



## Short-term preoperative smoking cessation and postoperative complications: a systematic review and meta-analysis

### Arrêt à court terme du tabagisme en préopératoire et complications postopératoires: revue systématique de la littérature et méta-analyse

Jean Wong, MD · David Paul Lam, BSc ·  
Amir Abrishami, MD · Matthew T. V. Chan, MBBS ·  
Frances Chung, MBBS

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#### Abstract

**Purpose** *The literature was reviewed to determine the risks or benefits of short-term (less than four weeks) smoking cessation on postoperative complications and to*

*derive the minimum duration of preoperative abstinence from smoking required to reduce such complications in adult surgical patients.*

**Source** *We searched MEDLINE, EMBASE, Cochrane, and other relevant databases for cohort studies and randomized controlled trials that reported postoperative complications (i.e., respiratory, cardiovascular, wound-healing) and mortality in patients who quit smoking within six months of surgery. Using a random effects model, meta-analyses were conducted to compare the relative risks of complications in ex-smokers with varying intervals of smoking cessation vs the risks in current smokers.*

**Principal findings** *We included 25 studies. Compared with current smokers, the risk of respiratory complications was similar in smokers who quit less than two or two to four weeks before surgery (risk ratio [RR] 1.20; 95% confidence interval [CI] 0.96 to 1.50 vs RR 1.14; CI 0.90 to 1.45, respectively). Smokers who quit more than four and more than eight weeks before surgery had lower risks of respiratory complications than current smokers (RR 0.77; 95% CI 0.61 to 0.96 and RR 0.53; 95% CI 0.37 to 0.76, respectively). For wound-healing complications, the risk was less in smokers who quit more than three to four weeks before surgery than in current smokers (RR 0.69; 95% CI 0.56 to 0.84). Few studies reported cardiovascular complications and there were few deaths.*

**Conclusion** *At least four weeks of abstinence from smoking reduces respiratory complications, and abstinence of at least three to four weeks reduces wound-healing complications. Short-term (less than four weeks) smoking cessation does not appear to increase or reduce the risk of postoperative respiratory complications.*

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**Author contributions** *Jean Wong* was involved in data abstraction, interpretation of data, drafting and revising, and final approval of the article. *David Paul Lam* was involved in data abstraction and drafting of the article. *Amir Abrishami* was involved in drafting and revising the article, data analysis, and interpretation of the data. *Matthew Chan* revised and approved the final version of the article. *Frances Chung* was involved in the conception and design, revising, and final approval of the article.

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J. Wong, MD (✉)  
Department of Anesthesia, Toronto Western Hospital, University Health Network, University of Toronto, 2-434 McLaughlin Wing, 399 Bathurst Street, Toronto, ON M5T 2S8, Canada  
e-mail: jean.wong@uhn.ca

D. P. Lam, BSc · A. Abrishami, MD  
Department of Anesthesia, Toronto Western Hospital, University Health Network, University of Toronto, 2-405 McLaughlin Wing, 399 Bathurst Street, Toronto, ON M5T 2S8, Canada

F. Chung, MBBS  
Department of Anesthesia, Toronto Western Hospital, University Health Network, University of Toronto, 2-433A McLaughlin Wing, 399 Bathurst Street, Toronto, ON M5T 2S8, Canada

M. T. V. Chan, MBBS  
Department of Anaesthesia and Intensive Care, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, NT, Hong Kong, SAR

## Résumé

**Objectif** *La littérature disponible a été passée en revue pour déterminer les risques ou avantages d'un arrêt du tabagisme à court terme (moins de quatre semaines) sur les complications postopératoires et pour en déduire la durée minimum d'abstinence tabagique préopératoire qui permet de diminuer la survenue de ces complications chez des adultes subissant une chirurgie.*

**Source** *Notre étude a porté sur les bases de données MEDLINE, EMBASE, Cochrane, et les autres bases de données pertinentes à la recherche d'études de cohortes ou d'études randomisées et contrôlées ayant décrit les complications postopératoires (c'est-à-dire respiratoires, cardiovasculaires, retard de cicatrisation) et la mortalité chez des patients ayant cessé de fumer dans les six mois ayant précédé l'intervention chirurgicale. Des méta-analyses ont été effectuées en utilisant un modèle à effets aléatoires pour comparer les risques relatifs de complications chez les anciens fumeurs, avec des délais variables d'arrêt du tabagisme, aux risques chez des fumeurs actifs.*

**Constatations principales** *Nous avons inclus 25 études. Comparés aux fumeurs actifs, les risques de complications respiratoires ont été comparables chez les fumeurs ayant cessé de fumer moins de deux semaines, ou entre deux et quatre semaines avant une intervention chirurgicale (rapport de risque [RR]: 1,20; intervalle de confiance [IC] à 95 %: 0,96-1,50, contre, respectivement, RR: 1,14; IC à 95 %: 0,90-1,45). Les fumeurs ayant cessé de fumer plus de quatre semaines et plus de huit semaines avant l'intervention chirurgicale avaient des risques de complications respiratoires moins élevés que les fumeurs actifs (RR: 0,77; IC à 95 %: 0,61-0,96 et RR: 0,53; IC à 95 %: 0,37-0,76, respectivement). Concernant les complications liées à la cicatrisation, le risque a été plus faible chez les fumeurs ayant cessé plus de trois à quatre semaines avant l'intervention que chez les fumeurs actifs (RR: 0,69; IC à 95%: 0,56-0,84). Peu d'études ont décrit des complications cardiovasculaires et il n'y a eu que peu de décès.*

