

TOBACCO & POSTSURGICAL OUTCOMES

- *Those who smoke, or even quit smoking, before surgery have a significantly increased risk of experiencing a range of postsurgical complications compared with non-smokers.*
- *Children exposed to second-hand tobacco smoke have a higher risk of peri-anaesthetic respiratory adverse events.*
- *Those who quit smoking approximately 4 weeks before surgery have a reduced risk of postsurgical complications. The optimum length of cessation varies depending on the type of postsurgical outcome assessed (i.e. wound healing or total complications).*
- *High-intensity behavioural interventions, which include weekly contact, provision of nicotine or non-nicotine (varenicline) replacement therapy and referrals to telephone cessation support and which are delivered for at least four weeks before surgery, are effective in reducing postsurgical complications. The impact of such interventions on smoking cessation can occur within one-week pre surgery.*
- *The surgical unit can play a vital role in the assessment of smoking status and initiation of smoking cessation interventions in its patients before surgery.*
- *Governments should promote the implementation of smoke-free hospital policies, access to nicotine or non-nicotine (varenicline) replacement therapy and access to community tobacco cessation services for presurgical patients.*

Tobacco use

Worldwide, more than 1.1 billion people smoke tobacco and at least 367 million people use smokeless tobacco (1). Tobacco smoking is known to cause adverse health effects, including cancer, cardiovascular and respiratory diseases (2), and was responsible for approximately 11.5% of total deaths in 2015 (3).

Surgery burden

Approximately one in 25 individuals (representing between 187 million and 280 million cases globally) undergoes major surgery annually for the treatment of disease, injury or illness (4, 5). Complications from surgery such as surgical site infections and respiratory and cardiopulmonary events represent a substantial burden for both patients and health-care systems. Major morbidity occurs in between 4% and 16% of all inpatient surgical procedures in developed countries, with perioperative mortality and severe disability occurring in 1% of cases (6-9). In developing countries, mortality rates reportedly increase to up to 0.24–10% of cases (9-11). Surgical procedures with major complications cost significantly more than surgery without any complications (12), suggesting that substantial savings can be made if such complications are prevented. Surgery and anaesthesia cause severe stress and trauma to the body (13).

Tobacco definitions

Smoked tobacco: any product made entirely or partly of leaf tobacco that is intended to be lit and the produced smoke inhaled. Examples include manufactured cigarettes, roll-your-own cigarettes, water pipes (e.g. hookah, shisha), cigars, kreteks and bidis.

Second-hand smoke (SHS): the combination of “mainstream” smoke (the smoke emerging from the mouth end of a cigarette during smoking) that is exhaled by the smoker, and “side-stream” smoke emitted into the environment from lit cigarettes and other tobacco products. The terms “Passive smoking or Involuntary smoking or Environmental tobacco smoke” are also often used to describe exposure to SHS.

Smokeless tobacco: any product that consists of cut, ground, powdered or leaf tobacco that is intended to be placed, loose or in sachets, in the oral or nasal cavity. Examples include snuff, chewing tobacco, gutka and mishri.

In the postsurgical period, the body undergoes a post-traumatic inflammatory response to fight infections and activates a wound-healing cascade for tissue recovery. The recovery process increases the body’s need for oxygen and other nutrients, and modifiable risk factors including high body mass index, risky alcohol consumption and active smoking are thought to interfere with this process (14, 15).

This evidence brief aims (a) to summarize the association between tobacco exposure (smoking, smokeless and second-hand smoke) and postsurgical complications; and (b) to describe the effectiveness of interventions to reduce presurgical tobacco use and tobacco-related complications.

The impact of tobacco use on postsurgical outcomes

Chronic exposure to tobacco causes adverse physiological changes in cardiovascular function, pulmonary function and tissue healing. These changes may interfere with the postsurgical recovery process and account for the increased occurrence of postsurgical complications observed in smokers (13). Additionally, there is some evidence that smoking even one cigarette can result in reduced blood flow which, in turn, can contribute to adverse surgical outcomes (16, 17).

Cardiovascular function Chemical substances contained in tobacco increase the body's need for oxygen, but reduce its capacity to use oxygen (18). Nicotine stimulates the central nervous system, increasing blood pressure, heart rate, peripheral vascular resistance and oxygen consumption. Nicotine is also thought to induce vasoconstriction and inhibit platelet aggregation, reducing oxygen transport. Carbon monoxide reduces the availability of oxygen for cellular processes by binding to haemoglobin, and also inactivates cardiac enzymes, leading to decreased oxygen transport and use (19). Together, these result in tissue hypoxia and increased blood viscosity, which increases an individual's risk of cardiovascular events.

Pulmonary function Smoking has an adverse impact on pulmonary function, primarily through decreased mucociliary clearance and abnormal small airway function (20). Cigarette smoking damages the ciliated epithelium and the tracheobronchial tree in the lungs, leading to increased mucus, obstruction in the bronchioles and reduced ciliary function, and increases the risk of infections and respiratory complications (14). Mucous hypersecretion leads to increased sputum volume, which may result in deterioration in the oxygen transport system, inflammation of the airway and increased pulmonary complications.

Impaired wound healing Smoking may impair surgical site healing and promote wounds opening along sutures (dehiscence) via a number of pathways including (a) peripheral tissue hypoxia leading to necrosis; (b) decreased inflammatory responses; and (c) delayed proliferative healing responses and reduced collagen synthesis (14). Increased oxidative stress inhibits the mechanisms of neutrophils, which slows down the wound-healing process and reduces the body's capacity to fight bacterial infections (21). Smoking also impairs production of pro- and anti-inflammatory cytokines responsible for regulating the immune function within the body, which may be a predisposing risk factor for infections in the postoperative period (14).

Impaired bone healing Smoking may also affect bone healing in several ways, including increased tissue hypoxia, vasoconstriction secondary to nicotine and direct impairment of osteoblast activity and collagen synthesis by tobacco smoke (22), with a systematic review identifying smoking as one of the top 10 risk factors for non-union of long bones (23).

