# Effect of preoperative smoking cessation interventions on postoperative complications and smoking cessation

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**Background:** The aim of this study was to examine the effect of preoperative smoking cessation interventions on postoperative complications and smoking cessation itself.

Methods: Relevant databases were searched for randomized controlled trials (RCTs) of preoperative smoking cessation interventions. Trial inclusion, risk of bias assessment and data extraction were performed by two authors. Risk ratios for the above outcomes were calculated and pooled effects estimated using the fixed-effect method.

**Results:** Eleven RCTs were included containing 1194 patients. Smoking interventions were intensive, medium intensity and less intensive. Follow-up for postoperative complications was 30 days. For smoking cessation it was from the day of surgery to 12 months thereafter. Overall, the interventions significantly reduced the occurrence of complications (pooled risk ratio 0.56 (95 per cent confidence interval 0.41 to 0.78); P < 0.001). Intensive interventions increased smoking cessation rates both before operation and up to 12 months thereafter. The effects of medium to less intensive interventions were not significant. Meta-analysis of the effect on smoking cessation was not done owing to heterogeneity of data.

**Conclusion:** Surgical patients may benefit from intensive preoperative smoking cessation interventions. These include individual counselling initiated at least 4 weeks before operation and nicotine replacement therapy.

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### Introduction

Smokers are at greater risk than non-smokers of postoperative wound healing complications, as well as postoperative pulmonary and cardiovascular complications<sup>1–3</sup>. Postoperative complications cause suffering and are costly for society<sup>4,5</sup>. Added to this, the long-term health hazards of smoking include cancer, respiratory and cardiovascular morbidity, reduced health-related quality of life, and premature death<sup>6,7</sup>.

Two clinical studies have reported that cessation of smoking more than 3 weeks before operation reduced the occurrence of wound healing complications in relation to head and neck and breast reduction surgery<sup>8,9</sup>. Similarly, an experimental trial has reported that 4 weeks of abstinence from smoking reduced the frequency of wound infections in healthy smokers to the frequency in healthy non-smokers<sup>10</sup>. The minimum duration of

abstinence necessary to confer benefit is unknown<sup>11</sup>. Hypothetically, cessation less than 3–4 weeks before surgery may benefit postoperative recovery. This being the case, preoperative intervention to encourage cessation of smoking even a few days before surgery might benefit many patients for whom the time from diagnosis to operation is short. Interventions for cessation of smoking before surgery appear relevant for postoperative risk reduction<sup>12,13</sup>. Abstinence from smoking in relation to surgery might further motivate long-term cessation. Preoperative smoking cessation interventions administered within the healthcare setting may, therefore, improve not only postoperative recovery but also long-term health.

The aim of this literature review was to answer the following questions. First, how does preoperative smoking cessation affect the occurrence of postoperative complications? Second, how does it affect short- and long-term cessation of smoking?

## **Methods**

## Search strategy

The databases PubMed, The Cochrane Library, Embase and CINAHL were searched using the following search strategy. For participants: tobacco use disorder OR smoking. For intervention: smoking cessation OR tobacco use cessation OR preoperative smoking cessation OR preoperative tobacco use cessation OR preoperative smoking intervention OR preoperative smoking cessation intervention OR smoking intervention OR smoking cessation intervention OR preoperative smoking cessation counselling OR smoking cessation counselling OR patient education OR preoperative patient education OR preoperative care OR preoperative preventive care OR health promotion programmes OR preoperative health promotion programmes. For outcomes: postoperative complication OR intraoperative complication OR postoperative pulmonary complication OR postoperative cardiovascular complication OR surgical procedures, operative OR wound healing OR wound healing complication OR postoperative morbidity OR surgery OR operation. For types of studies: controlled trial\* OR clinical trial\* OR randomized controlled trial OR randomized clinical trial OR review OR meta-analysis (\* these terms were included to broaden the search and ensure retrieval of as many potentially relevant studies as possible). The study was limited to patients aged 18 years or more. Language limits and date limits were not applied.

## Criteria for considering studies for this review

Only randomized controlled trials (RCTs) were included. All trials described smokers scheduled for elective surgery. Smoking interventions were administered before surgery in the hospital or primary-care setting. Interventions could include the five As (ask, advise, assess, assist, arrange), behavioural counselling tailored to stage of change, motivational interviewing or other methods of counselling (person to person, in groups, by telephone or via computer), all of these with or without pharmacotherapy and postoperative counselling. The intervention could also be pharmacotherapy *versus* placebo without behavioural counselling. Control interventions could include usual care or standardized brief advice with or without nicotine replacement therapy (NRT).