**Conclusion** *Un minimum de quatre semaines d'abstinence du tabagisme diminue le risque de complications respiratoires et un minimum de trois à quatre semaines réduit le risque de complications liées à la cicatrisation. L'arrêt à court terme (moins de quatre semaines) du tabagisme ne semble pas augmenter ou réduire le risque de complications respiratoires postopératoires.*

Smoking is associated with increased postoperative morbidity and mortality.<sup>1-3</sup> This is a major concern as up to 20% of surgical patients are smokers.<sup>4,5</sup> A recent large observational study of non-cardiac surgical patients reported that smoking is associated with a 38% increase in the risk of

perioperative death and a 30-109% increase in the risk of serious postoperative complications, depending on the type of complication.<sup>3</sup> However, this study did not examine whether short-term abstinence from smoking before surgery reduces the risk of postoperative complications.

A relatively long period of abstinence from smoking before surgery reduces postoperative complications.<sup>6,7</sup> Two systematic reviews showed that preoperative smoking cessation programs increased short-term (up to six months) abstinence.<sup>8,9</sup> Consequently, both the American Society of Anesthesiologists<sup>10</sup> and the Canadian Anesthesiologists' Society<sup>11</sup> recommend promoting smoking cessation before surgery. However, surgery is frequently scheduled within a few weeks of diagnosis of certain conditions, thus precluding longer periods of preoperative abstinence. As well, anesthesiologists typically see patients within one to four weeks of planned surgery. Anesthesiologists may be reluctant to advocate smoking cessation shortly before surgery because the benefits of a short period of abstinence (less than four weeks) are uncertain, and there could possibly be increased risks of postoperative respiratory<sup>12</sup> or cardiovascular complications, or mortality.<sup>13</sup> Interestingly, a paradoxical effect of lower mortality and improved outcome was observed in smokers compared with non-smokers after acute myocardial infarction, heart failure, and stroke.<sup>14-16</sup> These data suggest that it may be inappropriate to stop smoking shortly before surgery.

A recent meta-analysis found that smoking cessation less than eight weeks before surgery did not increase or decrease the rate of overall or respiratory complications.<sup>17</sup> However, the authors pooled studies with varying duration of smoking cessation (two to eight weeks before surgery) and did not examine wound-healing complications. Therefore, the effect of cessation of smoking shortly before surgery is still unclear.

It is important to determine the benefits or risks of short-term abstinence from smoking before surgery in order to guide anesthesiologists and other clinicians when providing preoperative advice to smokers. The objectives of this systematic review are to determine the benefits or risks of short-term (less than four weeks) abstinence from smoking compared with continued smoking on postoperative complications (respiratory, cardiovascular, wound-healing) and mortality and to determine the minimum duration of preoperative smoking cessation to reduce postoperative complications.

## Methods

### Search strategy

In collaboration with a research librarian, we searched Medline (January 1950 - April 2010 and May

2010 - January 2011), EMBASE (January 1980 - January 2011), Cochrane Database of Systematic Reviews (January 2005 - January 2011), and the Cochrane Controlled Trials Register (January 2011). Searches were conducted using two different components: 1) Smoking/Smoking cessation and related terms component 2) Preoperative/Surgery/Anesthesia and related terms component. Both text-word and index-word terms were used; the text word terms in our search strategies included smoke\*, nicotine?, cigar\*, preop\*, preoperat\*, perioperat\*, preanesthe\*, presurg\*, surger\*, surgical\*, operat\*, resect\*, operati\*, operation?, operative\*, anesthe\*, anaesthe\*, perisurg\*, preadmit\*, and preadmission\*. The following exploded index-word terms were used: 'tobacco use cessation', 'smoking cessation', 'smoking', 'tobacco', 'tobacco use disorder', 'nicotine', 'preoperative care', 'preoperative period', 'perioperative care', 'perioperative nursing', 'surgical procedures, operative', 'general surgery', 'anesthesiology' and 'anesthesia'. Articles were limited to human studies and to the English language (Appendix). The bibliographies of retrieved articles and relevant reviews were searched manually for further studies.

#### Study selection

Two reviewers (J.W., D.L.) independently screened titles and abstracts to identify studies reporting postoperative complications (respiratory, cardiovascular, wound-healing) or death in relation to timing of preoperative smoking cessation within six months before surgery. Any disagreements were resolved by consensus or by consulting the senior author (F.C.). All randomized controlled trials (RCT) and cohort studies were included.

Studies were excluded if the period of smoking cessation was more than six months before surgery or not reported. We included RCTs that offered interventions if the complications were reported according to the actual smoking behaviour (i.e., continued to smoke or abstained) regardless of the intervention that the patient was randomized to receive. We contacted the corresponding authors if complications were not reported according to actual smoking status. Strategies were used to avoid duplicate publications.