Second-hand smoke exposure and smokeless tobacco Little is known about the ways smokeless tobacco may influence postsurgical outcomes. In children, environmental exposure to tobacco smoke is associated with significantly higher odds of adverse surgical outcomes.

Association between tobacco exposure and postsurgical complications – reviews of observational trials

The link between tobacco smoking and the presence of postsurgical complications has been well studied. Overall, 28 systematic reviews published since 2004 were identified, examining the impact of smoking on a range of postsurgical outcomes (see Annex 1). All reviews reported that smoking, even when the smoker quits before surgery, was significantly associated with increased risk of at least one adverse postsurgical outcome, compared with the results for non-smokers (see Annex 1). A 2014 review (26) of 107 observational studies found a positive association between preoperative smoking status and

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a number of postoperative complications (within 30 days of surgery). The confounder-adjusted relative risks of surgical/intraoperative or postoperative complications were significantly higher in smokers in the case of: general morbidity/total complications (RR: 1.75, 95% CI: 1.40–2.20), wound complications (RR: 2.49, 95% CI: 1.91–3.26), general infections (RR: 2.05, 95% CI: 1.34–3.13), pulmonary complications (RR: 2.46, 95% CI: 1.74–3.48); neurological complications (RR: 1.71, 95% CI: 1.07–2.74); and admission to an intensive care unit after surgery (RR: 1.6, 95% CI: 1.14–2.25) (26). For wound healing in particular, a review of 140 cohort studies involving 479 150 patients found that smokers had significantly higher adjusted odds ratios for healing delay (OR: 2.07, 95% CI: 1.53–2.81) and dehiscence (OR: 1.79, 95% CI: 1.57–2.04), surgical site infection (OR: 2.27, 95% CI: 1.82–2.84) wound complications in hernia (OR: 2.07, 95% CI: 1.23–3.47), and lack of fistula or bone healing (OR: 2.44, 95% CI: 1.66–3.58) compared with non-smokers. These findings of increased risk of experiencing postsurgical complications are consistent with other reviews which include patients across all surgical specialities (14, 27–30), as well as reviews which include only patients undergoing surgery in specific sites, including hip and knee (31, 32), operation for Crohn’s disease (33), lower extremity grafting (34), periodontal surgery (35), spinal surgery (15), inguinal hernia surgery (36) and hip arthroplasty (37). The risk of delayed wound healing is similarly elevated in cosmetic surgery (OR: 2.50, 95% CI: 0.49–4.08) and bariatric surgery patients (OR: 3.30, 95% CI: 1.90–5.64) (38).

Association between cessation and postsurgical complications – reviews of controlled trials

A review of randomized controlled trials showed that interventions to increase cessation can significantly reduce the incidence of any postsurgical complication (RR: 0.42, 95% CI: 0.27–0.65) (39) and surgical site infections (OR: 0.43, 95% CI: 0.21–0.85) (14), and postoperative morbidity up to six months post-follow-up (40).

Association between exposure to second-hand smoke or use of smokeless tobacco and postsurgical complications

A systematic review and meta-analyses examining the impact of environmental tobacco smoke exposure on anaesthetic and surgical outcomes in children found that exposure significantly increased risk of peri-anaesthetic respiratory adverse events (RR: 2.52, 95% CI: 1.68–3.77) (41). Observational studies suggest that second-hand smoke exposure may be associated with adverse respiratory outcomes in both adults and children during general anaesthesia, as well as prolonged recovery time (42–47).

Association between tobacco exposure and postsurgical complications – summary of findings

Evidence from systematic reviews of observational studies shows a significantly increased risk of postoperative complications in smokers for all types of surgery, as well as in specific surgical sites including hip and knee, bowel resection and spinal surgery (40). The association between quitting smoking approximately 3–4 weeks before surgery and reduced postoperative complications has also been consistently reported in systematic reviews of randomized controlled trials (21).

Are there increased risks associated with short-term smoking cessation prior to surgery?

While there is a general consensus that stopping smoking before surgery can improve outcomes, there has been some controversy about the optimal timing of smoking cessation. Two studies published by Warner and colleagues (48–50) in a small sample of patients (< 200) undergoing coronary artery bypass grafting reported higher, but non-significant, rates of pulmonary complications among those who stopped smoking less than eight weeks prior to surgery, compared with those who continued to smoke.

Evidence from systematic reviews of observational studies has, however, reported no increase in adverse outcomes in people who cease smoking less than eight weeks before surgery (all complications: RR: 0.78, 95% CI: 0.57–1.07) (29), between two and four weeks (pulmonary complications: RR: 1.14, 95% CI: 0.90–1.45) and less than two weeks (pulmonary complications: RR: 1.20, 95% CI: 0.96–1.50) presurgery, compared with current smokers (27, 28). Longer abstinence periods (> 4 weeks) are, however, consistently associated with better postsurgical outcomes (21, 27, 28, 51), with a review reporting that each additional week of cessation resulted in an improvement of 19% in terms of reduction of postoperative morbidity (28).

Effectiveness of interventions to reduce presurgical tobacco use and related complications

Given the benefits of cessation for the reduction of adverse outcomes related to surgery, the presurgical period represents a key opportunity for interventions to reduce smoking and related complications. In our search, nine systematic reviews examining interventions to reduce smoking in patients undergoing surgery were identified. This includes a Cochrane systematic review published in 2014, which identified 13 randomized controlled trials examining interventions to reduce smoking in the presurgical period. Both low-intensity (RR: 1.30, 95% CI: 1.16–1.46) and high-intensity (RR: 10.76, 95% CI: 4.55–25.46) behavioural interventions were effective in reducing smoking immediately following the intervention. Only the two high-intensity interventions, which included weekly contacts (52, 53), were effective in reducing smoking rates at 12 months' follow-up (RR: 2.96, 95% CI: 1.57–5.55), with a corresponding reduction in postoperative complications (RR: 0.42, 95% CI: 0.27–0.65) (39). A narrative review of the efficacy of nicotine replacement therapy (NRT) in the perioperative period found limited evidence to indicate any increased risk of healing-related or cardiovascular-related complications (54). Only one trial examined the impact of non-NRT pharmacological interventions (varenicline), and found an increase in cessation