Outcome measures for postoperative complications were defined as wound healing complications, respiratory,

cardiovascular and urological complications, and other complications requiring treatment. Outcome measures for preoperative and postoperative smoking cessation were defined as either point prevalence or continuous abstinence.

Search results were scanned by the first author (T.T.) and obviously irrelevant studies removed. The remaining results were evaluated by two authors (T.T. and A.M.M.) according to the inclusion criteria. When in doubt, a third reviewer (H.T.) was called upon to assess and discuss relevance and potential inclusion. Furthermore, reference lists in studies retrieved through the search were checked for relevant studies. Included trials were evaluated according to The Cochrane Collaboration's tool for assessing risk of bias<sup>14</sup>.

### Extraction and analysis of data

The following data was extracted from each of the included studies: eligibility and exclusion criteria, study design, duration and degree of follow-up, sequence generation, allocation sequence concealment, blinding, number and characteristics of participants, types of preoperative smoking cessation and control interventions, number of patients with postoperative complications, length of hospital stay, number of patients not smoking before and after surgery, and biochemical validation of smoking cessation. The strictest criteria available were used for cessation of smoking, for example continuous abstinence rather than point prevalence. Data were initially extracted from each trial by T.T. and subsequently verified for consistency and accuracy by A.M.M.

Review Manager (RevMan) version 5.0 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark) was used for data analysis. Mantel–Haenszel methods were used to calculate risk ratios (RRs) and corresponding 95 per cent confidence intervals (c.i.). RRs were calculated using available-case analysis<sup>14</sup>.

The fixed-effect method was used to estimate pooled treatment effects. Heterogeneity among studies was calculated using the  $I^2$  statistic, which describes the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance).  $I^2$  values between 0 and 40 per cent were not considered important<sup>14</sup>. Meta-analyses were not considered appropriate if  $I^2$  values exceeded 40 per cent<sup>14</sup>.

The following strategies were used to assess the potential impact of missing data. First, missing participants were imputed as 'failures', excluding those who did not undergo surgery, and the number of patients initially randomized into each group was used as the denominator<sup>14</sup>. For

the complications outcome, missing participants were imputed as having had a postoperative complication requiring treatment. For the smoking cessation outcome, missing participants were imputed as continuing smokers. Second, sensitivity analyses were conducted excluding trials with more than 20 per cent dropout. Sensitivity analyses excluding trials that did not biochemically validate selfreported smoking cessation were conducted to explore any potential impact on overall effects. No subgroup analyses were planned. Assessment of reporting bias was planned using funnel plots<sup>14</sup>.

#### **Results**

The search yielded a total of 815 citations. Twenty potentially eligible studies were identified after reviewing the title, abstract and/or full text of the 815 citations. Six additional, potentially eligible studies were found from reference lists in studies retrieved through the search<sup>15–20</sup>, and three studies were obtained through personal communication<sup>21–23</sup>. Of the 29 potentially eligible studies, 18 were excluded in accordance with the inclusion criteria<sup>10,16–20,24–35</sup> (*Fig. 1*). Eleven RCTs involving initial recruitment of 1194 patients were included (*Table 1*). Azodi

and co-workers<sup>21</sup> reported smoking cessation data and Lindström and colleagues<sup>22</sup> postoperative morbidity data originating from the same trial; Villebro *et al.*<sup>23</sup> and Møller and co-workers<sup>37</sup> did the same.

## Characteristics of included studies

Six studies originated from Scandinavia, two from Australia, and the remaining three trials were from the UK, Canada and the USA. The studies were published from 2002 to 2008. Daily smokers, aged 18 years and above, with relevant language proficiency, and who were not pregnant were eligible for inclusion in the studies. To be eligible for a study on bupropion, patients had to want to stop smoking and not suffer from a range of prespecified co-morbidities; women were tested for pregnancy and asked to maintain contraception for the entire study period<sup>36</sup>. Exclusion criteria for the studies were excessive alcohol consumption, drug abuse, severe mental illness and dementia. Sørensen and Jørgensen<sup>39</sup> in addition excluded patients with inflammatory bowel disease from a trial of patients undergoing open colonic surgery. Definitions of daily smoking were: daily smoking with no further specifications; consumption of at least one or two