#### Data extraction

Two reviewers (J.W., D.L.) independently extracted study characteristics and rated study quality. The following information was extracted from each study: continent, number of study participants, description of intervention, study design, surgical procedure, duration of preoperative smoking cessation, and postoperative complications (as reported in the primary studies) for ex-smokers, current smokers, and non-smokers. Respiratory complications included: bronchospasm

needing treatment, atelectasis requiring bronchoscopy and/or assisted ventilation, pulmonary infection, pleural effusion, pneumothorax, empyema, pulmonary embolus, adult respiratory distress syndrome, respiratory failure or arrest, re-intubation and ventilation, tracheostomy, and high inspired oxygen required for 24 hr. Cardiovascular complications included: life-threatening arrhythmias, severe hemodynamic disturbances, myocardial infarction, congestive heart failure, and cerebral vascular accident. Wound-healing complications included: impaired wound healing requiring intervention (e.g., debridement or re-suturing), wound dehiscence, flap or fat necrosis, hernia, vessel thrombosis, wound hematoma, seroma, mediastinitis, wound infection with positive microbial culture or requiring antibiotic therapy, wound cellulitis and swelling. We also extracted information about study quality, including number of dropouts, comparability of groups, adjustment for confounders, blinding, follow-up period, biochemical validation of smoking cessation, and funding source. We categorized non-smokers as those who never smoked; ex-smokers were those who stopped smoking any time before surgery, and current smokers were those who continued to smoke up to the day of surgery.

#### Quality assessment

We did not assess the quality of the RCTs, as the objective of this review was not to determine the effectiveness of various interventions for reducing complications but rather to determine the effect of short-term smoking cessation on postoperative complications and the minimum duration of smoking cessation to reduce postoperative complications. We conformed to the *Meta-analysis of observational studies in epidemiology* (MOOSE) group guidelines.<sup>18</sup> The quality of the studies was considered high if the design, conduct, and reporting of the studies were unlikely to be susceptible to bias. High-quality studies fulfilled the following criteria: validation of self-reported smoking status with biochemical methods, comparability of patients, adjustment for potential confounders for postoperative complications, adequate length of follow-up, blinding of the outcome assessor, and reporting of the source of funding.

#### Data synthesis and analysis

The primary outcome was the respiratory complications among ex-smokers with less than two weeks and two to four weeks of abstinence compared with current smokers. Secondary outcomes included postoperative complications (respiratory, cardiovascular, wound-healing) and mortality among ex-smokers and smokers, smokers and non-smokers, ex-smokers and non-smokers.

Meta-analysis of the relative risks of complications (respiratory, cardiovascular, wound-healing) and mortality

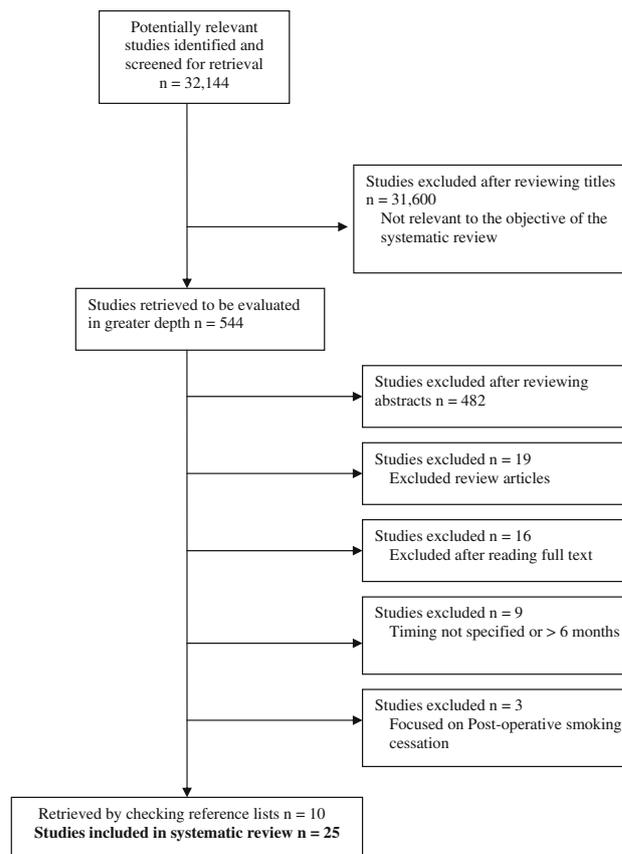
was performed in ex-smokers and smokers and ex-smokers and non-smokers when at least two studies comparing similar intervals were available. We also directly compared the relative risks of complications in different periods of preoperative smoking cessation with the risks in smokers and non-smokers. For the meta-analyses, we planned to categorize ex-smokers into different preoperative smoking cessation periods, i.e., less than two weeks, two to four weeks, more than four weeks, or more than eight weeks based on the cessation period reported in the original studies. Due to the clinical differences between the studies (e.g., patient population, study design, etc.), a random-effects model was used in all meta-analyses. The Mantel-Haenszel test was used to calculate the risk ratio (RR) and the corresponding 95% confidence interval (CI) for each meta-analysis. The  $I^2$  statistic was used to measure inconsistency among the study results.<sup>19</sup> A value > 50% may be considered moderate heterogeneity. Review Manager (RevMan) version 5.1 (The Nordic Cochrane Centre, The Cochrane Collaboration, 2011, Copenhagen) was used for all meta-analyses. Sensitivity analyses were performed for type of surgery (e.g., cardiac vs non-cardiac) and quality of study.

## Results

The search strategy yielded 32,144 citations. We identified 25 studies that fulfilled our inclusion criteria, for a total of 21,381 patients (Fig. 1). There were seven prospective cohort studies,<sup>12,20-25</sup> 16 retrospective cohort studies,<sup>26-41</sup> and two RCTs (Table 1).<sup>42,43</sup> Both RCTs offered nicotine replacement therapy.<sup>42,43</sup> There were 14 studies from North America,<sup>12,21,23,26,30-35,37,39-41</sup> six from Europe,<sup>22,27,28,38,42,43</sup> four from Asia,<sup>20,25,29,36</sup> and one from Australia.<sup>24</sup>

There were more male than female smokers, and smokers were younger than non-smokers or ex-smokers in many of the studies. The type of surgery, definition of complications, duration of smoking cessation, and the definition of “non-smokers”, “ex-smokers”, and “current smokers” reported in the individual studies varied between studies.