rates at 12 months' follow-up (RR: 1.45, 95% CI: 1.01–2.07), but no reduction in risk of postsurgical complications (RR: 0.94, 95% CI: 0.52–1.72) (55). Since the publication of the Cochrane review, other randomized controlled trials have found that a lower-intensity intervention that did not require weekly face-to-face sessions (NRT plus a telephone quitline), were effective in reducing smoking rates at 12 months' follow-up (RR: 3.0, 95% CI: 1.2–7.8) (56). Further, in a randomized controlled trial with non-NRT pharmacological interventions (varenicline) and telephone quitline follow-up, compared with a brief intervention without pharmacotherapy, an increase in cessation rates was found at 12 months' follow-up (1.62, 95% CI: 1.16–2.25, $P = 0.003$) (57). Consistent with reviews in hospitalized (58) and non-hospitalized populations (59), a small number of studies suggest that high-intensity behavioural interventions, with weekly face-to-face or telephone contact, the offer of NRT and referrals to the quitline, provided at least four weeks before surgery, are effective in reducing smoking and postoperative complications in presurgical patients.

Potential next steps

Research

There is strong evidence indicating that tobacco smoking is associated with an increased risk of a range of adverse postoperative outcomes. However, more prospective research, with longer follow-up times, is needed to assess the impact of smokeless tobacco use on these outcomes. Because of the negative impact of nicotine on cardiovascular function, research is also needed on the potential impact of use of electronic nicotine delivery systems on surgical outcomes, since these products can contain high and variable levels of nicotine. Finally, although current evidence suggests that effective intervention strategies exist for the reduction of smoking in preoperative patients, these results are based on a small number of trials conducted in developed countries. There has been only a small number of trials examining the use of pharmacotherapy (non-NRT) on smoking cessation in these patients. More intervention research examining different intervention intensities and

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modalities and the usefulness of pharmacotherapy is needed to inform future strategies to reduce smoking in this population.

Practice

Although a relatively large number of patients would like to quit smoking, and scheduled surgery provides a potential teaching opportunity to help smokers quit in the long term, patients are often poorly informed of the benefits of smoking cessation for surgical outcomes and unaware of the resources available to help them to quit (60). There is potential for surgeons and anaesthetists to be involved in the initiation and delivery of preoperative smoking cessation care. While their capacity to offer high-intensity behavioural interventions is likely to be limited, surgical staff can play an active role by identifying smokers and assessing their willingness to quit smoking, providing information on the potential implications of continuing to smoke for surgical outcomes, supporting the initiation of NRT and referring patients to cessation services.

Systems

Perioperative services have a considerable role to play in supporting smoking cessation among surgical patients (61). However, the involvement of other hospital staff, primary care physicians and community resources may help to support such services by ensuring that a comprehensive and individualized smoking cessation intervention is developed before a planned operation (60, 62). The introduction of smoke-free policies in hospitals such as those encouraged by the WHO Framework Convention on Tobacco Control is essential to facilitate efforts to reduce smoking in presurgical patients. Such policies should be accompanied by the provision of inpatient cessation care (in the form of brief advice and provision of NRT in preoperative and postoperative units) as well as outpatient community cessation care (in the form of tobacco quitlines and active referrals to primary care physicians for advice and/or NRT or non-NRT pharmacotherapy). Mechanisms to facilitate active referral to such cessation resources should be implemented as part of the provision of routine surgical care in order to ensure the best outcomes for surgical patients.

Methods

WHO conducted a systematic search of the peer-reviewed literature for systematic reviews that examined (a) the impact of reducing the use of smoked or smokeless tobacco and exposure to second-hand smoke on postsurgical outcomes; and (b) interventions to reduce preoperative smoking, published between 2004 and May 2016. To make the review as inclusive as possible, a broad definition of systematic review was used. Specifically, systematic reviews were defined as reviews that included defined inclusion/exclusion criteria and provided information to indicate that a systematic method of searching and selection of trials had been undertaken. Where insufficient evidence from systematic reviews was present, a selective examination of non-systematic reviews and high-quality studies were undertaken. Relevant high-quality systematic reviews known to the authors and undertaken outside the search period were also included. The inclusion criteria included humans only; subjects exposed to any form of tobacco who were scheduled to undertake surgery; and examination of association with and/or reduction of smoking in relation to postsurgical outcomes. The review was not limited by language, although few non-English studies were identified. Using standardized methods, one reviewer undertook data extraction for information pertinent to the objectives of the evidence brief. Findings from any meta-analyses (relative risk (RR)/odds ratios (OR) and corresponding 95% confidence interval (CI)) undertaken within the relevant reviews were reported within the text or in a supplementary table, where available.

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¹ WHO Collaborating Centre for Evidence-based NCD Program Implementation (Priority Research Centre for Health Behaviour, University of Newcastle, Australia); ² World Health Organization, Switzerland; ³ World Federation of Societies of Anaesthesiologists.

External reviewers: Davy Cheng,⁴ Jean Wong⁵ and Susan Ming⁶

⁴ London Health Sciences Centre, Canada; ⁵ University Health Network, Canada; ⁶ University of California San Francisco, USA

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Editorial assistance: Teresa Lander

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Annex 1. Summary of findings of included reviews

Author(s)	Synthesis	Number and type of studies	Search frame	Studies included	Aim	Surgery type	Pulmonary complications	Cardiovascular complications	Wound healing	Any complication	Other complications	Conclusions
Burcharth et al., 2015(36)	Narrative and meta-analysis	40 observational. (6 case-control; 15 database; 19 cohort)	Up to June 2013	Observational exploratory studies evaluating patient-related risk factors for recurrence after inguinal hernia surgery.	To provide a systematic overview of non-technical patient-related risk factors for recurrence after inguinal hernia surgery.	Inguinal hernia surgery	DNR	DNR	DNR	DNR	Smoking was found to be a risk factor for recurrence of surgery with a pooled OR of 2.53 (95% CI: 1.43-4.47, P =.001, I2 = 0%).	The meta-analysis found that smoking increased the risk of recurrence after inguinal hernia surgery..
Chiswell and Akram (41)7	Meta-analyses and narrative	28 observational studies	Up to 30 October 2014	Observational studies examining ETS exposure in children.	To undertake a systematic review of the impact of ETS on the paediatric surgical pathway and to establish if whether there is evidence of anaesthetic, intraoperative or postoperative harm.	Ear, nose and throat	Eleven studies examining respiratory adverse outcomes and laryngospasm outcome found association of such outcomes with ETS exposure (RR: 2.52, 95% CI: 1.68 – 3.77), P < 0.01, I2 = 23%).	DNR	DNR	DNR	Anaesthetic outcomes – 11 of 15 studies showed significant effects of ETS on anaesthetic outcomes.	ETS exposure increases the risk of anaesthetic complications and some negative surgical outcomes in children.