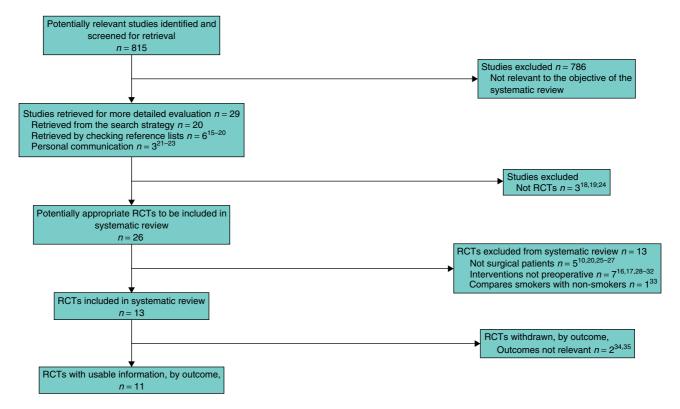


Fig. 1 Flow chart of systematic search. RCT, randomized controlled trial

Table 1 Overview of	fincluded	studies
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Reference	No. of patients	Types of surgery	Baseline smoking data	Type and duration of preoperative smoking cessation intervention	Dropout (%)
15	102	Elective surgery, not further specified	No data	One letter sent to patients 4 weeks before surgery	1
21	117(data from same trial as reference 22)	Hernia, laparoscopic cholecystectomy, hip/knee alloplasty	FTQ, cigarettes per day, years of smoking, CO, living with a smoker, previous smoking cessation, Swedish smokeless tobacco	Weekly counselling for 4 weeks before surgery + NRT + number to quit line	16
22	117 (data from same trial as reference 21)	Hernia, laparoscopic cholecystectomy, hip/knee alloplasty	Cigarettes per day, years of smoking, CO	See reference 21	13
36	47 (only 20 patients were operated)	General, orthopaedic, urological, ear, nose, throat, faciomaxillary	Years smoked, cigarettes per day, smokers in household, cigar/pipe, no. of previous attempts at cessation, FTNDS, CO, pulse oximetry	Bupropion 7 weeks before expected surgery + written and oral information + one telephone counselling	49
37	120 (data from same trial as reference 23)	Hip/knee alloplasty	Cigarettes per day, pack-years	Weekly counselling for 6–8 weeks before surgery + NRT	10
38	237	Cardiovascular, ophthalmology, plastics, urology	Stage of change, age of initiation, cigarettes per day, FTNDS, years since initiation	Counselling for 15 min 1–3 weeks before surgery + NRT	29
39	60	Open colonic or rectal surgery with formation of enteric anastomosis	Daily smoking, FTNDS, cotinine, CO, LASA score	Access to counselling for 2–3 weeks before surgery + NRT	5
40	180 (consecutive non-advised cohort not included)	Open incisional or inguinal day-case herniotomy	Smoking (g/day), CO, cotinine, FTNDS, LASA score	Telephone counselling for 10 min or 20 min counselling in outpatient clinic 1 month before surgery + NRT	17
23	120 (data from same trial as reference 37)	Hip/knee alloplasty	Cigarettes per day, FTNDS	See reference 37	16
41	121	Orthopaedic, intra-abdominal, spinal, genitourinary, otorhinolaryngological, gynaecological, other	Cigarettes per day, FTNDS, hours since last cigarette, CO, no. of previous cessation attempts, time since most recent attempt, duration of last cessation attempt, received encouragement to stop smoking at hospital, stage of change	Nicotine patch applied on day of surgery	4
42	210	Non-cardiac elective surgery for nervous, ear, nose, throat, digestive, hepatobiliary, pancreas, musculoskeletal, connective tissue, skin, subcutaneous tissue, breast, gynaecological systems	Stage of change, Heaviness of Smoking Index, previous attempts at quitting	Counselling 1–2 weeks before surgery in person + via computer and telephone + NRT for dependent smokers	14

FTQ, Fagerström's Tolerance Questionnaire, CO, end-expired carbon monoxide (parts per million), NRT, nicotine replacement therapy; FTNDS, Fagerström's Test for Nicotine Dependency Score; LASA score, linear analogue self-assessment scale.

cigarettes per day during the past week, with an average consumption of ten or more during the past 30 days; and consumption of at least ten cigarettes per day.

