



## Short title: Perioperative smoking BP

### 1. Purpose/benefits/justification

Tobacco use is a major global health problem and the single greatest preventable cause of death and disease in Australia and New Zealand.<sup>1,2</sup> Guidelines on smoking align with ANZCA's mission statement and are an integral part of its advocacy role in promoting the health of all patients and the community. Public health advocacy has been present from the earliest days of our profession as exemplified by John Snow instigating the removal of the handle from the Broad Street water-pump which prevented many deaths during the London cholera epidemic of 1854.<sup>3</sup>

Smokers are at increased risk of perioperative respiratory, cardiac and wound-related complications and quitting smoking may reduce the risk of complications.<sup>4</sup> Evidence suggests that the perioperative period is a "teachable moment" when many smokers quit or attempt to quit smoking, sometimes permanently.<sup>5,6</sup>

Anaesthetists and pain medicine physicians in Australia and New Zealand are highly trained to provide expert care in ensuring the best possible short-term clinical outcomes after surgery, but have few opportunities to otherwise improve the overall health of their patients. The purpose of PG12(POM) is to raise awareness amongst clinicians of the hazards of smoking in the perioperative period and assist them in answering questions of why they should promote smoking cessation, when and how. It is estimated that over 350,000 smokers have elective surgery in Australasia annually so even if the effects of such brief interventions were modest, great benefit would follow at little cost.<sup>7</sup>

### 2. Review of issues considered

#### 2.1 The burden of tobacco in Australia and New Zealand

Approximately 15,500 deaths are attributable to tobacco in Australia each year<sup>8</sup>, and 5000 in New Zealand<sup>2</sup>, the equivalent of the RMS Titanic sinking in the Tasman Sea every month. Smoking is the single greatest preventable cause of death and ill health, making up 8 per cent of the total disease burden in Australia<sup>8</sup> and costing the economy an estimated \$31.5 billion in tangible costs (that is, excluding intangibles such as pain and suffering).<sup>9</sup> Smokers are likely to be over-represented on operating lists for vascular, cardiac and cancer surgery. Estimates vary, but conservatively, half of all smokers will eventually die as the result of their smoking unless they quit.<sup>10</sup> Smokers lose at least one decade of life expectancy compared with those who have never smoked.<sup>11</sup> Cessation before the age of 40 years reduces the risk of death associated with continued smoking by about 90 per cent.<sup>11</sup>

#### 2.2 Prevalence of quitting before surgery

There is an underlying spontaneous quit rate in the general population of smokers which is estimated to be about 2 per cent per annum.<sup>12</sup> During 2010 in Australia, 29 per cent of the general population of smokers (aged >14) made at least one quit attempt<sup>13</sup> but tobacco addiction is characterised by poor spontaneous recovery rates and high rates of relapse.<sup>14</sup> In the United States, having surgery doubles the spontaneous quit rate in older adults (aged >50 years) compared to older adults not having surgery and approximately 8 per cent of all quit events are related to surgery.<sup>6</sup>

Little is known about how many smokers quit before surgery (or attempt to) in Australia. In 2011 at one Melbourne outer-metropolitan hospital, self-reported abstinence of 24 hours or more before surgery was relatively common, occurring in 24.9 per cent of patients who were smokers at the time they were placed on the surgical waiting list.<sup>5</sup> However, quit durations were usually short with periods of less than one week before surgery most common. A further 23.7 per cent tried to quit while on the waiting list but most attempts were brief, often ending within seven days of surgery.<sup>5</sup> At the time of this study, the hospital did not have any particular stop-smoking programs for surgical patients.