Author(s)	Synthesis	Number and type of studies	Search frame	Studies included	Aim	Surgery type	Pulmonary complications	Cardiovascular complications	Wound healing	Any complication	Other complications	Conclusions
Gronkjaer et al., 2014 (26)	Meta-analyses	107 (100 cohort, 7 case-control)	January 2000 – October 2011	Observational studies on the association between smoking status and postoperative complications occurring within 30 days of operation.	To identify associations between preoperative smoking status and postoperative complications (within 30 days of surgery).	All types of surgery	Non-adjusted: RR: = 1.73, 95% CI: 1.35–2.23; I2 = 79.3%; P < 0.001 Adjusted: RR: = 2.46, 95% CI: 1.74–3.48.	Non-adjusted: RR: = 1.07, 95% CI: 0.78–1.45, I2 = 60.4%; P = 0.007 Adjusted: RR: = 1.09, 95% CI: 0.69–1.72.	Non-adjusted: RR: = 2.15, 95% CI: 1.87–2.49, I2 = 63.9%; P < 0.001 Adjusted: RR: = 2.49, 95% CI: 1.91–3.26.	Non-adjusted: RR:1.52 95% CI: 1.33–1.74, I2=77%, p<0.001 Adjusted: RR: = 1.75, 95% CI: 1.40–2.20.	General infections: adjusted: RR: = 1.54, 95% CI: 1.32–1.79; I2 =28.6% and P = 0.165. Neurological complications: RR: = 1.38, 95% CI: 1.01–1.88, I2 = 0.0%; P = 0.529. Admission to intensive care unit: RR: = 1.60, 95% CI: 1.14–2.25; I2 = 66.3%, P = 0.018. Bleeding: RR: = 1.34, 95% CI: 0.59–3.07, I2 = 66.9%; P = 0.006.	Preoperative smoking was found to be associated with an increased risk of postoperative complications 30 days postsurgery.
Javed et al., 2012(35)	Narrative	24 (17 controlled trials, 3 case report, 4 case-control).	1968 to May 2010	The eligibility criteria encompassed the following: (1) original articles; (2) clinical and experimental studies; (3) case reports; (4) studies designed specifically to investigate the effect of smoking on clinical outcomes of periodontal surgical procedures.	To examine the effect of cigarette smoking on clinical outcomes after periodontal surgical interventions.	Periodontal surgery	DNR	DNR	DNR	DNR	Sixteen studies showed that reductions in probing depth and gains in clinical attachment levels were compromised in smokers in comparison with non-smokers. Three studies showed residual recession after periodontal surgical interventions to be significantly higher in smokers compared with non-smokers.	Although periodontal surgical interventions exhibit less favourable healing outcomes in smokers compared with non-smokers, the role of other confounding parameters needs to be considered.

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Author(s)	Synthesis	Number and type of studies	Search frame	Studies included	Aim	Surgery type	Pulmonary complications	Cardiovascular complications	Wound healing	Any complication	Other complications	Conclusions
Kanneganti et al., 2012(31)	Narrative	14	Inception to November 2011	Inclusion criteria included any English language clinical outcomes studies following ligamentous, meniscal or cartilage surgery of the knee with evidence levels I through IV according to the Oxford Centre for Evidence-Based Medicine.	To investigate the effects of smoking on ligament and cartilage knee surgery.	Knee surgery	DNR	DNR	DNR	DNR	All except one of the basic science and clinical studies exploring the relationship between smoking and knee ligaments found a negative association of smoking, either molecularly, biomechanically or clinically.	The current literature reveals a negative influence of smoking on the results of knee ligament surgery.
Kotsakis et al., 2015 (63)	Narrative and meta-analysis	8 CCTs	1977 – March 2014	Inclusion criteria: (1) original articles; (2) human controlled, clinical studies; (3) ≥10 participants; (4) ≥6 months of follow-up postintervention; (5) surgical interventions that included flap debridement surgery, modified Widman flap, and apically positioned flap procedures in smokers and non-smokers.	To assess the impact of cigarette smoking on clinical outcomes following periodontal flap surgical procedures.	Periodontal flap surgery	DNR	DNR	DNR	Reduction in probing depth is found to be highly significant in favour of non-smokers (P<0.001). Clinical attachment level gain was found in non-smokers vs. smokers (P<0.001).	None of the studies reported any adverse events associated with smoking status.	The magnitude of the therapeutic effect of periodontal flap surgical procedures is compromised in smokers compared with non-smokers.