Sample sizes ranged from 47 to 237 patients, with a mean of 133 (*Table 1*). Three trials recruited substantially fewer patients than planned according to the pretrial power

calculation<sup>21,22,39</sup>. Azodi and co-workers<sup>21</sup> and Lindström and colleagues<sup>22</sup> recruited 117 patients compared with a planned sample of 600. Sørensen and Jørgensen<sup>39</sup> recruited 60 patients compared with a planned sample of 300. Myles *et al.*<sup>36</sup>, who did not report a pretrial power analysis, also experienced slow accrual and so amended the primary outcome in the original study protocol from smoking cessation rates to daily cigarette consumption at hospital admission. The percentage of randomized patients *versus* eligible, non-randomized patients ranged from 10 to 91 per cent. Two studies did not report the number of randomized patients *versus* non-randomized eligible patients or the number of eligible patients who declined participation<sup>15,36</sup>. Intention-to-treat analysis was performed in all studies<sup>14</sup>. All trials performed available-case analysis<sup>14</sup>. Dropout rates ranged from 1 to 49 per cent (*Table 1*). Two trials had dropout rates exceeding 20 per cent<sup>36,38</sup>.

Patients were scheduled for operations spanning a variety of surgical specialties (Table 1). The pathologies requiring surgery and their severity were generally not described in detail. Patients were recruited between 1 and 14 weeks before operation. Mean ages ranged from 40 to 50 years<sup>36,38,41,42</sup> and median ages from 54 to 68 years<sup>21-23,37,39,40</sup>. A variety of baseline smoking data and other patient-related data were assessed in all but one study<sup>15</sup> (Table 1). Mean daily cigarette consumption ranged from 12 to 23<sup>38,41</sup> and median consumption from 15 to 17<sup>21,22,37,39,40</sup>. Overall, patients were similar across the intervention and control groups in terms of baseline smoking. Other patient-related factors and co-morbidity were similar across the groups, with three exceptions. In the trials by Azodi and co-workers<sup>21</sup> and Lindström and colleagues<sup>22</sup>, slightly more intervention group patients had co-morbidities. In the trial by Warner et al.<sup>41</sup>, patients in the intervention group were older and less likely to have a history of lung disease.

Preoperative smoking cessation interventions differed across the studies (Table 1). In four studies, the interventions were intensive<sup>21–23,37</sup>. Patients were offered weekly, individual behavioural counselling 4-8 weeks before surgery with professionally trained smoking cessation counsellors; NRT was tailored to nicotine dependency. Sørensen and Jørgensen<sup>39</sup> tested a mediumintensity intervention that gave patients access to counselling 2-3 weeks before surgery, also in combination with NRT. The remaining studies tested less intensive interventions that included brief counselling sessions (face to face, via computer and letter) with or without pharmacotherapy, or pharmacotherapy with no counselling<sup>15,36,38,40-42</sup>. The interventions are described in Table 1. Four studies offered patients postoperative smoking cessation support until discharge or up to 4 months after operation  $^{21,22,38,39}$ . Smoking cessation was encouraged from between 8 weeks to 24 h before surgery, and from between 10 and 30 days after operation. One study strongly encouraged smoking cessation but also gave patients the option to reduce

tobacco consumption by at least 50 per cent<sup>37</sup>. Ratner and colleagues<sup>38</sup> encouraged patients to remain permanently abstinent.

Control interventions differed. In the pharmacotherapy studies, patients received placebo drugs together with preoperative smoking cessation interventions identical to those received by the intervention groups<sup>36,41</sup>. Otherwise, control interventions included neutral information<sup>21–23,37</sup>, standard care with inconsistent and uncoordinated smoking cessation advice<sup>38</sup>, and standard advice about the risks of smoking in connection with surgery and anaesthesia<sup>15,40</sup>. In the study by Wolfenden and co-workers<sup>42</sup>, clinic staff had the option to provide advice on quitting and to prescribe NRT to control group patients. One study specifically asked control patients to maintain daily smoking habits<sup>39</sup>.

Five studies monitored the frequency of postoperative complications (*Table 2*)<sup>22,36,37,39,40</sup>. Definitions of postoperative complications varied between studies. Complications were monitored on the day of skin suture removal or 30 days after surgery. Warner and colleagues<sup>41</sup> recorded serious postoperative adverse events, but without predefining these as an outcome.