In the absence of any interventions to support quitting, longer term abstinence after surgery is low although successful permanent quitting does occur. In a randomised controlled trial of a stop-smoking intervention in a New South Wales regional hospital, even the control group (no intervention) had an abstinence rate of 5 per cent at three months.<sup>15</sup> In a Danish population having major orthopaedic surgery<sup>16</sup>, Moller et al reported 12 month smoking abstinence at 7.7 per cent in the absence of any intervention. The effect of interventions to increase quitting significantly increased long-term outcomes in those studies.<sup>15, 16</sup>

### 2.3 Prevalence and effect of physician advice to quit before surgery

Current evidence indicates advice to quit is inconsistently given. At one New South Wales preoperative clinic 39 per cent of smoking patients had received quit advice from an anaesthetist.<sup>17</sup> Myles et al reported surgeons advised quitting in only 6.5 per cent of cases in a sample of 200 ambulatory surgical patients at a Melbourne tertiary hospital, slightly more frequent than general practitioners (3 per cent).<sup>18</sup> Webb et al reported that less than 10 per cent of patients who smoked recalled advice from an anaesthetist to quit when surveyed on the day of surgery with rates of surgical quit advice at 22.6 per cent and general practitioner advice at 16.5 per cent.<sup>5</sup> When quit advice from clinicians occurred, the chance of patients stopping smoking before surgery was doubled.<sup>5</sup> Such findings are consistent with evidence from other patient settings that brief quit advice from clinicians is moderately effective.<sup>12</sup>

### 2.4 Evidence that smoking worsens surgical outcome

In 1944, a British anaesthetist published the first study on outcomes in smokers after surgery, showing a six-fold increase in pulmonary complications after abdominal surgery compared to non-smokers.<sup>19</sup> Since that time, over 300 studies have shown that smokers have increased perioperative risks across the range of surgical specialties, including respiratory, cardiovascular and wound-related complications.<sup>20</sup>

Turan et al compared 30-day outcomes in a cohort of 82,304 current smokers matched to 82,304 patients who had never smoked.<sup>21</sup> Adjusting for potential confounding factors such as age, gender and alcohol consumption, a significant dose-dependent increase in major and minor morbidity was shown in smokers.

Thirty-day mortality was 1.3 times higher than non-smokers (95%CI 1.2-1.5).<sup>21</sup> Unplanned intubation was 1.6 times higher (95%CI 1.1-2.3), pneumonia 1.8 times higher (95%CI 1.1- 2.9) and prolonged ventilation (>48 hours) 1.7 times higher (95%CI 1.2-2.5).<sup>21</sup> Turan et al also showed current smokers were at significantly increased odds of postoperative myocardial infarction (OR 2.1, 95% CI 1.8-2.4) and stroke (OR 1.5, 95% CI 1.3-1.8) compared to matched non-smokers.<sup>21</sup> Regarding infection, Turan et al showed 30 per cent higher odds of superficial wound infection (OR 1.3, 95%CI 1.2-1.4) and sepsis (OR 1.3, 95%CI 1.2-1.5) and 40 per cent higher odds for deep wound infection (OR 1.4, 95%CI 1.2-1.7).<sup>21</sup>

A similar case-control methodology was used by Sharma et al in 2012 to quantify the smoking risk in 43,574 patients having colorectal surgery.<sup>22</sup> Results were broadly similar to the Turan

study with smokers 47 per cent more likely to be dead at 30 days postoperatively, 30 per cent more likely to have a major complication, 32 per cent more likely to have an incisional infection and 31 per cent more likely to have some other infectious complication.<sup>22</sup>

In a large study of veterans having major joint arthroplasty, JA Singh et al found smokers had significantly higher mortality and risk of major complications.<sup>23</sup> They were 63 per cent more likely to have died within 12 months of surgery, 53 per cent more likely to develop pneumonia and there was a 41 per cent increase in incisional infection.<sup>23</sup>

## 2.5 Evidence that smoking cessation before surgery improves surgical outcome

Experimental and clinical studies have shown better outcomes when patients quit before surgery.<sup>16, 24-27</sup> Sorensen et al conducted a study in which healthy volunteers (smokers >20/day and never-smokers) agreed to have experimental sacral punch biopsies observed over a 12-week period.<sup>24</sup> Smokers were randomised to either continue smoking or quit, and quitting patients were randomised to receive either an active nicotine patch or placebo patch. The clean experimental wound had a high infection rate (12 per cent) in continued smokers compared to never smokers (2 per cent), and the infection rate of recent quitters was not significantly different from the never-smokers, regardless of which patch group patients were allocated to.<sup>24</sup>

