surgery.

*Arch Intern Med.* 2011;171(11):983-989.

Published online March 14, 2011.

doi:10.1001/archinternmed.2011.97

**C**IGARETTE SMOKING HAS been implicated as a risk factor for postoperative complications across a spectrum of surgical specialties.<sup>1-4</sup> Compared with nonsmokers, smokers who undergo surgery have longer

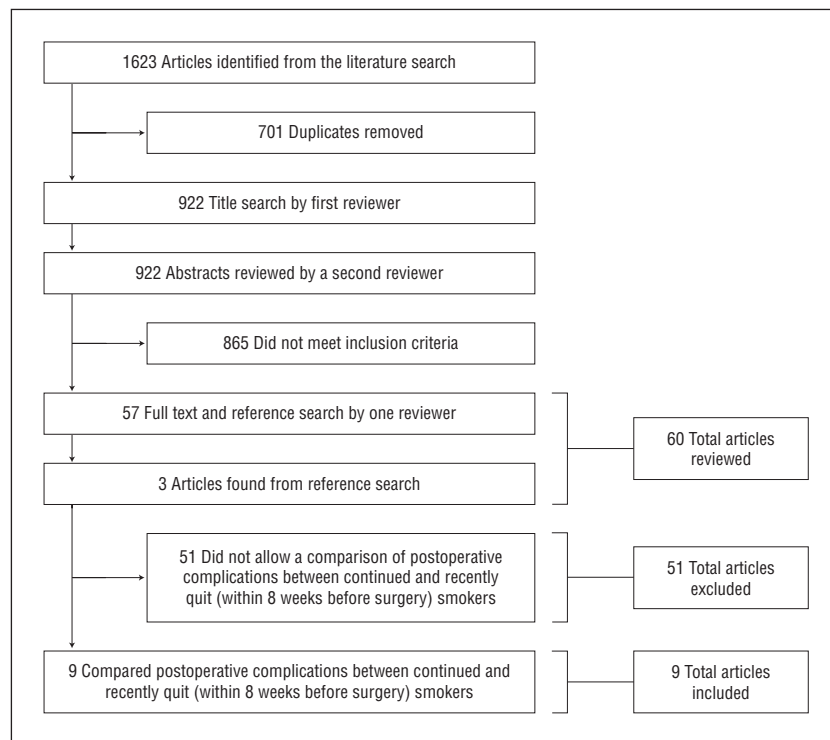
risk of in-hospital mortality.<sup>5-7</sup> Although stopping smoking before surgery can mitigate these risks<sup>8,9</sup> and longer periods of preoperative abstinence confer stronger benefits, the existing data do not allow clear advice on an optimal period of preoperative smoking cessation.<sup>10</sup>

The picture is complicated by a concern that has been circulating over the past 2 decades that stopping smoking within a few weeks before surgery may not just be ineffective in reducing postoperative complications, but that it can contribute to them. This concern originated from a

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hospital stays, higher risk of readmission, are more likely to be admitted to an intensive care unit, and have an increased

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**Figure 1.** Summary of identification and inclusion of smoking cessation articles.

1989 article that found postoperative pulmonary complications in 6 of 18 continuing smokers, compared with 12 of 21 ex-smokers who quit for less than 8 weeks prior to surgery.<sup>11</sup> The report did not include statistical analysis, but the authors suggested that losing the cough-promoting effect of cigarettes before any improvement in sputum clearance might predispose to retention of secretions and postoperative pulmonary complications. Although the difference between the 2 groups was not statistically significant ( $\chi^2=2.2$ ;  $P=.20$ ), the warning has in some instances become accepted as a proven fact. For example, an influential guidance document from the London Health Observatory states that “Cessation should occur at least 8 weeks prior to surgery to minimize the increase in pulmonary complications in recent quitters.”<sup>12(p13)</sup> The 8-week cutoff point has also been recommended by other sources.<sup>13,14</sup> Patients are often scheduled for operations at relatively short notice, and an opportunity to discuss smoking may arise fairly late. Clinicians faced with smoking patients, or even with patients who proactively ask for help with stopping smoking, are often un-

sure whether they should provide smoking cessation treatment shortly before surgery. The National Institute of Clinical Excellence, which provides guidance to the English National Health Service, has recently convened a meeting of experts to consider revoking its general recommendation to provide smoking cessation advice to preoperative patients. This was motivated by concerns about possible harm to patients who would be encouraged to quit less than 8 weeks before their operation. Similar concerns are anecdotally expressed by anesthesiologists and surgeons globally.

