Smoking and hazardous drinking are common and important risk factors for an increased rate of complications after surgery. The underlying pathophysiological mechanisms include organic dysfunctions that can recover with abstinence. Abstinence starting 3–8 weeks before surgery will significantly reduce the incidence of several serious postoperative complications, such as wound and cardiopulmonary complications and infections. However, this intervention must be intensive to obtain sufficient effect on surgical complications. All patients presenting for surgery should be questioned regarding smoking and hazardous drinking, and interventions appropriate for the surgical setting applied.

Keywords: alcohol, drinking; complications, postoperative; lifestyle intervention; risk factors; smoking; surgery

Hazardous drinking exceeds the intake defined as heavy drinking and the general WHO recommendation of a maximal annual intake at no more than 6 litre ethanol per capita (children and young adults excluded). It is obvious that patients with end-stage disease induced by alcohol, smoking, or another aetiology will be at higher risk during and after surgery, as would be predicted, for example, by a measure of functionality such as the ASA score.

Smoking and hazardous drinking affect human physiology in different ways even in the absence of end-stage disease. The systems most commonly affected by smoking are pulmonary function, cardiovascular function, the immune response, and tissue healing. In addition to the well-known alcohol-induced disorders of the liver, pancreas, and nervous system, heavy drinking affects cardiac function, immune capacity, haemostasis, metabolic stress response, and induces muscular dysfunction. Both smoking and drinking can alter the hepatic metabolization of commonly used drugs.

The most common perioperative complications related to smoking are impaired wound and tissue healing and wound infection, and cardiopulmonary complications. For alcohol, postoperative infections, cardiopulmonary complications, and bleeding episodes dominate.
the list of complications.67 The increase in risk seems to hold for all types of surgery and in all settings.11 62 67 So far, no trials have been powered to explore the effects on postoperative mortality.

This review will present the existing evidence of the following topics: the pathophysiology of damage related to smoking and hazardous drinking in the perioperative period and an evaluation of the effects of preoperative intervention on the perioperative course in these patients. We will look at some clinical applications such as introducing an intervention programme, quality management, and the implications for clinical practice and research.

Methods
We searched for literature in the following electronic databases: Pubmed, Cochrane Library, Embase, Biosis, and Cinnahl. We used no language or publication year limitations.

We included searches for clinical guidelines and health technology assessments.

We searched for systematic reviews, randomized controlled trials, clinical controlled trials, descriptive studies, expert, and medical textbooks (in that order) and referred to the level of evidence.65 We searched the following terms: smoking, alcohol drinking, complication, risk factors, identification, validation, smoking cessation, smoking intervention, nicotine replacement therapy, bupropion, varenicline, alcohol intervention, disulfiram, and benzodiazepines. We classified the retrieved articles according to level of evidence and graded strength of recommendation12 (Table 1).

Pathophysiology
The increased incidence of postoperative complications after smoking and hazardous drinking is caused by a variety of tobacco and alcohol-induced damage to organ systems in combination with the surgical trauma. The preoperative abnormalities can be represented by clinical symptoms or, more often, by subclinical characteristics, which are, at least to some degree, reversed by abstinence (Fig. 1).

<table>
<thead>
<tr>
<th>Table 1 Level of evidence and strength of recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Category of evidence</strong></td>
</tr>
<tr>
<td>Meta-analysis of randomized controlled trials</td>
</tr>
<tr>
<td>Randomized controlled trial</td>
</tr>
<tr>
<td>Controlled study without randomization</td>
</tr>
<tr>
<td>Type of quasi-experimental study</td>
</tr>
<tr>
<td>Descriptive studies, such as comparative studies, correlation studies, and case–control studies</td>
</tr>
<tr>
<td>Expert committee reports or opinions or clinical experience of respected authorities</td>
</tr>
</tbody>
</table>

Smoking
Studies of pathological changes in smokers undergoing surgery have shown that smokers have multiple organ changes with potential effects on their surgical course. Smokers have increased levels of carbon monoxide (CO) in their blood and up to 15% of the haemoglobin oxygen binding sites can be occupied by CO, thus significantly reducing the amount of oxygen available for cellular processes.24 47 In addition, high p-nicotine levels mimic the sympathetic reflexes resulting in increased heart rate and arterial pressure and reduced peripheral blood flow. The overall effects of these changes are an elevated oxygen consumption and a reduced oxygen delivery.25 This may produce a relative hypoxia particularly in the heart and the peripheral tissue including surgical wounds. However, the half-life of both CO and nicotine is <12 h and the effects diminish after short-term smoking abstinence.