There were few studies that fulfilled most of the criteria for high quality (Table 1). Four studies used biochemical methods, including exhaled carbon monoxide and urinary cotinine concentrations, to validate the smoking status of the patients.<sup>12,24,42</sup> Four studies had comparable groups among smokers, ex-smokers, and non-smokers.<sup>43</sup> Six of the observational studies adjusted for potential confounders (Table 1). The follow-up periods were not specified in 13 studies (Table 1).<sup>12,20,22,27-30,33-38,40</sup> The outcome assessor for postoperative complications was blinded to the smoking status of the patients in only five of the studies.<sup>12,29,36,42,43</sup> All five studies reporting the source of funding received



**Fig. 1** Flow chart of the literature search and study selection

public funding,<sup>21,24,36,42,43</sup> and the nicotine replacement products were provided by the manufacturers (Table 1).<sup>42,43</sup>

## Respiratory complications

Fifteen studies involving 19,323 patients reported respiratory complications (Table 2, available as electronic supplemental material [ESM]).<sup>12,20,21,23-32,40,42</sup> There were four different time points commonly reported by the studies for respiratory complications, i.e., less than two weeks, two to four weeks, more than four weeks, and more than eight weeks of smoking cessation before surgery. Fourteen studies involving 17,160 patients were included in the meta-analyses.<sup>12,20,21,23-26,28-32,40,42</sup> Eight of these studies involving 3,331 patients were prospective.<sup>12,20,21,23-25,42,43</sup> As there was only one study examining the effect of less than or more than 12 weeks cessation, we could not perform a meta-analysis of this time point.<sup>27</sup>

## Summary of meta-analyses of respiratory complications

(The individual meta-analyses are available as ESM, Figs 6-17).

**Table 1** Study characteristics and assessment of risk of bias

Authors	Study Design	Type of Surgery	# Patients	Interventions	# Dropouts	Comparability of groups	Adjustment for confounders	Outcome assessor blinded	Follow-up period	Validation of smoking cessation with biochemical method	Funding Source
Warner <i>et al.</i> , 1984 <sup>26</sup>	Retrospective	Cardiac	500	N/A	N/A	Not reported	No	No	30 days after surgery	Self-report	Not reported
Warner <i>et al.</i> , 1989 <sup>12</sup>	Prospective	Cardiac	200	N/A	7 eliminated 1 passed away	Not reported	No	Yes	7 days or discharge home	Yes – Urinary cotinine	Not reported
Ngage <i>et al.</i> , 2002 <sup>27</sup>	Retrospective	Cardiac	2,163	N/A	N/A	Yes	N/A	No	Not specified	Self-report	Not reported
Al-Sarraf <i>et al.</i> , 2008 <sup>28</sup>	Retrospective	Cardiac	2,587	N/A	N/A	No	Yes	No	Not specified	Self-report	Not reported
Azarasa <i>et al.</i> , 2009 <sup>20</sup>	Prospective	Cardiac	600	N/A	N/A	No	No	No	Not specified	Self-report	Not reported
Nakagawa <i>et al.</i> , 2001 <sup>29</sup>	Retrospective	Pulmonary	288	N/A	N/A	No	Yes	Yes	Not specified	Self-report	Not reported
Vaporiyan <i>et al.</i> , 2002 <sup>30</sup>	Retrospective	Pulmonary	261	N/A	4 passed away	No	No	No	Not specified	Self-report	Not reported
Barrera <i>et al.</i> , 2005 <sup>21</sup>	Prospective	Pulmonary	300	N/A	N/A	No	No	No	30 days after surgery	Self-report	Public
Groth <i>et al.</i> , 2009 <sup>31</sup>	Retrospective	Pulmonary	213	N/A	92 did not complete pulmonary function tests	No	No	No	30 days after surgery	Self-report	Not reported
Mason <i>et al.</i> , 2009 <sup>32</sup>	Retrospective	Pulmonary	7,990	N/A	25 passed away	No	Yes	No	30 days	Self-report	Not reported
Chang <i>et al.</i> , 2000 <sup>33</sup>	Retrospective	Reconstructive	718	N/A	N/A	No	Yes	No	Not specified	Self-report	Not reported
Padubidri <i>et al.</i> , 2001 <sup>34</sup>	Retrospective	Reconstructive	748	N/A	N/A	Yes	N/A	No	Not specified	Self-report	Not reported
Goodwin <i>et al.</i> , 2005 <sup>35</sup>	Retrospective	Reconstructive	515	N/A	N/A	No	Yes	No	Not specified	Self-report	Not reported
Kuri <i>et al.</i> , 2005 <sup>36</sup>	Retrospective	Head & neck	188	N/A	N/A	No	No	Yes	Not specified	Self-report	Public
Spear <i>et al.</i> , 2005 <sup>37</sup>	Retrospective	Reconstructive	200	N/A	N/A	No	No	No	Not specified	Self-report	Not reported
Chan <i>et al.</i> , 2006 <sup>38</sup>	Retrospective	Reconstructive	169	N/A	4 patients excluded due to small volume reductions mammoplasty	No	Yes	No	Not specified	Self-report	Not reported
Araco <i>et al.</i> , 2008 <sup>22</sup>	Prospective	Reconstructive	84	N/A	N/A	Yes	N/A	No	Not specified	Self-report	Not reported
Glassman <i>et al.</i> , 2000 <sup>39</sup>	Retrospective	Orthopedic	395	N/A	34 lost to follow-up 2 passed away 2 refusals	No	No	No	2 years	Self-report	Not reported
Møller <i>et al.</i> , 2002 <sup>43</sup>	Randomized Controlled Trial	Orthopedic	120	Counselling and Nicotine Replacement Therapy	12 excluded, dropped out, or operation cancelled	Yes	N/A	Yes	Discharge home	Yes - Expired Carbon Monoxide	Public; Industry provided nicotine substitution products
Moore <i>et al.</i> , 2005 <sup>40</sup>	Retrospective	Urogynecologic	887	N/A	N/A	No	No	No	Not specified	No	Not reported