Most studies reported smoking cessation as selfreported continuous abstinence; two used self-reported point prevalence (Table 3). One study did not distinguish between smoking cessation and smoking reduction<sup>39</sup>. Eight studies validated self-reported smoking cessation with measurements of carbon monoxide in expiratory air and/or cotinine in urine/saliva (Table 3). Carbon monoxide levels of 10 parts per million or less were considered indicative of smoking cessation<sup>21,22,36,38</sup>. Four trials did not define cut-off points for smoking cessation<sup>23,37,39,40</sup>. Cessation of smoking was assessed before operation, and 1, 3, 6 and 12 months after surgery. Definitions of preoperative abstinence varied considerably. Four studies defined preoperative cessation as abstinence for a minimum of 1 month before surgery 23,36,37,40, two studies as abstinence for at least 1 week before surgery<sup>21,22</sup>, and one study as being abstinent on the day of surgery<sup>15</sup>.

## Assessment of risk of bias

The studies were assessed to be at low risk of bias overall (*Table 4*). Generation of sequence allocation and allocation concealment was adequate in all studies. Blinding of participants, personnel and outcome assessors was considered adequate for trials examining the effect of pharmacotherapy *versus* placebo if blinding of participants, key study personnel and outcome assessors was ensured, and it was unlikely that the blinding could have been broken. For trials examining the effect of behavioural

Reference	Intensity of preoperative smoking intervention	Definition of postoperative complication	Risk ratio for postoperative complications
Lindström <i>et al.</i> <sup>22</sup>	Intensive	Events causing additional medical or surgical treatment or investigation, prolonged hospital stay, unscheduled postoperative check-ups within 30 days Any wound complication	0.51 (0.27, 0.97) 0.48 (0.20, 1.16)
Møller et al. <sup>37</sup>	Intensive	Death or postoperative morbidity requiring treatment within 30 days Wound-related complications	0.34 (0.19, 0.64) 0.17 (0.05, 0.56)
Sørensen and Jørgensen <sup>39</sup>	Medium intensive	Adverse events within 30 days needing medical or surgical intervention	0.94 (0.51, 1.73)
Sørensen <i>et al</i> . <sup>40</sup>	Less intensive	Postoperative wound infection with swollen, red, hot, painful wound with or without pus discharge and surgical or medical intervention evaluated at skin suture removal	0.71 (0.21, 2.41)
Myles <i>et al</i> . <sup>36</sup>	Less intensive	Postoperative wound infections	0.82 (0.06, 11.33)
Warner et al. <sup>41</sup>	Less intensive	Serious postoperative adverse events	0.86 (0.24, 3.03)

#### Table 2 Effects of the preoperative smoking cessation interventions on postoperative complications

Values in parentheses are 95 per cent confidence intervals.

			terventions		

Reference	Intensity of preoperative smoking intervention	Definition of smoking cessation	Biochemical validation of smoking cessation	Follow-up	Risk ratio for smoking cessation
Azodi <i>et al.</i> <sup>21</sup>	Intensive	Continuous abstinence	со	Preop.1 month postop.12 months postop.	31.50 (4.45, 222.82) 31.50 (4.45, 222.82) 2.05 (1.01, 4.14)
Lindström et al.22	Intensive	As in reference 21	As in reference 21	As in reference 21	As in reference 21
Møller et al. <sup>37</sup>	Intensive	Continuous abstinence	CO	Preop.	8.36 (3.19, 21.86)
Villebro <i>et al</i> . <sup>23</sup>	Intensive	Continuous abstinence	СО	Preop.1 month postop.12 months postop	As in reference 37. 5.89 (1.88, 18.44) 5.22 (1.24, 21.96)
Sørensen and Jørgensen <sup>39</sup>	Medium intensity	Abstaining or reduction by more than half of daily smoking	CO + cotinine	Day before surgery At skin suture removal	Smoking cessation and smoking reduction assessed in combination
Andrews et al. <sup>15</sup>	Less intensive	Point prevalence	No validation	Preop.	2.21 (1.06, 4.60)
Myles et al. <sup>36</sup>	Less intensive	Continuous abstinence	СО	Preop.	0.82 (0.06, 11.33)
Ratner <i>et al</i> . <sup>38</sup>	Less intensive	Continuous abstinence	CO + cotinine	Preop.6 months postop.12 months postop.	1.38 (1.12, 1.69) 1.54 (0.96, 2.50) 1.04 (0.63, 1.71)
Sørensen <i>et al.</i> <sup>40</sup>	Less intensive	Continuous abstinence	CO + cotinine	Preop.3 months postop.	1.82 (0.79, 4.18) 1.54 (0.53, 4.49)
Warner <i>et al</i> . <sup>41</sup>	Less intensive	Continuous abstinence	No validation	1 month postop.6 months postop.	1.14 (0.63, 2.09) 0.60 (0.21, 1.67)
Wolfenden <i>et al</i> . <sup>42</sup>	Less intensive	Point prevalence	No validation	Preop.3 months postop.	1.29 (1.09, 1.53) 1.64 (0.83, 3.25)

