November 2019

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).

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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 online for description of all reviews included). 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 online for table of findings). A 2014 review (26) of 107 observational studies

found a positive association between preoperative smoking status and 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

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.

N.B. Reference List and all articles included in the literature review (Annex 1) available at www.who.int/tobacco.

www.who.int/tobacco

Suggested citation: Yoong SL[1], Tursan d'Espaignet E[1,2], Wiggers J[1], St Claire[2], S Mellin-Olsen J[3], Grady A[1], Hodder R[1], Williams C[1], Fayokun R[2] and Wolfenden L[1] (2019). WHO tobacco knowledge summaries: tobacco and postsurgical outcomes. Geneva: World Health Organization.

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Editorial assistance: Teresa Lander

Design by: Denis Meissner, WHO Graphics
Printed by: WHO Document Production Services, Geneva, Switzerland

WHO/NMH/PND/2019.10