Table 1 continued

Authors	Study Design	Type of Surgery	# Patients	Interventions	# Dropouts	Comparability of groups	Adjustment for confounders	Outcome assessor blinded	Follow-up period	Validation of smoking cessation with biochemical method	Funding Source
Lindström <i>et al.</i> , 2008 <sup>42</sup>	Randomized Controlled Trial	Orthopedic/ General Surgery	117	Weekly meeting or telephone counselling and free nicotine substitution.	15 dropped out	Yes	N/A	Yes	30 days after surgery	Yes – Expired Carbon Monoxide	Public; Industry provided nicotine substitution products
Bluman <i>et al.</i> , 1998 <sup>23</sup>	Prospective	Mixed	410	N/A	N/A	No	Yes	No	Until hospital discharge	Self-report	Not reported
Myles <i>et al.</i> , 2002 <sup>24</sup>	Prospective	Mixed Ambulatory	489	N/A	N/A	No	Yes	No	7 days	Yes – Expired Carbon Monoxide	Public
Taber, <i>et al.</i> , 2009 <sup>41</sup>	Retrospective	Donor Nephrectomy	221	N/A	N/A	No	No	No	Until hospital discharge	Self-report	Not reported
Yamashita <i>et al.</i> , 2004 <sup>25</sup>	Prospective	Mixed	1,011	N/A	3 excluded	No	No	No	30 days after surgery or hospital discharge	Self-report	Not reported

N/A = not applicable

The relative risk (RR) of postoperative respiratory complications was higher in those who continued smoking at the time of surgery compared with non-smokers (RR 2.11; 95% CI 1.51 to 2.94;  $I^2 = 61%$ ;  $P < 0.0001$ ). When the period of abstinence from smoking was more than eight weeks, the risk was similar in ex-smokers and in non-smokers (RR 1.16; 95% CI 0.76 to 1.77;  $I^2 = 50%$ ;  $P = 0.50$ ), but a shorter period of abstinence failed to reduce the risk to values as low as those in non-smokers (Fig. 2). The type of surgery largely explained the heterogeneity, and grouping similar types of surgery together, i.e., cardiac vs non-cardiac surgery, reduced heterogeneity.

Compared with current smokers, the risk of respiratory complications was not higher in ex-smokers who abstained less than two weeks or two to four weeks before surgery (Fig. 3). On the other hand, the risks of respiratory complications in those who quit more than four weeks before surgery were significantly lower compared with current smokers (Fig. 3). The RR was 0.77 (95% CI 0.61 to 0.96;  $I^2 = 64%$ ;  $P = 0.02$ ) with more than four weeks of smoking cessation, and the RR was further reduced to 0.53 (95% CI 0.37 to 0.76;  $I^2 = 52%$ ;  $P = 0.0005$ ) in those who quit more than eight weeks before surgery. The type of

surgery, i.e., cardiac vs non-cardiac surgery, explained part of the heterogeneity at more than eight weeks but not at more than four weeks. The number of high-quality studies with similar smoking cessation intervals was insufficient to perform sensitivity analyses.

Direct comparisons of different intervals of smoking cessation and respiratory complications showed that there was no difference between patients who stopped smoking less than two weeks vs two to four weeks before surgery (Fig. 4). Notably, the risk of respiratory complications was lower in those who stopped smoking more than four weeks vs less than four weeks before surgery. Similarly, the RR was less in ex-smokers who quit more than eight weeks vs less than eight weeks before surgery (Fig. 4). The type of surgery, i.e., cardiac vs non-cardiac surgery, largely explained the heterogeneity at four weeks but not at eight weeks.

Cardiovascular complications

Cardiovascular complications were evaluated in only five studies involving 1,818 patients.<sup>20,31,40,42,43</sup> One of the RCTs did not report cardiovascular complications

Comparisons	No of Patients	RR [95% CI]	$I^2\%$	P value	References
CS vs. NS	4565	2.11 [1.51, 2.94]	61%	<0.0001	12, 22, 23-26, 29,30, 32
< 2 wk vs. NS	3568	2.51 [1.85, 3.39]	35%	<0.00001	25, 26, 29, 32
2 - 4 wk vs. NS	1646	2.80 [1.73, 4.52]	40%	<0.0001	26, 29, 32
> 4 wk vs. NS	5897	1.39 [1.18, 1.65]	52%	0.0001	20, 24, 26, 29, 30, 32, 40
> 8 wk vs. NS	1742	1.16 [0.76, 1.77]	50%	0.50	12, 20, 21, 25, 26