The randomised controlled trial from Moller et al on major joint arthroplasty showed six to eight weeks cessation resulted in markedly lower wound infections, cardiovascular complications, reduced hospital stay and lowered need for reoperation.<sup>16</sup> Similar findings were found in general surgical patients if randomised to an intensive smoking cessation intervention four weeks before surgery.<sup>26</sup> Three weeks' abstinence improved wound healing in a head and neck surgery population in another study.<sup>27</sup> A recent meta-analysis of studies showed that wound healing complications across all surgical specialities was significantly lower with four weeks quitting.<sup>28</sup>

## 3. When to quit? Brief smoking cessation and pulmonary complications

While there is agreement that longer quitting is best, some uncertainty has existed as to whether short quits are worthwhile or may even be harmful.<sup>29</sup> Improved function occurs over time:

1. Quitting for a day will lower carboxyhaemoglobin and nicotine levels and could be expected to improve tissue oxygen delivery.<sup>30</sup>
2. Quitting for as little as three weeks was shown to improve wound healing.<sup>27</sup>
3. Six to eight weeks quitting means sputum volumes are not increased compared to non-smokers<sup>31</sup> and pulmonary function is improved.<sup>32</sup>
4. Immune function is significantly recovered by six months quitting.<sup>33</sup>

Concerns are sometimes expressed that stopping smoking shortly before surgery (<8 weeks) increases postoperative pulmonary complications. For example, in the current edition of Miller's Anaesthesia, Roizen and Fleisher write "the fact that anesthesiologists rarely see their patients four weeks or more before surgery presents a dilemma: if one is unable to advise the patient to stop smoking eight weeks or more before surgery, is it preferable for the patient to continue smoking?"<sup>34</sup> The 2007 version of ANZCA professional statement *PG12(POM) Guideline on smoking as related to the perioperative period* concluded "patients who smoke should be encouraged to stop smoking at least six to eight weeks before surgery."<sup>35</sup>

Such concerns over short quit times are increasingly recognised as a misinterpretation of data indicating postoperative pulmonary complications may be higher in recent quitters (<8 weeks) than those who continue smoking.<sup>35-38</sup> Speculation has been made that recent quitters' possible loss of the cough

promoting effects of cigarettes before there is a reduction in mucous hyper-secretion could be a mechanism for increased pulmonary complications.<sup>36</sup> Data regarding this became available in the early 1980s and although studies were limited in both quantity and quality, beliefs regarding the harms of quitting just a few weeks before surgery are well entrenched and appear in guidelines and recent review articles as though irrefutable.<sup>35, 36, 39, 40</sup> As elective surgery in public and private hospitals is frequently performed within a six week waiting period, the question of optimal timing to quit smoking is of paramount importance in order to best assist patients.<sup>41</sup>

In evaluating the evidence, there were three studies referenced in the ANZCA statement which made claims about recent quitters.<sup>36-38</sup> The first was a 1982 prospective study from Mitchell et al which sought to identify risk factors for postoperative respiratory morbidity in 200 general surgical patients.<sup>37</sup> Among the findings were that seven out of the 14 patients (50 per cent) who had stopped smoking within eight weeks of surgery had purulent sputum postoperatively compared to ex-smokers greater than eight weeks (many of whom could have had years of abstinence), where the prevalence of purulent sputum was only 22 per cent (10 out of 45 patients).<sup>37</sup> This result just reached statistical significance ( $\chi^2=4.02$   $p=0.045$ ) and the difference in sputum rate between recent ex- smokers and those with prolonged abstinence (28 per cent) had a wide 95 per cent confidence interval (95%CI 0-50%). The Mitchell et al study did not analyse those who continued to smoke with the 14 recent quitters but had this been done, no significant differences in sputum would have been found. Furthermore, the actual quit times of the recent quitters (less than eight weeks) were not stated and it may have been only a few days in many cases. Data on arguably more important pulmonary complications than purulent sputum such as bronchospasm, fever and segmental lung collapse was not reported in the Mitchell study.<sup>37</sup>