Author(s)	Synthesis	Number and type of studies	Search frame	Studies included	Aim	Surgery type	Pulmonary complications	Cardiovascular complications	Wound healing	Any complication	Other complications	Conclusions
Lassig et al., 2012 (64)	Narrative	36 (RCTs; cohort studies; case series)	1990–2010	We included all articles evaluating the effects of smoking (current or former) on perioperative complications in head and neck oncological surgery.	To assess whether smoking increases postoperative wound healing and systemic complications in patients undergoing head and neck surgery.	Head and neck surgery	DNR	DNR	Overall, 47% of studies supported an association between smoking and complications of surgery.	DNR	DNR	Evidence from the existing clinical literature is inconclusive on an association between cigarette smoking and perioperative complications after head and neck surgery.
Mills et al., 2011(28)	Meta-analyses	15 (6 RCTs and 9 observational studies)	Inception to September 2009	Observational studies and randomized trials were included that evaluated the incidence of postoperative complications among populations who achieved smoking abstinence at a defined time point before surgery.	To determine the strength of evidence supporting the role of smoking cessation and the duration of cessation required in preventing postoperative complications.	All types of surgery	Former vs. current smokers: (RR: 0.81, 95% CI: 0.70–0.93, I2 = 7%; P < 0.003).	DNR	Former smokers vs. current smokers: (RR: 0.73, 95% CI: 0.61–0.87, I2 = 0%; P = 0.0006).	Findings from the 6 RCTs: RR: 0.59 (95% CI: 0.41–0.85, I2 = 14%, P = 0.01), 4 weeks cessation vs. > 4 weeks) decrease of 20% (RR: 0.80, 95% CI: 3–33, I2 = 68%, P = 0.02) Observational studies, former vs. current smokers: RR: 0.76, 95% CI: 0.69–0.84, I2 = 15%, P < 0.0001.	DNR	There is a reduction in complications among former smokers vs. current smokers. Longer-term cessation is associated with improved outcomes.

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Author(s)	Synthesis	Number and type of studies	Search frame	Studies included	Aim	Surgery type	Pulmonary complications	Cardiovascular complications	Wound healing	Any complication	Other complications	Conclusions
Molle and Villebro, 2005 (65)	Meta-analyses	4 RCTs	Inception to February 2005	Only RCTs examining the impact of preoperative intervention to help patients awaiting surgery quit smoking were included.	The objective of this review was to assess the effect of preoperative smoking cessation in the postoperative period and longer-term. We also set out to determine the effect of smoking cessation on the incidence of postoperative complications.	All types of surgery	DNR	Benefits of cessation: two studies examined cardiovascular complications. One found a significant reduction and the other did not.	Benefits of cessation: two studies examined wound healing. One found a significant reduction and the other did not.	Benefits of cessation: two studies examined total complications. One found a significant reduction and the other did not.	DNR	Preoperative smoking interventions are effective for changing smoking behaviour perioperatively. Direct evidence that reducing or stopping smoking reduces the risk of complications is based on two small trials with differing results.
Myers et al., 2011(29)	Meta-analyses	9 observational studies	Inception to May 2010	All 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.	To identify whether there was any evidence that stopping smoking within 8 weeks of surgery is associated with postoperative complications.	All types of surgery	Recent quitters vs. smokers: (RR:1.18, 95% CI: 0.95–1.46); I2 = 0, P = 0.13).	DNR	DNR	Recent quitters vs. smokers: (RR: 0.78, 95% CI: 0.57–1.07), I2 = 66.1, P = 0.13).	DNR	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.

Author(s)	Synthesis	Number and type of studies	Search frame	Studies included	Aim	Surgery type	Pulmonary complications	Cardiovascular complications	Wound healing	Any complication	Other complications	Conclusions
Nolan and Warner, 2015 (54)	Narrative	DNR	January 1990 – May 2015	Studies were selected for inclusion according to their relevance to the preclinical and clinical evidence pertaining to the way NRT affects surgical outcomes and long-term rates of abstinence from tobacco.	To discuss the current evidence for the efficacy and safety of NRT in patients scheduled for surgical procedures.	All types of surgery		No evidence that NRT increases risk of cardiovascular complications.	Smokers at increased risk for development of wound-related complications, including surgical site infections and wound dehiscence. No evidence that NRT increases risk of healing-related complications.	No effect or reduction in complication rates from use of NRT.	Abstinence from smoking reduces cardiovascular and healing-related risks. Smoking-related diseases and multiple pharmacological compounds in cigarette smoke, including nicotine, may contribute to risk.	Patients who smoke are at increased risk for perioperative complications, including healing-related and cardiovascular. Abstinence from smoking reduces these risks.
Pluvy et al., 2015a (38)	Meta-analysis	60 observational studies	1972 – July 2014	RCTs and observational studies reporting on the incidence of perioperative and postoperative complications secondary to tobacco consumption in the context of plastic surgery.	To develop concrete responses as well as assessment of the scientific level of evidence on the elevated risk of complications incurred in plastic surgery by active smokers in comparison with abstinent smokers and non-smokers.	Plastic surgery (cosmetic, bariatric, microsurgery, breast reconstruction)	DNR	DNR	Cosmetic: OR 2.5 [1.49–4.08] P < 0.001 for delayed wound healing. OR: 1.8 [1.04–3.09] P = 0.03 for wound dehiscence. Bariatric: combined OR of 3.3 [1.90–5.64] P < 0.001 with regard to delayed wound healing.	Cosmetic: combined OR: 3.6 [2.25–5.91] P < 0.001 for overall complications. Bariatric: combined OR: 1.9 [1.00–3.84] P = 0.04 for overall complications.	Cosmetic: OR: 7.3 (1.31–40.77), P = 0.02; with regard to cytosteatonecrosis, 2.3 (1.51–3.54), P < 0.001 for surgical site infections. Bariatric: OR: 3.1 (1.39–7.13) P = 0.006 for cutaneous necrosis. OR: 2.7 (0.70–10.76). P = 0.14 for surgical site infections.	Patients with smoking habit run significantly heightened risk of cutaneous necrosis, particularly in event of major detachment, additionally delayed wound healing and additional surgical site infections. Rigorous preoperative evaluation of smokers could help diminish risks.

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Author(s)	Synthesis	Number and type of studies	Search frame	Studies included	Aim	Surgery type	Pulmonary complications	Cardiovascular complications	Wound healing	Any complication	Other complications	Conclusions
Pluvy et al., 2015b (66)b	Narrative	39 included studies	1972 – 2014	The keywords were “wound healing”, “physiopathology”, “smoking cessation”, “nicotine replacement therapy”, “smoking”, “tobacco” and “nicotine”. RCTs and observational studies were retained for further examination. English and French language publications were included.	To provide an update on the negative impact of smoking, especially on wound healing, and also about the indisputable benefits of quitting.	All types of surgery	DNR	DNR	Hypoxia, tissue ischaemia and immune disorders induced by tobacco cause alterations in the healing process. Some effects are reversible by quitting.	DNR	DNR	Total smoking cessation of 4 weeks preoperatively and lasting until primary healing of operative site (2 weeks) appears to optimize surgical conditions without heightening anaesthetic risk. Tobacco withdrawal assistance, human and drug-based, is recommended.