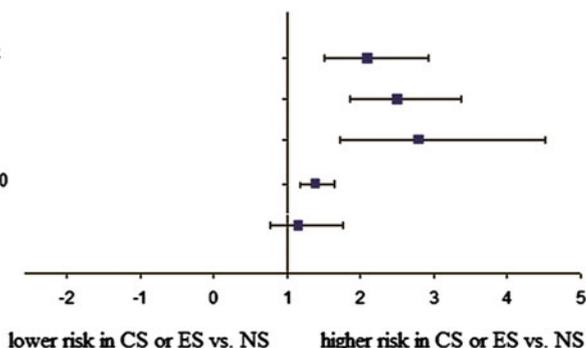


Fig. 2 Summary of the meta-analyses of postoperative respiratory complications in current smokers or ex-smokers compared with non-smokers. The squares indicate the overall relative risk and the

horizontal lines indicate the 95% confidence interval for each time interval. CS = current smoker; NS = non-smoker; ES = ex-smokers

Comparisons	No. of Patients	RR [95% CI]	$I^2\%$	P value	References
< 2 wk vs. CS	559	1.20 [0.96, 1.50]	0%	0.10	25, 26, 42
2 - 4 wk vs. CS	2210	1.14 [0.90, 1.45]	6%	0.27	26, 29, 31
> 4 wk vs. CS	5659	0.77 [0.61, 0.96]	64%	0.02	24, 26, 28-32
> 8 wk vs. CS	1426	0.53 [0.37, 0.76]	52%	0.0005	12, 20, 21, 25, 26

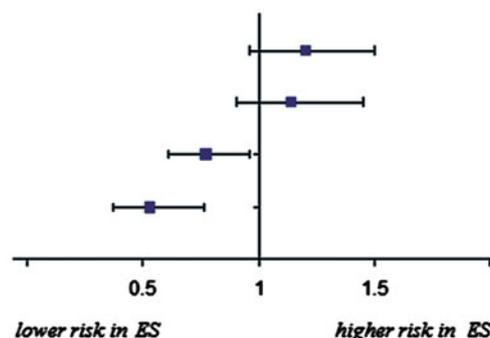
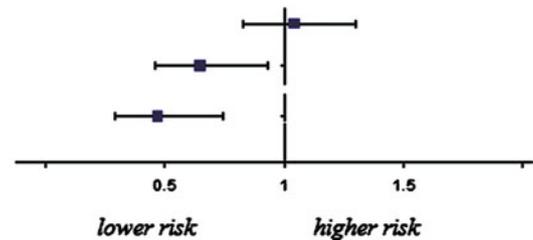


Fig. 3 Summary of the meta-analyses of postoperative respiratory complications in ex-smokers compared with current smokers. The squares indicate the overall relative risk and the horizontal lines

indicate the 95% confidence interval for each time interval. CS = current smoker; NS = non-smoker

Comparisons	No. of Patients	RR [95% CI]	I <sup>2</sup> %	P value	References
< 2 wk vs. 2 - 4 wk	2170	1.04 [0.83, 1.30]	0%	0.74	26, 29, 32
> 4 wk vs. < 4 wk	5592	0.65 [0.46, 0.93]	82%	0.02	26, 28, 32
> 8 wk vs. < 8 wk	1309	0.47 [0.29, 0.74]	76%	0.001	12, 20, 21, 25, 26



**Fig. 4** Summary of the meta-analyses of postoperative respiratory complications with direct comparisons of ex-smokers based on time of smoking cessation before surgery. The squares indicate the overall

relative risk and the horizontal lines indicate the 95% confidence interval for each time interval

according to actual abstinence or continued smoking, and the authors did not respond to our request for these data.<sup>43</sup> There were no differences in risks for cardiovascular complications among current smokers, ex-smokers (one to eight weeks abstinence), and non-smokers (Table 3; available as ESM). However, a meta-analysis on this outcome was not performed as there were few cardiovascular complications reported in the studies, and the sample sizes were limited.

#### Wound-healing complications and studies for performing a meta-analysis

There were 15 studies involving 9,536 patients that reported wound-healing complications (Table 4, available as ESM).<sup>22,24,27,28,33-43</sup>

There was only one time point (i.e., less than or more than three to four weeks before surgery) with an adequate number of studies for meta-analysis. Thirteen studies involving 7,265 patients were included in the meta-analysis.<sup>22,24,28,33-42</sup> There was twice the risk of wound-healing complications in those who continued smoking at the time of surgery vs non-smokers (RR 2.08; 95% CI 1.60 to 2.71;  $I^2 = 8%$ ;  $P < 0.00001$ ) (Fig. 18, available as ESM).

The risk remained higher in ex-smokers who quit smoking within three to four weeks before surgery vs non-smokers (RR 1.64; 95% CI 1.40 to 1.92;  $I^2 = 0%$ ;  $P < 0.00001$ ) (Fig. 19, available as ESM). However, risks of wound-healing complications in patients who abstained from smoking beyond three to four weeks before surgery were similar to those in patients who had never smoked (RR 1.44; 95% CI 0.97 to 2.15;  $I^2 = 76%$ ;  $P = 0.07$ ) (Fig. 20, available as ESM). The type of surgery did not explain the heterogeneity.