Values in parentheses are 95 per cent confidence intervals. CO, carbon monoxide in expiratory air; preop., preoperative; postop., postoperative.

counselling, participants could not be blinded, and complete blinding of personnel was considered difficult to uphold. In these studies, blinding was considered adequate if outcome assessment was blinded. Blinding was therefore assessed as adequate in seven of 11 trials. Four trials did not describe whether assessors of self-reported smoking data were blinded, resulting in assessment of blinding as unclear<sup>15,21,23,40</sup>. In the study by Sørensen and colleagues<sup>40</sup> postoperative complications were initially assessed by a study nurse before further referral for blinded assessment.

Incomplete outcome data were addressed adequately in all but two studies<sup>36,40</sup>. The dropout rate in one of these was

 Table 4 Risk of bias assessment of included studies

Reference	Adequate sequence generation	Allocation concealment	Blinding	Incomplete outcome data addressed	Free from selective reporting	Free from other bias
Andrews et al. <sup>15</sup>	+	+	?	+	+	+
Azodi <i>et al</i> . <sup>21</sup>	+	+	?	+	+	+
Lindström et al. <sup>22</sup>	+	+	+	+	+	+
Myles et al. <sup>36</sup>	+	+	+	-	+	+
Møller et al.37	+	+	+	+	+	+
Ratner et al.38	+	+	+	+	+	+
Sørensen and Jørgensen <sup>39</sup>	+	+	+	+	+	+
Sørensen <i>et al</i> . <sup>40</sup>	+	+	?	?	+	+
Villebro et al.23	+	+	?	+	+	+
Warner <i>et al</i> . <sup>41</sup>	+	+	+	+	+	+
Wolfenden et al.42	+	+	+	+	+	+

+, Low risk of bias; -, high risk of bias; ?, risk of bias unclear.

49 per cent and this could have induced clinically relevant bias in the observed effect size<sup>36</sup>. The other study did not specify reasons for dropout according to interventions and so it was unclear whether dropout from this study represented a risk of bias<sup>40</sup>. All studies were assessed to be at low risk of selective outcome reporting and other biases.

#### **Postoperative complications**

Two studies reported significant reductions in postoperative complications in the intervention *versus* the control groups<sup>22,37</sup> (*Table 2*). Lindström and co-workers<sup>22</sup> found that the number of patients with any postoperative complication was halved in the intervention group; the difference between intervention and control groups in frequencies of any wound complication was not significant (*Table 2*). Møller *et al.*<sup>37</sup> found that both the number of patients with any postoperative complication, and the number of patients with wound-related complications, was more than halved in the intervention group (*Table 2*). Preoperative smoking interventions were intensive in both studies. Lindström and colleagues<sup>22</sup> also offered 4 weeks of postoperative counselling. Control interventions included neutral information.

The four remaining studies that assessed postoperative complications found non-significant differences in the number of patients with such complications between groups  $(Table 2)^{36,39,40,41}$ . Preoperative smoking interventions in these studies were medium to less intensive. Control interventions included maintenance of daily smoking, standard advice, placebo and counselling identical to that received in the intervention group, and placebo with no counselling.

Length of hospital stay was reported in four studies. This did not differ significantly between intervention and control groups<sup>22,36,37,39</sup>. Median length of hospital stay for

intervention groups ranged from 1 to 11 days and that for control groups from 1 to 13 days<sup>22,36,37,39</sup>.

Overall, preoperative smoking cessation interventions significantly reduced the occurrence of postoperative complications after surgery (RR 0.56 (95 per cent c.i. 0.41 to 0.78); P < 0.001) (*Fig.* 2). The effect remained significant when missing participants were imputed as having complications (RR 0.66 (95 per cent c.i. 0.51 to 0.84)), when studies with a dropout rate over 20 per were removed (RR 0.56 (95 per cent c.i. 0.40 to 0.78)) and when studies without biochemical validation of smoking cessation were excluded (RR 0.54 (95 per cent c.i. 0.30 to 0.76)).