Our preparatory examination of the existing literature on this topic identified 2 important methodologic issues. First, most existing studies focus on comparisons of early quitters (usually, those smoke free for more than 2 months before their surgery) and recent quitters (those smoke free for only a few weeks or up to 2 months before their surgery) with never smokers.<sup>10</sup> Of these 3 groups, recent quitters often have the poorest outcomes. This seems to form one of the sources of warnings about recent quitting. However, showing that recent quitters have more complications than

early quitters and/or never smokers may simply mean that recent quitting is less beneficial than early quitting. Only a comparison with continuing smokers can show whether recent quitting poses a risk.

The second issue concerns biochemical validation of self-reported abstinence. Hospital patients are often acutely aware that smoking may have contributed to their illness; consequently, they worry about the disapproval of clinical staff and tend to misreport their smoking status.<sup>15,16</sup> If the sample of patients classified as recent ex-smokers contains a proportion who are in fact still smoking, this is likely to dilute any potential risks or benefits of recent quitting. Compared with studies based on self-reported smoking status, studies that objectively validate self-reported abstinence from smoking provide more reliable evidence. The 2 validation methods commonly used, salivary cotinine levels and end-expired carbon monoxide readings, are both reliable.<sup>17</sup>

We present herein an analysis of the existing literature that takes into account these methodologic issues. The study sought to determine the following: Is there any evidence that stopping smoking within 8 weeks before surgery is associated with postoperative complications?

## METHODS

We identified and analyzed all existing studies that allowed comparisons of postoperative complications in patients who stopped smoking 8 weeks or less prior to surgery (recent quitters) with those who continued to smoke. All types of postoperative complications were considered from all specialties and populations. All study designs were included if they provided data on postoperative complications (as defined by the authors in that specialty) in both recent quitters and continuing smokers.

## SEARCH STRATEGY AND SELECTION CRITERIA

Electronic databases were examined using the KA24 (Knowledge Access 24 hours a day) Internet-based resource. The databases included the British Nursing Index (BNI) (from 1985), the Cumulative Index to Nursing and Allied Health Literature (CINAHL) (from

**Table. Methodologic Characteristics of Included Studies**

Source	Study Period	Study Design	Definition of Recent Quitters	Type of Surgery	Complications Assessed	Validation of Smoking Abstinence
Barrera et al, <sup>5</sup> 2005	30 d post surgery	Prospective	Smoke free 1-2 wk before surgery	Thoracotomy for lung tumors	Pulmonary complications	None
Chan et al, <sup>22</sup> 2006	During hospital stay	Retrospective	Smoke free less than 4 wk before surgery	Bilateral breast reduction	Wound complications	None
Glassman et al, <sup>2</sup> 2000	During hospital stay	Retrospective	Smoke free up to 1 mo before surgery	Posterior instrumental fusion at either L4-L5 or L4-S1	Wound complications	None
Groth et al, <sup>23</sup> 2009	During hospital stay	Retrospective	Smoke free up to 1 mo before surgery	Pulmonary resection	All complications	None
Kuri et al, <sup>24</sup> 2005	During hospital stay	Retrospective	Smoke free up to 6 wk before surgery	Reconstructive head and neck surgery	Wound complications	None
Lindström et al, <sup>25</sup> 2008	30 d post surgery	Randomized controlled trial	Smoke free up to 3 wk before surgery	Hernia repair, laparoscopic cholecystectomy, hip and knee replacement	All complications	Carbon monoxide reading
Møller et al, <sup>1</sup> 2002	During hospital stay	Randomized controlled trial	Smoke free for up to 8 wk before surgery	Primary elective hip or knee alloplasty	All complications	Carbon monoxide reading
Warner et al, <sup>26</sup> 1984	30 d post surgery	Retrospective	Smoke free for up to 8 wk before surgery	Coronary artery bypass grafting	Pulmonary complications	None
Warner et al, <sup>11</sup> 1989	7 d post surgery	Prospective	Smoke free for up to 8 wk before surgery	Elective coronary artery bypass grafting	Pulmonary complications	Urinary cotinine