Author(s)	Synthesis	Number and type of studies	Search frame	Studies included	Aim	Surgery type	Pulmonary complications	Cardiovascular complications	Wound healing	Any complication	Other complications	Conclusions
Reese et al., 2008 (33)	Meta-analyses	16 observational studies	1966 – 2007	Studies had to compare Crohn's disease patients treated with surgery who smoked versus those who had never smoked or were ex-smokers.	The aim of the study was to quantify the risk of disease recurrence associated with cigarette smoking for individuals with Crohn's disease after disease-modifying surgery.	Surgery for Crohn's disease	DNR	DNR	DNR	DNR	Clinical relapse: 58.3% of smokers vs. 39.0% of non-smokers (OR: 2.07, 95% CI: 1.25–3.44; I ² = 52.8; P < 0.005). Surgery in the follow-up period: 40.3% smokers vs. 36.3% non-smokers (OR: 1.35, 95% CI: 0.84–2.17, P = 0.21). Five-year reoperation rates: 34.2% smokers vs. 31.1% non-smokers (OR: 1.06, 95% CI: 0.32–3.53; P = 0.92). Ten-year reoperation rates: smokers 55.5% vs. non-smokers 32.1% (OR: 2.56, 95% CI: 1.79–3.67, P < 0.001).	Crohn's disease patients who continue to smoke after surgery suffer more clinical relapses and are more likely to require further surgery. Ex-smokers do not share these increased risks.

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Author(s)	Synthesis	Number and type of studies	Search frame	Studies included	Aim	Surgery type	Pulmonary complications	Cardiovascular complications	Wound healing	Any complication	Other complications	Conclusions
Santiago-Torres et al., 2015 (67)	Narrative	10 studies	PubMed (1950 – September 2013), CINAHL (1994 – September 2013), SPORTDiscus (1975 – September 2013), and Cochrane Library (1994 – September 2013)	English language clinical outcomes studies after ligamentous, tendinous or cartilaginous surgery of the shoulder with Oxford Centre for Evidence-Based Medicine evidence levels I through IV.	To determine whether smoking has a negative influence on tendinous, ligamentous and cartilaginous shoulder surgery.	Shoulder surgery	DNR	DNR	Nicotine was found to have a deleterious effect on healing and strength of repair in an animal rotator cuff (RTC) tear model.		Clinically, outcomes of RCR are likely to be worse when associated with smoking. Smoking was found to be associated with an increased rate of early failure of SLAP repairs but likely does not affect long-term outcomes.	Smoking has a negative influence on RCR clinical outcomes and is associated with decreased healing of small-medium rotator cuff tears after repair. Smoking cessation would benefit patients undergoing RCR and improve clinical outcomes. The relationship of smoking and labral/SLAP repair or articular cartilage is less clear.
Schmidt-Hansen et al., 2013(68)	Narrative	7 observational studies	Inception to September 2011	Any original study published in English and investigating the effect of preoperative smoking cessation or preoperative pulmonary rehabilitation on operative and longer-term outcomes in 50 or more patients who received surgery with curative intent for lung cancer.	The objectives of this systematic review were to determine the effectiveness of (1) preoperative smoking cessation and (2) preoperative pulmonary rehabilitation on peri- and postoperative outcomes in patients who undergo resection for lung cancer.	Curative surgery for lung cancer	DNR	DNR	DNR	DNR	Majority of studies reported higher risk in smokers compared with non-smokers however significant limitations were present in all included studies.	The results tentatively seem to suggest that preoperative smoking is associated with worse outcomes of lung cancer surgery than no preoperative smoking as the majority of the included studies have found that non-smokers have better outcomes than smokers of different categories.

Author(s)	Synthesis	Number and type of studies	Search frame	Studies included	Aim	Surgery type	Pulmonary complications	Cardiovascular complications	Wound healing	Any complication	Other complications	Conclusions
Sepehrpour et al., 2012 (69)	Narrative	5 cohort studies	Inception to December 2011	All study designs were included.	The question addressed was whether smoking cessation prior to cardiac surgery would result in a greater freedom from postoperative complications.	Cardiac surgery	The largest of the best-evidence studies demonstrated a significant reduction in pulmonary complications in non-smokers ($P < 0.001$).	DNR	DNR	DNR	There were non-significant reductions in neurological complications, infective complications and readmissions to intensive care.	There is convincing evidence presented that patients who are not active smokers at the time of cardiac surgery have improved outcomes postoperatively in comparison with smokers.
Singh, 2011 (32)	Meta-analyses	21 observational studies	Inception to March 2010	Studies were included if they were fully published reports that included smoking and any peri- or postoperative clinical outcome in patients with either TKA or THA. Studies were excluded if they were abstracts, reviews or editorials or did not provide clinical outcomes data.	The objective of this systematic review was to assess the association of smoking and postoperative outcomes following THA or TKA.	THA or TKA	DNR	DNR	DNR	Current vs. non-smokers: (RR: 1.24, [95% CI: 1.01–1.54]) Current vs. former smokers: (RR: 1.32 [95% CI: 1.05–1.66]).	DNR	This systematic review found that smoking is associated with significantly higher risk of postoperative complications and mortality following THA or TKA.