#### Smoking cessation

Cessation of smoking before operation was significantly increased by intervention in five of seven studies<sup>15,21,37,38,42</sup>, at 1 month after operation in two of three studies<sup>21,23</sup>, and at 12 months after surgery in two of three studies<sup>21,23</sup> (*Table 3*). Two studies, testing intensive preoperative smoking cessation interventions, retained significantly increased smoking cessation rates in intervention *versus* control groups from before operation to 12 months after operation<sup>21,23</sup>. Patients in the intervention groups in these trials also had significantly fewer postoperative complications than controls who received neutral information (*Table 2*)<sup>22,37</sup>.

There were non-significant differences in smoking cessation rates between intervention and control groups at 3 months in two of two studies<sup>40,42</sup>, and at 6 months in two of two studies<sup>38,41</sup>. Two of these studies also found non-significant differences across interventions in the number of patients with postoperative complications<sup>40,41</sup>. The remaining two studies did not assess postoperative

	Postoperative complication rate								
Reference	Smoking intervention	Standard care	Weight (%)	Risk ratio			Risk ratio		
Møller <i>et al.</i> <sup>37</sup>	10 of 56	27 of 52	38.7	0.34 (0.19, 0.64)					
Sørensen and Jørgensen <sup>39</sup>	11 of 27	13 of 30	17.0	0.94 (0.51, 1.73)			— <b>o</b> —		
Myles <i>et al.</i> <sup>36∗</sup>	1 of 11	1 of 9	1.5	0.82 (0.06, 11.33)			•		
Warner <i>et al.</i> 41 <sup>†</sup>	4 of 56	5 of 60	6.7	0.86 (0.24, 3.03)		-			
Sørensen <i>et al.</i> <sup>40</sup>	6 of 101	4 of 48	7.5	0.71 (0.21, 2.41)					
Lindström et al.22	10 of 48	22 of 54	28.6	0.51 (0.27, 0.97)			-0		
Total	42 of 299	72 of 253	100.0	0.56 (0.41, 0.78)			•		
Total events	1 D 0 00 12 150					1		1	
Heterogeneity: $\chi^2 = 5.87$ , 5 d.f., $P = 0.32$ , $l^2 = 15\%$ Test for overall effect: $Z = 3.44$ , $P < 0.001$					0.01	0.1	1	10	100
Test for overall effect. $Z = 3.4$	H, F < 0.001				Favo	urs interver	ntion Favo	urs standar	d care

**Fig. 2** Meta-analysis of the effects of preoperative smoking cessation interventions on postoperative complications. \*Includes only wound healing complications; †postoperative complications not predefined as an outcome. Risk ratios are shown with 95 per cent confidence intervals

complications<sup>38,42</sup>. Preoperative smoking cessation interventions were less intensive in these studies. Control interventions included standard care, standard advice, provision of NRT at the discretion of clinical staff, and placebo with no counselling.

Heterogeneity, measured by the  $I^2$  statistic, exceeded 40 per cent in meta-analyses of smoking cessation rates at all follow-up times, with the exception of 3-month follow-up. It was therefore not appropriate to calculate pooled effects of preoperative smoking cessation interventions on smoking cessation.

## **Reporting bias**

A funnel plot was not drawn because of the limited number of trials (11 RCTs originating from nine study groups). As a rule of thumb, tests for funnel plot asymmetry should be used only when there are at least ten study groups<sup>14</sup>. With fewer, the power of the test is too low to distinguish chance from real asymmetry<sup>14</sup>.

#### **Discussion**

The aim of this review was to evaluate how preoperative smoking cessation interventions affect the frequency of postoperative complications, and short- and long-term cessation of smoking. Preoperative smoking interventions were primarily expected to reduce the frequency of wound healing complications<sup>43</sup>. For colorectal surgery, a reduction in anastomotic leakage and fascial dehiscence was expected, and for upper abdominal and cardiothoracic surgery, a reduction in respiratory complications<sup>43</sup>. Overall, the results of this review indicate that preoperative smoking cessation interventions can reduce the occurrence of postoperative complications, specifically wound healing complications and other complications requiring intervention. One small study tested the effect of a medium-intensity intervention on complications in colorectal surgery, but the effect on anastomotic leakage and fascial dehiscence was not significant<sup>39</sup>. The results also indicate that preoperative smoking cessation interventions can increase smoking cessation rates before operation and for up to as long as 12 months after surgery.