The second study cited in PG12(POM) (2007) was a 1989 study of cardiac surgical patients by Warner et al. It found that 12 out of 21 recent quitters (<8 weeks) had postoperative respiratory complications (57 per cent) compared with six out of 18 patients (33 per cent) who continued to smoke.<sup>36</sup> Patients who stopped smoking longer than 8 weeks had a 14.5 per cent pulmonary complication rate which was similar to the rate in patients who never smoked (11.9 per cent).<sup>36</sup> While there is no argument that longer periods of cessation before surgery are preferable, the data from this paper does not provide evidence that short periods of cessation were harmful, as is sometimes stated.<sup>38</sup> No analysis was undertaken on the difference in complications between the current smokers and recent ex-smokers. Had this been pursued, the 24 per cent difference in complications between the groups in the small sample size (95% CI -10-50) would not have been statistically significant ( $\chi^2=2.2$ ;  $p=0.2$ ).

The third study was by Bluman et al who found that the 36 patients who self-reported that they had reduced their cigarette intake in the preoperative period had 6.7 times (95%CI, 2.6-17.1) more postoperative respiratory complications than the 105 who said they smoked their usual amount.<sup>38</sup> This claim is undermined by the difficulty in verifying self- reported cigarette reductions or cessation.<sup>42</sup> It also ignores the well-described phenomenon of compensatory smoking whereby smokers may consume fewer cigarettes but extract a similar smoke volume by modifying the pattern of inhalation.<sup>43</sup> The patient's total smoke exposure is thus not simply a function of cigarette numbers, but behavioural characteristics which can achieve a greater yield per cigarette.<sup>43</sup>

Citing the Mitchell and Warner papers, PG12(POM) (2007) stated that "compared to non- smoking patients, production of purulent sputum in the postoperative period is 50% higher in patients who stopped smoking <8 weeks prior to surgery, 25% higher in those who ceased to smoke >8 weeks prior to surgery and no different to non-smokers if cessation of smoking occurred >6 months."<sup>35</sup> At face value, this would seem enough to encourage any smoker to continue smoking, however a critical assessment of their data reveals the sputum production of recent quitters is little different from continuing smokers. This is supported by the largest study to date on the relationship between smoking, quitting and intra-operative sputum volumes which involved over 1000 participants in Fukushima, Japan.<sup>31</sup> Sputum volumes were determined by endotracheal tube suctioning during elective surgery. As expected, the prevalence of current smokers with increased sputum volumes (18.2 per cent) was higher than non-

smokers (9.3 per cent). However 18.8 per cent of recent quitters (>2 weeks but <2 months) had increased sputum which was not significantly different from 18.2 per cent in current smokers.<sup>31</sup> The prevalence of patients with increased sputum was not significantly higher than current smokers for those quitting for between one day and two weeks (22.9 per cent) and no differences in postoperative pulmonary complications were found based on length of smoking abstinence.<sup>31</sup>

The issue of timing smoking cessation before surgery was recently reviewed by Myers et al who published a meta-analysis of studies that compared complication rates between smokers who stopped <8 weeks before surgery with those who continued to smoke.<sup>44</sup> Myers et al identified nine studies for inclusion in the meta-analysis totalling 448 recent quitters and 441 continuing smokers, most of whom did not report statistically significant results.<sup>44</sup> Analysing results of all studies together, the composite endpoint for total complications was 22 per cent lower in recent quitters (relative risk 0.78, 95% CI 0.57-1.07).<sup>44</sup> Pulmonary complications were reported endpoints of five studies, occurring in 115 of 261 recent quitters and 75 of 251 continuing smokers; a relative risk of 1.18 (95% CI, 0.91-1.46) meaning recent quitters were at slightly higher risk). However as these confidence intervals include the number one, they were not statistically significant. Similar results were found in a second meta-analysis on this topic in 2012.<sup>45</sup> Ascertaining optimal timing of smoking cessation before surgery therefore demands larger studies.<sup>46</sup> The bottom line from critical analysis of the studies is that recent quitters have fewer postoperative complications overall.<sup>25</sup> It would seem they are no worse off than continuing smokers in terms of pulmonary complications, but may be no better off.<sup>30, 44, 46</sup> Further data is needed on this important question but current available evidence should not dissuade anaesthetists and surgeons from advising patients to quit at any time before surgery.