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Author(s)	Synthesis	Number and type of studies	Search frame	Studies included	Aim	Surgery type	Pulmonary complications	Cardiovascular complications	Wound healing	Any complication	Other complications	Conclusions
Sorensen 2012 (14)	Narrative	140, 4 RCTs	Inception to May 2010 for cohort, January 2011 for RCTs	Cohort studies with 100 patients or more assessing healing complications in smokers and former smokers were included. RCTs assessing the effect of perioperative smoking cessation on postoperative healing complications were included. Only RCTs with a minimum of 1 week of preoperative intervention and assessment of healing outcome after specified elective surgical procedures were included. RCTs with a dropout rate greater than 40% were excluded.	To clarify the evidence on smoking and postoperative healing complications across surgical specialties and to determine the impact of perioperative smoking cessation intervention.	All types of surgery	DNR	DNR	Smokers vs. non-smokers: healing delay: (adjusted OR: 2.07 [95% CI: 1.53- 2.81]) wound complications: (adjusted OR: 2.27 [95% CI: 1.82–2.84]) Smokers vs. former smokers: healing complications: adjusted OR: 1.31 [95% CI: 1.10–1.56]) Former vs. current smokers: adjusted OR: 0.28 [95% CI: 0.12–0.72]) Evidence from RCTs: healing complications OR: 0.48 [95% CI: 0.19-1.25).	DNR	Smokers vs. non-smokers, Necrosis: adjusted OR: 3.60 [95% CI: 2.62-4.93]) Surgical site infection: OR: 1.79 (95% CI: 1.57-2.04) Evidence from RCT: surgical site infection: OR: 0.40 (95% CI: 0.20–0.83).	Smokers have a higher incidence of infectious and non-infectious healing complications after surgery compared with non-smokers across all surgical specialties. Former smokers appear to have a lifetime higher risk of healing complications compared with patients who never smoked.

Author(s)	Synthesis	Number and type of studies	Search frame	Studies included	Aim	Surgery type	Pulmonary complications	Cardiovascular complications	Wound healing	Any complication	Other complications	Conclusions
Teng et al., 2015 (37)	Meta-analysis	6 cohort studies	Inception – August 2013	Studies that: (1) used a cohort study design; (2) evaluated the association between smoking and the risk of any prosthesis-related complication after THA; and (3) provided sufficient data for calculating the risk ratio or weighted mean difference with a 95% CI.	To quantitatively evaluate the association between smoking and the risk of prosthesis-related complications after THA.	THA	DNR	DNR	DNR	DNR	Compared with the patients who never smoked, smokers had significantly increased risk of aseptic loosening of prosthesis (summary RR = 3.05, 95% CI: 1.42–6.58), deep infection (summary RR: 3.71, 95% CI: 1.86–7.41) and all-cause revisions (summary RR: 2.58, 95% CI: 1.27–5.22). No significant difference in risk of implant dislocation or length of hospital stay (WMD = 0.03, 95% CI: 0.65–0.72).	Smoking is associated with significantly increased risk of aseptic loosening of prosthesis, deep infection and all-cause revisions after THA.
Theadom and Cropley, 2006 (51)	Narrative	12 prospective cohort designs	Inception to 2005	Prospective cohort designs exploring the effects of preoperative smoking cessation on postoperative complications were included.	To establish the effect of preoperative smoking cessation on the risk of postoperative complications, and to identify the effect of the timing of preoperative cessation.	All types of surgery	Two out of the four studies identified significant associations with increased pulmonary complications.	DNR	DNR	Five of the nine studies stated that current smokers had a significantly higher risk of overall complications than non-smokers.	One study examined wound infection and found a significant association.	Longer periods of smoking cessation appear to be more effective in reducing the incidence/risk of postoperative complications; there was no increased risk in postoperative complications from short-term cessation.

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Author(s)	Synthesis	Number and type of studies	Search frame	Studies included	Aim	Surgery type	Pulmonary complications	Cardiovascular complications	Wound healing	Any complication	Other complications	Conclusions
Thomsen et al., 2009 (70)	Meta-analyses	11 RCTs	NS	Only RCTs were included. All trials described smokers scheduled for elective surgery. Smoking interventions were administered before surgery in the hospital or primary care setting.	The aim of this study was to examine the effect of preoperative smoking cessation interventions on postoperative complications and smoking cessation itself.	All types of surgery	DNR	DNR	DNR	RR: 0.56 (95% CI: 0.41–0.78); I2 = 15%; P < 0.001).	DNR	The results of this systematic review indicate that patients scheduled to undergo surgery can benefit from intensive preoperative smoking cessation interventions.
Thomsen et al., 2014 (39)	Meta-analyses	13 RCTs	Up to January 2014	RCTs that recruited people who smoked prior to surgery, offered a smoking cessation intervention, and measured preoperative and long-term abstinence from smoking or the incidence of postoperative complications or both outcomes.	To assess the effect of preoperative smoking intervention on smoking cessation at time of surgery and 12 months postoperatively and on incidence of postoperative complications.	All types of surgery	No studies detected significant differences between groups in regard to postoperative pulmonary or cardiovascular complications.	No studies detected significant differences between groups in regard to postoperative pulmonary or cardiovascular complications.	Intensive interventions: RR: 0.31, 95%CI: 0.16–0.62 (210 participants). Brief interventions: RR: 0.99, 95% CI: 0.70–1.40 (325 participants).	Intensive interventions: (RR: 0.42, 95% CI: 0.27–0.65, I2 = 0%, P = 0.54). Brief interventions: RR: 0.92, 95% CI: 0.72–1.19, I2 = 0%, P < 0.0001).	DNR	Intensive interventions initiated at least four weeks before surgery and including multiple contacts for behavioural support and the offer of pharmacotherapy are beneficial for changing smoking behaviour perioperatively and in the long term, and for reducing the incidence of complications.