1981), The Cochrane Library database (from 1800), Embase (from 1980), Medline (from 1950) and PsycINFO (from 1806), all searched through May 2010. The search terms were developed within the study team.<sup>18-21</sup> The following search terms were used: (smoking AND cessation) or (tobacco AND cessation) or (stop\$ AND smok\$) or quit\$ or (smoking AND status) and (post-op\$ or postop\$ or pre-op\$ or preop\$ or peri-op\$ or periop\$) and (complication\$ or morbidity or mortality or pulmonary). The search was limited to electronic databases and to articles in English.

**Figure 1** shows the flow of studies through the reviewing process. One reviewer filtered titles and abstracts of the articles returned in the search for information on postoperative complications (complications were defined by the authors in that specialty and so differed depending on surgical procedure) in recent quitters (stopped smoking within 8 weeks before surgery) and continuing smokers. Reports identified as potentially relevant were screened by a second reviewer. Hard copies were obtained of all 57 articles classified as potentially relevant. A hand search of the references from these articles identified a further 3 publications. The 60 articles were examined independently by 2 of us (K.M. and H.M.). Their conclusions were checked by a third reviewer (P.H.), who also reconciled any differences. The 9 ar-

ticles that included interpretable data were rated for methodologic quality independently by the first 2 reviewers, and their conclusions were again checked by the third reviewer, who reconciled any differences.

For each study we extracted the number of postoperative complications for both continuing smokers and recent quitters. We also extracted data on the study period, duration of abstinence in recent quitters, whether their smoking status was biochemically validated, study design, the type of surgery, and the postoperative complications that were assessed (**Table**).

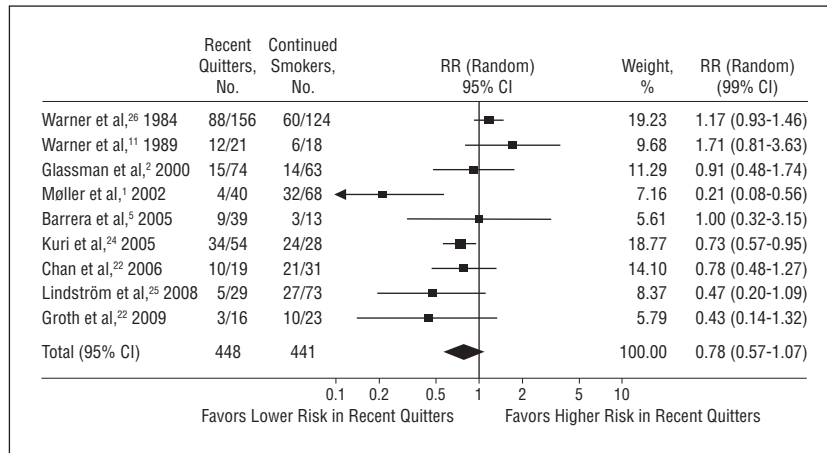
Where a study collected relevant data but did not report them in a form usable for our analysis, we contacted the authors. David Lindström, MD, PhD, provided data on pulmonary complications that were not reported in his 2008 article.<sup>25</sup>

### QUALITY ASSESSMENT

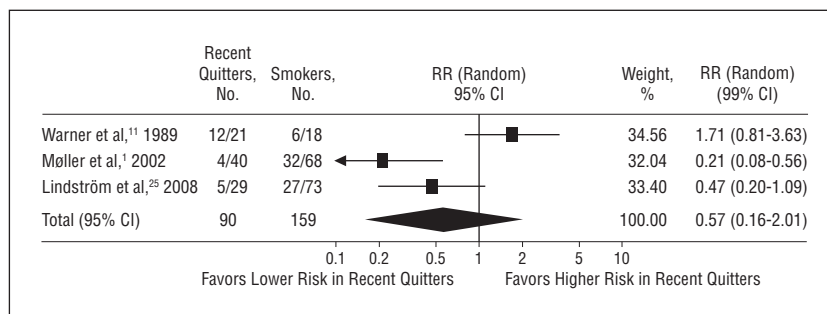
The quality of the included articles<sup>1,2,5,11,22-26</sup> was assessed according to national guidelines for undertaking systematic reviews<sup>27</sup> and using indicators of susceptibility to bias specific for the purpose of the review. The key issue for our purpose concerns the reliability of classifying patients as recent quitters. Misclassification of smoking status presents by far the most serious risk of bias. Real differences could be diluted or even