#### 4. Assisting patients quit before surgery

There is an underlying spontaneous quit rate in the general population of smokers which is estimated to be about 2 per cent per annum.<sup>12</sup> During 2010 in Australia, 29 per cent of the general population of smokers (aged >14) made at least one quit attempt<sup>13</sup> but tobacco addiction is characterised by poor spontaneous recovery rates and high rates of relapse.<sup>14</sup> In the US, having surgery doubles the spontaneous quit rate in older adults (>50 years) compared to older adults not having surgery and approximately 8 per cent of all quit events are related to surgery.<sup>6</sup>

Many smokers try to quit on their own but in the absence of additional support, each quitting attempt will only have a 4-7 per cent success rate.<sup>47</sup> Quitting success tends to be greater in patients having surgery, and advice and encouragement delivered by physicians is known to improve quitting success.<sup>12</sup> Further, this group may be more motivated to quit. Perioperative clinicians cannot be expected to be smoking cessation specialists but should know how and why to refer patients to professionals who are. The Smoking Cessation Taskforce of the American Society of Anesthesiology developed a simple three-point cessation strategy (A-A-R=Ask, Advise, Refer) that may be used in everyday practice.<sup>48</sup> These are consistent with guidelines for Australian general practice<sup>49</sup> and recommendations of the Australian National Health Preventative Taskforce.<sup>50</sup>

**A=Ask.** Patients should always be asked about their smoking status. It is suggested to always ask even when the answer is already known (for example, the smell of cigarette smoke is evident) as it reinforces the message to the patient that his or her doctor believes tobacco use is a significant issue. Asking about smoking is not universally done. One large audit showed hospital doctors asked about smoking status in less than half the cases.<sup>51</sup> In another audit, anaesthetists documented smoking status in only 25 per cent of cases.<sup>52</sup>

**A=Advise.** Most smokers are aware of the risks that are printed on the packet regarding future cardio-respiratory disease and cancer, but data show that few have awareness of the specific perioperative risks that smoking poses.<sup>5, 6</sup> By understanding the benefits of quitting before surgery, the likelihood of behavioural change prior to surgery may be increased.<sup>5</sup>



**R=Refer.** An awareness of locally available smoking cessation support and referral of patients is likely to significantly improve quit rates. In randomised controlled trials of perioperative quit programs, more intensive interventions produced significantly greater abstinence.<sup>25</sup> General practitioners, pharmacists, quit counsellors at local community health centres and telephone Quitlines may be appropriate referral points. Compared to the provision of self-help material alone, multi-session counselling delivered via telephone Quitlines increased smoking abstinence at 12 months by a significant 25-50 per cent.<sup>53</sup> A Victorian study showed that multi-session Quitline counselling resulted in 24 per cent of participants being abstinent at three months.<sup>54</sup> Fax referral and online referral are options at Quitlines in Australia and New Zealand.

#### 4.1 Evidence based cessation support

This could be broadly classified into pharmacotherapy and non-pharmacotherapy options, or a combination of these. In several perioperative studies, nicotine replacement therapy (NRT) has often been provided to assist cessation in nicotine dependent patients (generally >10 cigarettes/day)<sup>25</sup> and its safety is well established.<sup>24, 55</sup> The addition of NRT to counselling increased quitting by 50-70 per cent in a review of perioperative studies without impairing wound healing.<sup>56</sup> The nicotine partial receptor agonist varenicline has also been successful in supporting long-term abstinence in a perioperative population.<sup>57</sup>

A summary of studies smoking interventions (mostly in community settings) from the Cochrane database is shown below.

**Table 1. Summary of meta-analysis related to smoking cessation from the Cochrane Library of Systematic Reviews: Pharmacotherapy**