Smoking also impairs immune function leading to an increased risk of infection.21 The immune system appears to recover after 4–6 weeks of abstinence from smoking. The wound healing process is affected by smoking due to interference with the production of collagen.27

Finally, even young, asymptomatic smokers have reduced pulmonary capacity, increased mucus production, and reduced ciliary function.20 This may lead to perioperative pulmonary complications. These pulmonary changes will improve over 6–8 weeks of abstinence from smoking22 33 (Table 2).

Hazardous drinking
Several mechanisms by which hazardous drinking can influence the perioperative course have been identified.

A daily intake of more than 2–3 drinks produces a reduction in the immune capacity in most patients or volunteers.67 The effect is most marked on the cellular element, which can be measured by a significant suppression of delayed type hypersensitivity (DTH). DTH is a preoperative indicator for development of infectious complications after surgery.48 DTH is also decreased by surgical trauma per se, thus resulting in a very poor response in hazardous drinkers undergoing surgery compared with other surgical patients.48 64 71 After withdrawal from alcohol, DTH improves significantly after 2 weeks and is normal after 8 weeks.69 Correspondingly, the response improved after 4 weeks of preoperative abstinence in asymptomatic alcohol abusers, thus adding to the explanation for the improved outcome after surgery related to abstinence from alcohol.72

Subclinical cardiac insufficiency and arrhythmias are also characteristic of hazardous drinkers undergoing surgery,71 and both are important risk factors for development of postoperative complications. Preoperative abstinence significantly reduces the incidence arrhythmia in the postoperative period measured by Holter recording.72

The influence of alcohol on haemostasis is well known and produces a prolonged bleeding time in the perioperative
Fig 1 The effect of smoking on postoperative (a) pulmonary complications, (b) wound complications, and (c) the effect of hazardous drinking on postoperative morbidity.
period. This alone cannot explain the increased episodes of perioperative bleeding in hazardous drinkers.\textsuperscript{70} During abstinence, the reversibility of this effect in surgical patients is shown by a normalized bleeding time.\textsuperscript{72}

The endocrine stress response to surgery is significantly increased in hazardous drinkers during and immediately after the surgical procedure. This is most marked in the changes in the concentrations of epinephrine,
norepinephrine, and cortisol,\textsuperscript{64,71} which may aggravate existing alcohol-induced organ dysfunction. The increased stress response to surgery can be treated by stress-reducing therapy, but this does not, however, aid the recovery of the other alcohol-induced dysfunctions.\textsuperscript{63} Four weeks of abstinence from alcohol result in a more normal stress response to surgery\textsuperscript{72} (Table 2).

Future research should include a clarification on necessary duration of abstinence and an evaluation of to which degree the dysfunctioning organ systems should improve in order to avoid clinical complications after surgery.

**Effect of preoperative intervention on postoperative outcome**

**Smoking intervention**

Six randomized studies of preoperative smoking cessation intervention have been published, and they all showed a beneficial effect upon smoking habits, with quit rates of 40–89%.\textsuperscript{36,40,50,57,59,61,79}

Only three of these randomized studies evaluated the effect upon postoperative morbidity. One study included two groups of 60 patients undergoing knee or hip replacement and evaluated the effect of 6–8 weeks smoking cessation intervention. In this study, the intervention groups developed significantly fewer complications requiring treatment, 18% compared with 52% ($P=0.0003$), especially wound complications, 5%, and 31% ($P=0.001$). There was no effect of smoking reduction on postoperative complications.\textsuperscript{40} A recently published study of 102 patients undergoing general surgery showed that a 3–4 weeks smoking cessation programme reduced the incidence of postoperative complications from 41% to 21%, $P=0.03$. The evidence level is 1b and the recommendation strength A for preoperative smoking cessation programmes of 3–4 and of 6–8 weeks duration.

A further study did not show any beneficial effect of 1–3 weeks preoperative smoking cessation before scheduled colorectal resection (41% and 43%).\textsuperscript{59} However, this study added to our understanding that short-term abstinence from tobacco does not increase the risk of complications after surgery,\textsuperscript{6} a concept that was previously suspected from extrapolation from descriptive studies.\textsuperscript{76} In the three studies, the intervention groups received a comprehensive programme delivered by clinical experts, and the programme was intimately linked to the surgical organization.