masked if the classification of abstinence was inaccurate. Studies that validated self-reported abstinence biochemically thus present the best evidence available. This consideration is included in the Table. It reflects the reliability of data of interest to the present review rather than the overall quality of the studies, which had mostly different purposes and priorities.

The included studies differed in a number of other ways, but we are not aware of any other feature that would exaggerate or diminish the difference between the 2 study groups in a systematic manner. The included studies used a range of study designs, but the key comparison of postsurgical complications in patients who stopped smoking shortly before surgery and those who continued to smoke is largely independent of study design and not affected by it. For example, while 2 studies randomized smokers to either a stop-smoking intervention or a control procedure, some smokers in the control group stopped smoking and many in the intervention group did not. For our purpose, the comparison of the randomized groups is less informative than the comparison of quitters and continuing smokers across both conditions (both studies provide the necessary information). For these reasons, no quality points were assigned to study designs. The different designs would not be expected to differ in accuracy of detect-



**Figure 2.** All included studies. Total events, 180 recent quitters and 197 continued smokers. Test for heterogeneity,  $\chi^2=23.61$  ( $P=.003$ ),  $I^2=66.1\%$ . Test for overall effect,  $Z=1.52$  ( $P=.13$ ). CI indicates confidence interval; RR, relative risk.



**Figure 3.** Studies with biochemical validation of self-reported smoking abstinence. Total events, 21 recent quitters and 65 continued smokers. Test for heterogeneity,  $\chi^2=13.21$  ( $P=.001$ ),  $I^2=84.9\%$ . Test for overall effect,  $Z=0.88$  ( $P=.38$ ). CI indicates confidence interval; RR, relative risk.

ing postsurgical complications or produce any systematic bias in reporting complications in continuing smokers and recent quitters. Similarly, as the sub-analysis of interest to us was not the main focus of the included studies, publication bias was unlikely: there was no obvious reason that would lead researchers or publishers to prefer one result over another.

## DATA ANALYSIS

Data extracted from the included studies were entered into the RevMan (Review Manager) program (version 5.0) developed for Cochrane meta-analyses. Analyses of adverse effects typically use the Peto odds ratio, which is the preferred statistic for rare occurrences, but in this case the rate of complications was high (over 50% in some studies), and we calculated a pooled risk ratio using a fixed-effects model. We assessed statistical heterogeneity using the  $I^2$  statistic. Where there was significant heterogeneity, a random-effects model was used.<sup>28</sup> We conducted 3 meta-analyses. The first meta-analysis included all available studies to check for any effects of recent quitting, beneficial or detrimental.

We repeated this analysis using only studies with validated self-reported abstinence and least risk of bias. Finally, we analyzed separately studies that focused specifically on pulmonary complications to assess possible detrimental effects in this particular area.

## SEARCH OUTPUT

A total of 889 patients participated in the relevant studies. The characteristics of the 9 studies that met the inclusion criteria are listed in the Table.

Two additional studies were close to meeting the inclusion criteria. One of these reported data separately for patients who stopped smoking 2 to 4 weeks prior to the operation and those who quit earlier.<sup>29</sup> Those quitting 2 to 4 weeks preoperatively did not differ significantly from continuing smokers in the incidence of postoperative pulmonary complications (54% vs 44%). However, the analysis included a comparison of smokers who stopped smoking within 2 weeks before the operation with continuing smokers. This makes the interpretation of the findings difficult, and the study is not included in the meta-analyses results reported herein. However, including this

study in the relevant meta-analyses did not alter the results.