Intervention	Relative risk* (95% confidence interval)	Effectiveness	Comments
Nicotine patch <sup>58</sup>	1.9 (1.4-2.7)	Yes. Other nicotine forms similarly effective.	Skin irritation possible. No increase in myocardial infarction.
Anxiolytics <sup>59</sup>		Low. Few trials, wide confidence intervals.	Evidence does not rule out possible effect.
Bupropion (Zyban™) <sup>60</sup>	1.7 (1.5-1.9)	Yes. Similar effect size as NRT	36 studies. Seizure risk 1:1000. ?Suicide association.
Nortriptyline <sup>60</sup>	2.0 (1.5-2.8)	Yes. Similar or better than NRT.	6 studies. Tricyclic side-effects.
Selective serotonin reuptake inhibitors (SSRI), for example, Fluoxetine <sup>60</sup>	0.9 (0.7-1.2)	No.	4 studies. Other SSRI drugs similarly ineffective.
Clonidine (oral or transdermal) <sup>61</sup>	1.7 (1.2-2.8)	Yes.	6 trials. Dry mouth and sedation common.
Nicotine receptor partial agonists, for example, Varenicline (Champix™) <sup>62</sup>	2.3 (2.0-2.7)	Yes. Lower doses than standard also appear effective.	10 trials. Mild transient nausea? Depression and suicide association.

\* Relative risk (RR) refers here to the “risk” of successful cessation, usually measured at 12 months. Thus a RR of 1.7 for nicotine patches means patients receiving patches were 70 per cent more likely to succeed at 12 months than control group patients.

**Table 2. Summary of meta-analysis related to smoking cessation from the Cochrane Library of Systematic Reviews: Non-pharmacological**

Intervention	Relative risk* (95% confidence interval)	Effectiveness	Comments
Hypnotherapy <sup>63</sup>		Low. Possibly not as good as counselling.	11 trials, very different designs.
Individual counselling <sup>64</sup>	1.4 (1.2-1.6)	Yes.	30 trials, >7000 patients.
Group behaviour therapy <sup>65</sup>	2.0 (1.6-2.5)	Yes.	53 trials. If patients like group attendance works better than individual counselling.
Rapid smoking aversive therapy <sup>66</sup>	2.0 (1.4-3.0)	Yes.	12 trials. Problems with methodology in most.
Acupuncture and related techniques <sup>67</sup>	1.1 (0.8-1.4)	Low. Little or no different from placebo.	33 studies, most affected by bias.

## 5. Tobacco as an addictive product

Cigarettes typically weigh one gram and contain around 10 mg of nicotine, of which 1 mg will be delivered to the smoker, giving it a “bioavailability” of 10 per cent.<sup>68</sup> However, depending on how intensively the cigarette is smoked, this may vary from 3-40 per cent.<sup>68</sup> When smokers are given low nicotine/low tar cigarettes, they are able to extract the same nicotine dose by varying the frequency and depth of inhalation so such cigarettes offer no health benefit.<sup>69</sup> Manufacturers achieve low nicotine/tar in most cases simply by adding multiple fine ventilation holes in the paper of the cigarette filter.<sup>68, 70</sup> When tested by a robotic smoking device under standard (International Organization for Standardization) conditions, such cigarettes will achieve low measured levels due to the entrainment of air through ventilation holes. When smoked by nicotine addicted smokers, true yields of tar and nicotine are markedly higher due to more intensive ventilation patterns and/or occlusion of the ventilation holes by fingers or lips.<sup>68, 69</sup>

Patients who report “cutting down” on cigarette numbers before surgery may not achieve any worthwhile health benefit due to this behavioural adaptation in smoking fewer cigarettes more intensively to achieve a certain nicotine blood level.<sup>43</sup> This is also known as “compensatory smoking” and explains the lack of reduction of health risk in smokers who transitioned to “low tar/nicotine” cigarettes.<sup>71</sup>

Nicotine is a weak base with a pH of 8, but the smoke of flue-cured Virginian tobacco found in the majority of Australian cigarettes is relatively acidic, with pH 6.0-7.0, meaning relatively little is in the unionised (free) form that readily crosses biological membranes such as the blood-brain-barrier.<sup>69, 70</sup> A number of manufacturers add ammonia (pKa 9.25) to tobacco, increasing the pH of the inhaled smoke and markedly increasing unionised nicotine.<sup>69</sup> Such “free-basing” agents added to tobacco increase the “kick” from nicotine, increasing its addictiveness and making quitting harder.<sup>69</sup> As unionised nicotine has greater volatility than its ionized counterpart, this also allows better separation of nicotine from particulate phase to gas phase, allowing better distribution to the lungs.<sup>69, 72</sup>