Author(s)	Synthesis	Number and type of studies	Search frame	Studies included	Aim	Surgery type	Pulmonary complications	Cardiovascular complications	Wound healing	Any complication	Other complications	Conclusions
Tonnesen et al., 2009 (19)	Narrative	6 RCTs	DNS	All study designs but only findings from RCTs were reported.	Examined impact of both alcohol and smoking on cessation and mortality.	All types of surgery	DNR	DNR	Two RCTs reported a reduction in total complications for interventions 3–4 weeks and 6–8 weeks in length.	Two RCTs reported a reduction in total complications for interventions 3–4 weeks and 6–8 weeks in length.	DNR	Abstinence starting 3–8 weeks before surgery will significantly reduce the incidence of several serious postoperative complications, such as wound and cardio-pulmonary complications and infections. However, this intervention must be intensive to obtain sufficient effect on surgical complications.
Vieira Vavichio et al., 2014 (21)	Narrative	12 (1 meta-analysis; 3 systematic reviews; 3 experimental; 3 non-experimental; 2 narrative reviews)	Inception – Sep 2012	The inclusion criteria were: studies involving human beings aged 18 years old or older and articles published in Portuguese, English and Spanish.	To find scientific evidence about the duration of preoperative smoking cessation required to reduce surgical wound healing complications.	All types of surgery	Smoking cessation restored tissue oxygenation and metabolism. Within four weeks, cellular inflammatory response was partly reversed, whereas proliferative response remained impaired; nicotine did not affect the tissue, but appeared to impair inflammation and stimulate proliferation.	DNR	Ten studies showed smoking cessation for a minimum of four weeks is beneficial. One study concluded smoking cessation for period < 3 weeks was a risk factor. Another study showed duration of preoperative smoking abstinence to prevent or reduce healing complications remains unknown.	Smoking cessation for short period (< 4 weeks) compared with > 4 weeks resulted in 20% reduction in relative risk of total complications (RR: 0.80, 95% CI: 3-3, P = 0.02); each additional week of smoking cessation generated a significant impact on postoperative complications.	Vitamin C lower in smokers than in those never smoked (average 54.13 and 110.6, respectively, P < 0.010); four-week cigarette abstinence needed to restore levels of vitamin C and collagen, improving inflammatory cell response. Significant increase in vitamin C after smoking cessation ($\beta = 2.23 \pm 0.86$, P = 0.01).	The period required for preoperative smoking cessation was at least 4 weeks for restoration of oxygen levels in tissues, decreased oxidative stress, reduction of negative impact on function of macrophages and increased levels of vitamin C and collagen.

TOBACCO & POSTSURGICAL OUTCOMES

Author(s)	Synthesis	Number and type of studies	Search frame	Studies included	Aim	Surgery type	Pulmonary complications	Cardiovascular complications	Wound healing	Any complication	Other complications	Conclusions
Willigendael et al., 2005 (34)	Narrative	29 (4 randomized RCTs, 12 prospective studies, and 13 retrospective studies)	From 1950-2004	Studies considered for inclusion were those that evaluated the influence of smoking on the primary, secondary or cumulative patency rates of arterial reconstructive surgery in the lower extremities in patients with PAD.	To establish the best estimate of the effect of smoking, smoking cessation and the dose-response relationship on the patency of lower extremity bypass grafts.	Arterial reconstructive surgery in the lower extremities in patients with PAD.	DNR	DNR	DNR	DNR	Graft patency failure: OR: 3.09 (95% CI: 2.34–4.08; I2 = 37%, P<0.0001).	Continued smoking after lower limb bypass surgery results in a threefold increased risk of graft failure. Smoking cessation, even if instigated after the operation, restored graft patency to nearer the patency of never-smokers.
Wong et al., 2012 (27)	Meta-analyses	25 (7 prospective, 16 retrospective and 2 RCTs)	Inception to January 2011	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.	To examine the risks or benefits of short-term (less than 4 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.	All types of surgery	There were no differences in risks for cardiovascular complications among current smokers, ex-smokers (1–8 weeks' abstinence), and non-smokers. No meta-analysis performed.	Smokers vs. non-smokers: RR: 2.11, 95% CI: 1.51–2.94; I2 = 61%; P < 0.0001). Cessation 2-4 weeks vs. non-smokers: RR: 2.51 (95% CI: 1.85–3.39; I2 = 52%; P = 0.0005) Cessation > 4 weeks vs. non-smoker: RR= 0.77 (95% CI: 0.61–0.96; I2 = 64%; P = 0.02) Cessation > 8 weeks vs. non-smokers: RR: 0.53 (95% CI: 0.37–0.76; I2 = 52%; P = 0.0005).	Smokers vs. non-smokers (RR: 2.08, 95% CI: 1.60–2.71; I2 = 8%; P < 0.00001). Cessation 3 - 4 weeks vs. non-smokers: RR: 1.22, 95% CI: 0.56–2.67, I2 = 86%; P = 0.61). Cessation > 4 weeks vs. non-smoker: RR: 0.69, 95% CI: 0.56–0.84; I2 = 0%; P = 0.0003).	DNR	In conclusion, at least 4 weeks of preoperative smoking cessation is necessary to reduce respiratory complications, and at least 3–4 weeks of abstinence is needed to reduce wound-healing complications.	

Author(s)	Synthesis	Number and type of studies	Search frame	Studies included	Aim	Surgery type	Pulmonary complications	Cardiovascular complications	Wound healing	Any complication	Other complications	Conclusions
Xing et al., 2013 (15)	Narrative	36 cohort studies	Inception to June 2011	Observational studies	To identify the independent risk factors, based on available evidence in the literature, for patients developing SSI after spinal surgery.	Spinal surgery	DNR	DNR	DNR	DNR	There were 46 potential independent risk factors that were identified by more than one study and were included in the final analysis. Six were identified as strong evidence factors, including obesity/BMI, longer operation times, diabetes, smoking, history of previous SSI and type of surgical procedure.	Although the available observations form a heterogeneous group, and there is no conclusive evidence, we have identified six strong evidence risk factors including obesity/BMI, longer operation times, diabetes, smoking, history of previous SSI and type of surgical procedure.

* BMI: body mass index; CCT: controlled clinical trial; DNR: did not report; ETS: environmental tobacco smoke; NRT: nicotine replacement therapy; OR: odds ratio; PAD: peripheral arterial disease; RCR: rotator cuff repair; RCT: randomized controlled trial; RR: relative risk; SLAP: superior labral anterior to posterior; SSI: surgical site infection; THA: total hip arthroplasty; TKA: total knee arthroplasty; WMD: weighted mean difference.

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