The second study concerned pulmonary complications following resection of lung cancer.<sup>30</sup> It reported data separately for patients quitting 2 to 4 weeks prior to the operation but also merged those who quit within 2 weeks before the operation with continuing smokers. The incidence of complications was not significantly different in recent quitters and continuing smokers (6.2% vs 6.9%). The study is not included in the meta-analysis, but its inclusion does not affect the results.

Two other excluded studies require a special mention because they have been cited as demonstrating risks of recent quitting and an explanation of such risks.<sup>12</sup> Bluman et al<sup>13</sup> found that 36 smokers who self-reported reducing their smoking rate in the weeks to months prior to surgery had a higher risk of postoperative pulmonary complications than 105 who reported smoking at their usual rate (relative risk, 6.7; 95% confidence interval [CI] 2.6-17.1). Self-reported smoking reduction may not reflect any real change in the inhaled volume of smoke. Even when there is a genuine reduction in the number of cigarettes, the reduction is usually undermined by compensatory smoking<sup>31,32</sup>; this finding is therefore difficult to interpret.

Yamashita et al<sup>33</sup> compared intraoperative sputum production among recent quitters, continuing smokers, and nonsmokers.<sup>33</sup> The study is not included in our meta-analysis because volume of intraoperative sputum production is not a surgical complication. Patients were categorized into having or not having a high sputum volume. Those abstaining from smoking for less than 2 months preoperatively were more likely to have a higher sputum volume than nonsmokers (23% vs 9%;  $P < .01$ ), but there was no significant difference between recent ex-smokers and current smokers (23% vs 18%).

## RESULTS

Only 1 of the 9 included studies reported a significant result, and this was in favor of recent abstainers.<sup>1</sup> When all 9 studies are combined, there is no beneficial or detrimental effect of quitting within 8 weeks before surgery compared with continued smoking (**Figure 2**). Because there is substantial heterogeneity between these studies, the result needs to be interpreted with caution.

**Figure 3** presents the results of the 3 reports that validated self-



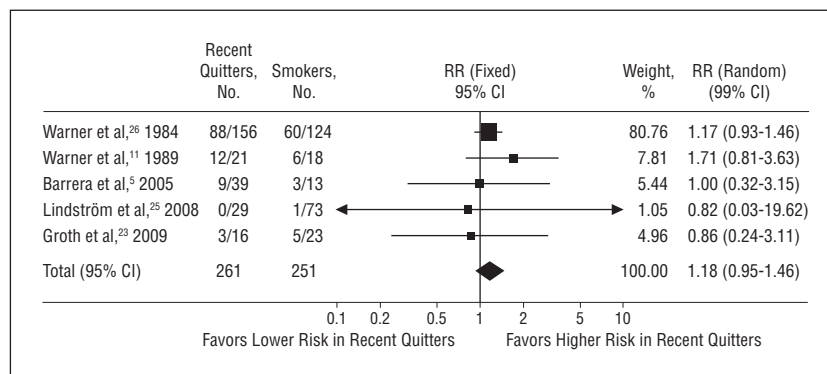
reported abstinence and had the highest quality scores.<sup>1,11,25</sup> These studies provide the best evidence available. The results again show no significant benefit or detrimental effect of recent quitting compared with continued smoking, but there is once more substantial heterogeneity in the data.

The effect of smoking cessation on postoperative pulmonary complications is shown in **Figure 4**. The results are homogeneous, and they show no significant increase in risk in those who stopped smoking less than 8 weeks prior to surgery compared with those who continued smoking.

## COMMENT

The present analysis does not support the suggestion that quitting smoking less than 8 weeks before surgery has a negative impact on surgical outcomes. A hypothetical explanation of the presumed risks of quitting before surgery, as suggested by Warner et al<sup>11</sup> and repeated by others,<sup>13</sup> is based on an assumption that stopping smoking leads to a decrease in coughing and an increase in sputum production. Both of these claims remain unconfirmed. Smoking seems to suppress rather than enhance cough reflex sensitivity.<sup>34-36</sup> Stopping smoking was reported to lead to a mild increase in coughing in 2 studies<sup>37,38</sup> and a decrease in 2 other reports.<sup>39,40</sup> Regarding mucociliary clearance shortly after smoking cessation, we are aware of only 1 study in which intraoperative sputum production was measured. The investigation found no difference between recent quitters and continuing smokers.<sup>33</sup>