Ex-smokers who quit less than three to four weeks before surgery had similar risks for wound-healing complications as current smokers (RR = 1.22; 95% CI 0.56 to 2.67;  $I^2 = 86%$ ;  $P = 0.61$ ) (Fig. 21, available as ESM). The type of surgery did not explain heterogeneity, but the

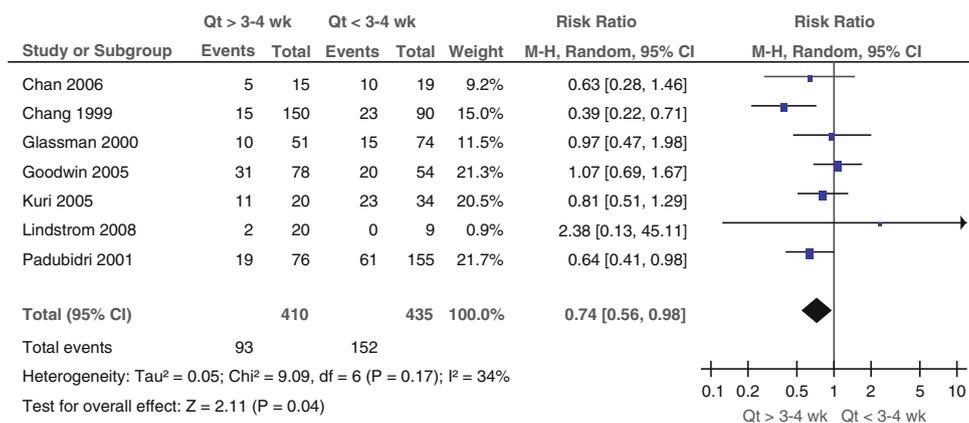
number of studies was limited at this time interval. The risks of wound-healing complications in ex-smokers who stopped smoking more than three to four weeks before surgery were significantly lower than in current smokers (RR 0.69; 95% CI 0.56 to 0.84;  $I^2 = 0%$ ;  $P = 0.0003$ ) (Fig. 22, available as ESM). In addition, direct comparisons showed the risk was significantly lower in ex-smokers who stopped smoking more than three to four weeks before surgery vs those who stopped less than three to four weeks before surgery (RR 0.74; 95% CI 0.56 to 0.98;  $I^2 = 34%$ ;  $P = 0.04$ ) (Fig. 5). Therefore, more than three to four weeks of preoperative abstinence is necessary to reduce risks of wound-healing complications.

#### Mortality

Ten of the studies reported mortality rates.<sup>12,20,21,23,27,28,30,32,42,43</sup> One large retrospective study in pulmonary resections for lung cancer reported higher mortality in current and ex-smokers compared with non-smokers (1.5% vs 0.3%, respectively;  $P < 0.05$ ).<sup>32</sup> The other nine studies did not report differences in mortality among smokers who quit at different intervals before surgery and current and non-smokers.<sup>12,20,21,23,27,28,30,42,43</sup> However, there were few deaths reported in the included studies, and the individual studies were not large enough to detect differences in mortality.

#### Discussion

This review supports the notion that there is a time-related decrease in the risk of respiratory complications, i.e. the relative risk decreases as the duration of preoperative smoking cessation increases. Most importantly, cessation of smoking more than four weeks before surgery reduced the risk of respiratory complications by 23%. Those who stopped smoking more than eight weeks before surgery had greater benefits, and the risk of respiratory complications



**Fig. 5** Ex-smokers who quit more than three to four weeks before surgery had lower relative risks of postoperative wound-healing complications than those who quit less than three to four weeks before surgery. The squares indicate the overall relative risk and the

horizontal lines indicate the 95% confidence interval for each time interval. The diamond represents the pooled estimate. Qt = quit time; CI = confidence interval; M-H = Mantel Haenszel; wk = weeks

was reduced by 47%. Indeed, the risk of respiratory complications in those who stopped smoking more than eight weeks before surgery was comparable with non-smokers. In all probability, patients should stop smoking at least four weeks, and preferably eight weeks, before surgery to reduce postoperative respiratory complications. However, there was no evidence that short-term abstinence from smoking (less than four weeks) before surgery increases or reduces postoperative respiratory complications compared with continued smoking, but only a few studies examined this interval. There was no difference in mortality between smokers and ex-smokers, but there were few deaths reported in the included studies.

Our meta-analysis shows that smokers who abstained more than three to four weeks before surgery had fewer wound-healing complications than current smokers. As well, smokers who quit more than three to four weeks before surgery had fewer wound-healing complications than those who quit less than three to four weeks before surgery. Our results are consistent with a well-conducted study in wound healing following excisional punch biopsy that reported a reduction in the incidence of wound infections with four weeks of abstinence from smoking.<sup>44</sup> However, this study was not included in our review as it did not involve a surgical procedure.

We did not find evidence to support that short-term abstinence from tobacco may lead to acute withdrawal, increased sympathetic activity, and increased cardiovascular complications. However, a limited number of studies reported cardiovascular complications. Therefore, we could not determine the risk or benefits of smoking cessation for prevention of cardiovascular complications.