Flavourings are frequently added to tobacco to disguise the unpleasant taste of nicotine and other tobacco components. Licorice, peppermint, cocoa and sugar may be added<sup>72, 73</sup> which reduce what tobacco scientists term “throat grab”; the unpleasant coughing and spluttering that would occur when a person first initiates smoking. Although these are seemingly harmless ingredients, such additives allow smoke to be better drawn into the lungs, allowing the impact of the addictive nicotine to unfold.<sup>73</sup>

## 6. Pharmacology of tobacco smoke

Tobacco smoke is a complex mixture of around 4,500 chemical compounds.<sup>74</sup> Additives such as those listed above may contribute up to 600 further chemicals.<sup>74</sup> The combustion products vary depending on whether they are formed by burning in the hotter conditions of mainstream smoke (inhaling on the cigarette 860-900 degrees Celsius) or side-stream smoke (when the cigarette is smouldering in the air, 500-650 degrees Celsius).<sup>69</sup> Disturbingly (for those exposed to second-hand smoke), side-stream smoke contains many toxins in much higher concentrations than mainstream smoke and larger particulate size.<sup>69</sup> A number of these products are carcinogenic, as below.

**Table 3. Major carcinogens in cigarette smoke (incomplete list)/non-filter cigarette<sup>69</sup>**

Toxin group	Example/amount	International Agency for Research on Cancer Carcinogenic Risk*
Polycyclic aromatic hydrocarbons	Benzopyrene 20-40ng	2A
Heterocyclic compounds	Furan 18-37ng	2B
N-Nitrosoamines	N-Nitrosodimethylamine 2-180ng	2A
Aromatic amines	2-Naphthylamine 1-334ng 4-Aminobiphenyl 2-5ng	1 1
Aldehydes	Formaldehyde 70-100mcg	2A
Volatile hydrocarbons	Benzene 20-70mcg	1
Misc. organic compounds	Vinyl chloride 11-15ng	1
Heterocyclic amines	Aac 25-260ng	2B
Metals	Arsenic 40-120mcg	1
Other	Ethylene oxide 7mcg	1



Cigarette smoke induces liver enzymes in the cytochrome P450 system, which performs such (Phase 1) reactions as drug oxidation/hydroxylation.<sup>75</sup> Polycyclic aromatic hydrocarbons in smoke are principally involved in induction the isoenzymes CYP1A1, CYP1A2 and CYP2E1.<sup>75</sup> Some anaesthetic drugs are also metabolised via these enzymes so this in part may explain some of the literature such as the increased requirements for vecuronium and rocuronium in smokers.<sup>75</sup> Smokers also have higher opioid requirements after surgery and experience more postoperative pain, although pharmacokinetic explanations via enzyme induction are unlikely to account fully for this.<sup>76</sup>

## 7. Literature search strategy

All references in PG12(POM) (2007)<sup>35</sup> were obtained and critically read. Background reading on tobacco science, policy and effects of public health was provided from a number of academic sources.<sup>14, 77, 78</sup> Searches for documents from the Australian Government (Australian Institute of Health and Welfare) and Ministry of Health (New Zealand) on tobacco, health and drug policy yielded further useful documents on tobacco use in each country.

Electronic databases (PubMed and Cochrane) were searched through to January 2013 for relevant English language randomised controlled trials and reviews using search terms including “smoking”, “tobacco”, “preop\$”, “periop\$”, “postop\$”, “quit\$”, “cessation”, “surgery”, “outcome”, “complication”. Further references were obtained through examination of the bibliographies of relevant reviews and trials.

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#### **Process of document review**

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ANZCA regional/national committees  
Faculty of Pain Medicine Board  
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Airway Management Special Interest Group (SIG)  
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Cardiothoracic, Vascular and Perfusion SIG  
Communication in Anaesthesia SIG  
Day Care Anaesthesia SIG  
Diving and Hyperbaric Medicine SIG  
Medical Education SIG  
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Obstetric Anaesthesia SIG  
Perioperative Medicine SIG  
Regional Anaesthesia SIG  
Rural SIG  
Simulation and Skills Training SIG  
Welfare of Anaesthetists SIG

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