There are several limitations to this systematic review. The results are based on observational data. Quitting behavior may be determined by the same factors that determine postoperative outcomes. For example, patients who stop smoking may be more likely to access postoperative care, perhaps masking a detrimental effect of recent quitting. Conversely, those with more serious illness may be more likely to stop smoking, possibly ob-



**Figure 4.** Studies of pulmonary complications. Total events, 112 recent quitters and 75 smokers. Test for heterogeneity,  $\chi^2=1.32$  ( $P=.86$ ),  $I^2=0\%$ . Test for overall effect,  $Z=1.53$  ( $P=.13$ ). CI indicates confidence interval; RR, relative risk.

scuring beneficial effects of recent quitting. Another potential limitation is that our search covered only studies in English.

Our meta-analyses combined different types of surgical procedures and various definitions of postoperative complications. Although no detrimental effect was found in any single investigation or the various study combinations, it remains possible that there are particular types of surgery and/or complications that may reveal a different result. Amalgamating different types of studies makes it necessary to interpret the results with some caution. This, however, does not disqualify the approach we took. Given the relatively limited number of studies available, as long as the appropriate caveats are kept in mind, such a meta-analysis, combined with a systematic review of all individual studies, is the only way to arrive at a conclusion based on all currently available evidence.

Two of the meta-analyses included substantial heterogeneity, and where this is the case, the review of individual studies is more informative. It is reassuring that no single study within either group showed a significant risk, and that in the key analysis concerning pulmonary complications, the test of heterogeneity was nonsignificant.

Apart from showing no evidence of risk of recent quitting on pulmonary or any other complications, the results also show no evidence of benefit in wound healing or other areas of postsurgical recovery. Stopping smoking shortly before surgery may be unrelated to its

immediate aftermath, but smokers prompted to quit in this context are of course likely to benefit in the long term.

Studies that did not validate smoking status may misclassify smokers as abstainers, making it less likely that any beneficial or detrimental effects of quitting will be detected. Future studies should verify self-reported abstinence biochemically and report details of exactly how and when smoking status was established.

No data are available on the effects of only a few days' abstinence from smoking. Early abstinence generates more intense withdrawal discomfort,<sup>41,42</sup> but there is no clear rationale to expect this to translate into postoperative complications. Nevertheless, future studies should focus on smokers quitting within 1 week of surgery and report their results separately.

In view of these limitations and the relatively small number of available studies, our findings are necessarily only tentative and may be modified when more data become available. The combined number of participants in the relevant trials was 889, and a small detrimental or beneficial effect may still emerge with further extension of this work. This is of course true for most meta-analytical verdicts.

In conclusion, there is currently no suggestion, either from any single study or from combinations of studies, that quitting smoking shortly before surgery increases postoperative complications. Future studies should focus on patients with a very short duration of abstinence and

should use biochemical validation of self-reported abstinence. In the meantime, until some new evidence of harm emerges, firm advice to stop smoking and an offer of smoking cessation treatment to those who need it can be provided to pre-surgical patients at any time.

**Accepted for Publication:** January 7, 2011.

**Published Online:** March 14, 2011.  
doi:10.1001/archinternmed.2011.97

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**Author Contributions:** All authors had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Myers, Hajek, and McRobbie. *Acquisition of data:* Myers, Hajek, and McRobbie. *Analysis and interpretation of data:* Myers, Hajek, Hinds, and McRobbie. *Drafting of the manuscript:* Myers, Hajek, Hinds, and McRobbie. *Critical revision of the manuscript for important intellectual content:* Myers, Hajek, Hinds, and McRobbie. *Statistical analysis:* Myers, Hajek, and McRobbie. *Obtained funding:* Myers and McRobbie. *Administrative, technical, and material support:* Myers, Hajek, and McRobbie. *Study supervision:* Myers.

**Financial Disclosure:** Drs Hajek and McRobbie have received research funds from and provide consultancies to the following manufacturers of smoking cessation medications: Glaxo SmithKline, Novartis, Pfizer Global, and Johnson & Johnson.