A randomized study of smokers who volunteered to undergo experimental incisions in the sacral region found that after 4 weeks of stopping smoking, there was a lower infection rate.\textsuperscript{61} The beneficial effects of smoking intervention have been shown to be most important for wound healing and pulmonary complications.\textsuperscript{36,40} However, no clinical studies have determined the optimal duration of preoperative smoking cessation intervention, but pathophysiological studies indicate the positive effect of short-term intervention.\textsuperscript{77}

**Alcohol cessation intervention**

A randomized clinical trial of the effect of individual alcohol intervention before colorectal resection on 42 patients consuming 60–420 g of ethanol per day aimed at stopping alcohol completely for 4 weeks before surgery. The quit rate was more than 90% in the intervention group, who received a comprehensive intervention programme delivered by clinical experts.\textsuperscript{72} The same study evaluated the effect on postoperative morbidity and found it to be significantly reduced, from 74% to 31% ($P=0.02$). The most frequent complications requiring treatment were cardiopulmonary, infections, bleeding episodes, and wound complications.\textsuperscript{72} The study was not powered to explore effects on the separate types of complications. Coincidently, underlying organ dysfunction recovered in the intervention group, but not in the control group. The evidence level is 1b, and the recommendation reaches strength A.

An intended randomized clinical controlled study compared one session of brief intervention with no intervention.\textsuperscript{54} The intervention aimed at reducing alcohol consumption to <40 g per day for men and 20 g for women. Owing to recruiting problems, it was changed to a controlled trial. The intervention group developed more complications compared with the control group, 44% vs 25%, but this difference disappeared after adjusting for differences between the groups.\textsuperscript{54}

A multicentre study of interventions in non-surgical patients using acamprosate, naltraxone, and behavioural intervention recruited 1383 alcohol abusers in nine arms. This study showed only minor differences among the arms, with 66–71% of the patients relapsing to heavy drinking during the treatment period.\textsuperscript{29} In addition, the use of naltraxone, which also acts as an antagonist to morphine, would be inconvenient in several surgical settings.

Several programmes of brief interventions have been evaluated in different groups of alcohol abusers and in different settings including hospitals—but not as preoperative intervention. Most, including a meta-analysis of patients from general practice and trauma patients from emergency rooms,\textsuperscript{59} report that a brief intervention has an effect, when measuring the effect as any reduction in alcohol intake. A more relevant effect for surgical patients is the effect defined as the rate of alcohol abusers, who change to a non-abusing drinking pattern. This effect is low, especially in the high-quality studies. A recent meta-analysis of randomized controlled trials from general practice showed an effect rate of 2–3% after 1 yr.\textsuperscript{7} A review of brief intervention in a hospital setting concluded that the evidence is still unclear.\textsuperscript{14} In spite of the relative low effect rate, these programmes are often cost-effective, since the intervention costs are limited. They are therefore recommended, in general, to alcohol abusers.

More studies are needed to clarify the most beneficial intervention programme and the duration of preoperative alcohol intervention. The pathophysiological studies,
Long-term effect of preoperative intervention

One study has follow-up on the preoperative smoking cessation. The intervention group had significantly higher quit rate 1 yr after preoperative smoking cessation programme, 22% vs 3%, *P*<0.01. One year smoking cessation is related to gender (men), low nicotine dependency, non-smoking spouse, and preoperative smoking intervention. All patients gave the same reasons for smoking cessation: improved health and saving money.

The long-term effect of preoperative alcohol intervention in surgical patients has not been evaluated in a high-quality design.

Clinical applications

Identification of smokers and hazardous drinkers by self-reporting

In general, risk factors should be documented in the medical records at first contact to hospital, including the history of tobacco and alcohol. The minimum criteria to record are daily or non-daily smoker, and hazardous drinker or non-hazardous drinker. This helps to identify high- and low-risk patients.

Much of the literature relating to increased postoperative morbidity and effect of intervention is based upon self-reported consumption of tobacco and alcohol, as this is very simple to use in clinical practice. This may, however, be an underestimate, as high consumers may well under-report their intake. In contrast, over-reporting of drinking and smoking among patients is unknown. Thus, all patients who report a high intake can be regarded as higher risk, but a number of the patients reporting low intake may actually be in the high-risk group.