The findings of our systematic review and meta-analysis are consistent with previous reviews and extend their

findings.<sup>6,7,17</sup> Our review included more studies than a previous review which was limited to a comparison of smokers vs ex-smokers who quit less than eight weeks before surgery.<sup>17</sup> We also examined wound-healing complications, and we did not pool the results of studies with different periods of cessation. In contrast, by comparing different intervals of short-term cessation with continued smoking and including studies that directly compared different intervals of cessation (e.g., less than two weeks vs two to four weeks) on postoperative complications, we were able to determine the minimum duration of preoperative smoking cessation necessary to reduce postoperative respiratory and wound-healing complications. Our findings also confirm that smokers have higher risks for postoperative respiratory and wound-healing complications than non-smokers.<sup>3</sup>

The results of our review should be interpreted with caution due to several limitations of the included studies. Few studies had high methodological quality, and most of the included studies were retrospective observational studies. However, it would be difficult to perform a prospective trial with randomization of patients to different periods of abstinence before surgery. Our conclusions are based on the best evidence that is currently available. The majority of the studies relied on self-reporting of smoking status, which may have led to the status being inaccurately reported. Many of the studies did not adjust for confounding factors between groups. The study designs and definition of postoperative complications varied among the studies. As well, the smoking cessation intervals in some studies were not clearly defined, and intervals overlapped with more than one time interval. To overcome this problem, we grouped together similar intervals of the reported smoking cessation periods and compared them collectively.

In addition, many of the studies did not report clinically significant outcome measures, including recovery room and hospital length of stay. Another limitation of this review is our exclusion of articles not published in English.

The heterogeneity was moderate or high for a few of the meta-analyses. The type of surgery could explain some of the heterogeneity; however, smoking increases complications across all non-cardiac surgical procedures<sup>3</sup> and including different types of surgery increases generalizability of our findings. The number of high-quality studies with similar smoking cessation intervals was insufficient to perform the relevant sensitivity analysis. Other factors that explain the heterogeneity may include the wide range of time intervals *vs* clearly defined intervals reported in individual studies. Sensitivity analyses of other potential factors explaining heterogeneity, such as disease severity, patient morbidity, etc., were not possible due to limited data reported in the individual studies. However, heterogeneity exists in the amount of overall effect, not in the direction of the effect, i.e., although the RRs were different, all were on the same side of the Forest plot. Nonetheless, we used the random effects method, which is more suitable when heterogeneity exists.<sup>45</sup>

In conclusion, at least four weeks of preoperative smoking cessation is necessary to reduce respiratory complications, and at least three to four weeks of abstinence is needed to reduce wound-healing complications. Based on the available studies examining short-term (less than four weeks) abstinence from smoking, short-term abstinence does not increase or reduce postoperative respiratory complications. However, given the known long-term benefits of smoking cessation, including an improvement in long-term health, and the “teachable moment” a pre-admission visit provides, our findings should not deter anesthesiologists and other perioperative clinicians from counselling surgical patients to stop smoking regardless of the time of visit. Future studies should examine the ideal time frame for smoking cessation prior to surgery, consider adjusting for confounders, and target more clinically significant outcomes, such as hospital length of stay.

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## Appendix

#	Searches Smoking/Smoking Cessation & Related Terms Component
1	“tobacco use cessation”/
2	smoking cessation/
3	exp Smoking/
4	smoking.mp.
5	smoke*.mp.
6	exp Tobacco/
7	[Tobacco Smoke Pollution/ ==> removed April 28, 2010]
8	[Tobacco Industry/ ==> removed April 28, 2010]
9	tobacco?.tw. [changed to textword to avoid MeSH terms above]
10	exp “tobacco use disorder”/
11	[exp nicotinic agonists/ ==> removed April 28, 2010]
12	exp nicotine/
13	nicotine?.mp.
14	cigar*.mp.
15	[marijuana*.mp. ==> removed April 28, 2010]
16	[cannabis/ ==> removed April 28, 2010]
17	[cannabis.mp. ==> removed April 28, 2010]
18	[hookah?.mp. ==> removed April 28, 2010]
19	[waterpipe?.mp. ==> removed April 28, 2010]
20	[water-pipe?.mp. ==> removed April 28, 2010]
21	or/1-20
Preoperative / Surgery / Anesthesia & Related Terms Component	
22	exp Preoperative Care/
23	preoperative period/
24	preop*.mp.
25	pre-op*.mp.
26	peroperat*.mp.
27	Perioperative Care/
28	Perioperative Nursing/
29	perioperat*.mp.
30	peri-operat*.mp.
31	prean?esthe*.mp.
32	pre-an?esthe*.mp.
33	presurg*.mp.
34	pre-surg*.mp.
35	(before adj2 surger*).mp.
36	(before adj2 surgical*).mp.
37	(prior adj2 surger*).mp.
38	(prior adj2 surgical*).mp.
39	(before adj2 operat*).mp.
40	(prior adj2 operat*).mp.
41	(before adj2 resect*).mp.
42	(prior adj2 resect*).mp.
43	(advance adj2 surger*).mp.
44	(advance adj2 surgical*).mp.

## Appendix continued

## Preoperative / Surgery / Anesthesia &amp; Related Terms Component

- 45 (advance adj2 operati\*).mp.  
 46 (ahead adj2 surger\*).mp.  
 47 (ahead adj2 surgical\*).mp.  
 48 (ahead adj2 operat\*).mp.  
 49 exp Surgical Procedures, Operative/  
 50 General Surgery/  
 51 surger\*.mp.  
 52 surgical\*.mp.  
 53 operative\*.mp.  
 54 operation?.mp.  
 55 anesthesiology/  
 56 exp anesthesia/  
 57 anesthe\*.mp.  
 58 anaesthe\*.mp.  
 59 su.fs.  
 60 perisurg\*.mp.  
 61 peri-surg\*.mp.  
 62 preadmission\*.mp.  
 63 pre-admission\*.mp.  
 64 preadmit\*.mp.  
 65 pre-admit\*.mp.  
 66 or/22-65  
 67 21 and 66  
 68 limit 67 to (English language and human)

**Duplicate records within Medline removed →  
 minus 91 duplicates →**

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