**Funding/Support:** Dr McRobbie is supported by the UK Centre for Tobacco Control Studies, a UKCRC Public Health Research Centre of Excellence.

**Additional Information:** Analyses in RevMan software are available from Ms Myers.

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## INVITED COMMENTARY

### ONLINE FIRST

# The Optimal Timing of Smoking Cessation Before Surgery

There is strong evidence that smoking cessation is beneficial to long-term health.<sup>1</sup> Globally, over 230 million adults undergo major surgery annually, and millions of these patients experience major respiratory and cardiovascular complications.<sup>2</sup> Upwards of 30% of patients undergoing surgery are smokers at the time of their surgery, and smoking is associated with an increased risk of postoperative complications, the strongest evidence being for respiratory complications.<sup>3,4</sup> All patients are forced to become nonsmokers, if only for a short period, around the time of surgery. The perioperative period presents a unique opportunity to try and get patients to permanently stop smoking.

A recent systematic review of 5 perioperative trials demonstrated that a preoperative smoking cessation intervention reduced a broad composite outcome of any postoperative complication compared with standard care: in a total of 176 events observed in 535 participants, the relative risk (RR) was 0.70 (95% CI, 0.56-0.88) ( $I^2=69\%$ ).<sup>5</sup> More intense interventions (4-8 weeks) were associated with a greater risk reduction compared with brief interventions (single episode) ( $P=.01$  for heterogeneity). The exact time of smoking cessation prior to surgery with either type of intervention was not explicitly examined. The review did not report pooled results for major cardiovascular or pulmonary complications. Preoperative smoking cessation interventions were positively associated with long-

term (12 months) self-reported smoking cessation (RR, 1.61 [95% CI, 1.12-2.33]) ( $I^2=58\%$ ).<sup>5</sup>

Although these data are limited to a few studies and a small number of events, this is encouraging evidence that smoking cessation prior to surgery may prevent postoperative complications and increase long-term abstinence from tobacco. These data do not, however, provide guidance on the optimal timing of smoking cessation prior to surgery. The importance of clarifying this timing issue is that some studies have raised the concern that smoking cessation just prior to surgery may be associated with greater harm.<sup>6</sup> Some perioperative guidelines have reflected this concern and have recommended that patients quit 8 weeks or more prior to surgery to minimize pulmonary complications that may occur when patients quit smoking within a few weeks of surgery.<sup>7</sup> There exist related data that support this potential paradoxical occurrence of harm associated with smoking withdrawal immediately prior to surgery. Some large observational studies of patients with acute coronary syndrome have demonstrated a paradoxical effect of smoking on mortality: smokers were found to have initially lower risk-adjusted in-hospital mortality rates after their acute event compared with past or nonsmokers.<sup>8</sup> It is possible that the sympathetic activity associated with recent tobacco withdrawal may predispose patients to perioperative cardiovascular or

respiratory complications that predominantly occur during the first few days after surgery.<sup>9</sup>

This uncertainty regarding the presence or absence of harm associated with smoking cessation shortly prior to surgery leaves clinicians uncertain as to what to advise patients, particular those for whom surgery is imminent. Myers and colleagues attempt to address the question of the impact of the timing of smoking cessation prior to surgery by undertaking a systematic review and meta-analysis. They identify 9 studies reporting data on a total of 377 events in 889 smokers (448 recent quitters and 441 continuous smokers). The RR of any complication among recent quitters compared with continuous smokers was 0.78 (95% CI, 0.57-1.07), and there was significant heterogeneity ( $P=.003$ ) that was not explained. Pulmonary complications occurred in 115 of 261 recent quitters and 75 of 251 continuous smokers (RR, 1.18 [95% CI, 0.91-1.46]).

The definition of a *recent quitter* in the included studies suggests that a patient who quit 2 to 3 days before surgery would fall into this category, as would a patient who quit 8 weeks prior to surgery. It would seem possible that the separation in the timing of the last smoking episode prior to surgery between recent quitters and patients who continued to smoke may not have been very large, and this may partly explain the demonstrated heterogeneity and the lack of effect demonstrated in the pooled estimates. Lack of or suboptimal risk factor adjustment is another major limi-