Specifically, intensive smoking cessation interventions with individual counselling, and including NRT, administered 1–2 months before surgery, increase short- and long-term cessation of smoking. Furthermore, these interventions are associated with a significantly reduced risk of postoperative complications. The evidence supporting these effects comes from two small internally validated trials with relatively homogeneous patient groups, interventions, outcomes and follow-up periods<sup>21–23,37</sup>. Future trials with similar interventions before different types of surgery would strengthen the evidence.

Medium intensity and less intensive interventions with NRT are not associated with long-term cessation or with significant reductions in postoperative complications<sup>36,39,40,41</sup>. The three largest trials included in this review examined less intensive interventions, with provision of NRT, and found insignificant effects on smoking cessation in the long term<sup>38,40,42</sup>. This indicates that intensive smoking interventions with persistent counselling are more effective in supporting smoking cessation and that a minimum intervention period of 4 weeks may be necessary to ameliorate the deleterious effects of smoking on postoperative recovery.

Length of hospital stay did not differ between interventions. This may be due to the trend towards shorter length of hospital stay and use of ambulatory day surgery over the past decade. An increasing proportion of complications may, of course, occur after discharge from hospital<sup>44</sup>.

Overall, definitions of postoperative complications focused on clinically important events requiring intervention. However, the definitions were not consistent across studies. Judgement of complication status would also to some degree have been subjective, with a risk of intraobserver and interobserver variation<sup>45</sup>. These factors hamper comparison of complication rates between studies and the strength of the conclusions that can be drawn from this review.

The confidence intervals in studies testing less intensive interventions may not exclude a potential benefit of such interventions<sup>36,38,40–42</sup>. Failure to detect a significant incremental benefit should not, therefore, be interpreted as firm evidence that these interventions are not effective. Within the individual studies, insignificant differences may be explained by the fact that the relative additional effect of less intensive interventions is smaller when control interventions include standard advice, brief advice from medical staff or counselling and NRT<sup>36,38,40–42</sup>. The relatively small sample sizes in these studies may also make detection of smaller, but significant, intervention effects difficult.

Smoking cessation and control interventions also varied considerably in the studies with medium to less intensive interventions, as did definitions of preoperative smoking cessation. This challenges rigorous comparison of the effects of medium to less intensive interventions, and may also be considered a limitation to this review.

The preoperative smoking cessation interventions were tested across heterogeneous surgical populations and this increases the external validity of the reviewed studies. However, smoking interventions in the reviewed studies were primarily administered by research nurses professionally trained in smoking cessation counselling. Perioperative patient care is a multidisciplinary task and smoking cessation interventions should reflect this as well as the short contact patients often have with the hospital. Therefore, the effect of intensive collaborative interventions between the primary care sector, and anaesthetic, surgical and outpatient units, with proactive counselling from general practitioners and clinical nursing and medical staff at all preoperative and postoperative patient contacts, should be evaluated.

All studies originated from Western high-income countries that, to a large extent, are comparable in regard to smoking prevalence, tobacco control policies and attitudes to smoking<sup>46</sup>. Low- and middle-income countries, on the other hand, differ widely in smoking prevalence, methods of tobacco use, tobacco control policies, and beliefs

about and attitudes towards smoking<sup>47,48</sup>. This affects the applicability of the results of this review to low- and middleincome countries<sup>48,49</sup>. However, given that 70 per cent of the world's 10 million tobacco-attributable deaths expected by the year 2030 will occur in these countries, there is an urgent need to develop ways to translate effective cessation interventions to suit local settings and cultures<sup>48,49</sup>.

The results of this systematic review indicate that patients scheduled to undergo surgery can benefit from intensive preoperative smoking cessation interventions lasting at least 4 weeks and including NRT. Benefit accrues not only in terms of postoperative recovery but also in long-term health. This is in accord with current Cochrane Review<sup>50</sup> evidence. There is also increasing evidence of the importance of adding NRT to counselling in this setting<sup>50</sup> as NRT increases the rate of smoking cessation by 50-70 per cent. The effectiveness of NRT appears to be largely independent of the intensity of support<sup>51</sup>. There is no suggestion that NRT has any adverse effect on wound healing<sup>10,41</sup>. The effect of brief preoperative smoking intervention with additional intensive postoperative intervention warrants research. Outcomes should be standardized in future studies.

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