Questionnaires have been developed in non-surgical settings, particularly for identification of alcohol abuse. These questionnaires focus on problems related to dependence, as described in the International Classification of Diseases or DSM classifications, rather than current consumption. They include: CAGE (Questionnaire including for questions regarding 'Cut down, Annoyed, Guilty, Eye-opener'), MAST (Michigan Alcoholism Screening Test), and AUDIT (Alcohol Use Disorder Identification Test). However, periods of abstinence for <6–12 months in the DSM and AUDIT, and even longer in the other tests, are not detectable. This is inappropriate for surgical patients, where you are looking for as little as 1 month of abstinence. Furthermore, hazardous intake without dependence could be overlooked, because most of the questions are related to symptoms of addiction.

The use of biochemical markers such as cotinine concentration, CO, carbohydrate-deficient transferrin, or alcohol concentration in blood may seem attractive, but they have not been shown to be better for identification in the surgical setting. This is due to the introduction of uncertainties and variances, leading to problems in interpreting both positive and negative test results. Therefore, it is possible to misclassify smokers and non-smokers and both hazardous and non-hazardous drinkers. Finally, these markers and questionnaires have not been shown to be associated with the surgical outcome.

Intervention programmes

The agenda for surgical patients is often different from that in other hospital settings or general practice. It is characterized by a fixed preoperative period, limited by the referral date and the date of operation. The relevant preoperative intervention should take place in this period in order to reduce the risk at surgery. The surgical patient therefore needs an intensive intervention programme, which has to be effective, because of the tight preoperative schedule that does not leave time to repeat the programme in case of failure. The number needed to treat to produce one extra complication-free patient after surgery increases five- to 10-fold when using a lifestyle intervention programme with a quit rate up to 10% compared with an intensive programme with a quit rate 64–90% as described below.

Intensive preoperative smoking cessation intervention

Individual counselling is a key point of preoperative smoking cessation intervention. The frequency should be adjusted to the time of starting the smoking intervention and the scheduled time of surgery. In general, one weekly meeting will be suitable. The optimal period of intervention is still to be determined, but both 3–4 and 6–8 week programmes have proven to be effective.

At the first meeting, the magnitude and profile of nicotine dependence is estimated by the Fagerstrom test. A personalized nicotine substitution schedule should be devised in accordance with the test results and patient’s preference. Smoking status is monitored by CO in expired air. Nicotine substitution products should be given to the patients without charge. At all subsequent meetings, tobacco consumption is recorded. Patients are given advice about smoking cessation, benefits and side-effects, how to manage immediate withdrawal symptoms, and how to keep weight gain to a minimum.

Intensive preoperative alcohol cessation intervention

Individual counselling is also a key point in alcohol intervention. Intensive programmes include a meeting every week with an expert nurse or physician in alcohol...
intervention. At the first meeting, the magnitude and profile of alcohol intake and dependence is estimated according to the International Classification of Diseases. A personalized schedule for treatment of alcohol withdrawal symptoms (benzodiazepines, e.g. chlordiazepoxide) and supportive medication (disulfiram and B-vitamins) is devised in accordance with the results and patient’s preference. The status should be monitored by ethanol in expired air. At all subsequent meetings, alcohol intake should be recorded. Patients are given advice about alcohol cessation, benefits and side-effects, and how to manage immediate withdrawal symptoms.

Prevention and treatment of withdrawal symptoms are important elements in the intervention programme. It is important to initiate the prevention and treatment of withdrawal symptoms as soon as possible after the patient has abstained from alcohol, because the withdrawal symptoms may develop before the patient is completely sober and because the symptoms may develop to a life-threatening condition. Long-lasting benzodiazepines, such as chlordiazepoxide, are the first choice, for surgical patients. In general, benzodiazepines have replaced the barbiturates as they have fewer side-effects, broader therapeutical window, and an antagonist is available. Long-lasting benzodiazepines are preferable due to better prevention of seizures and lower potential for abuse. Supplemental disulfiram (with reservations for contraindications) to support the abstinence is recommended, since it is the only medical treatment evaluated for this group. Disulfiram should not be given unless the alcohol concentration in expired air or in blood has been proven zero. Short-term treatment with disulfiram is not followed by more complications than placebo. However, disulfiram does not influence the symptoms of craving or withdrawal.

Patients
The patient perspective is based on prospective studies of intervention and description, which reflects the level 2–3 of evidence and strength B–C of recommendation. Patients undergoing surgery seem to be highly motivated to change their lifestyle. When informed about the increased risk of complications, about 80% want the hospital to support them in changing their lifestyle before surgery with regard to smoking, hazardous drinking, and being overweight. Smokers who had enrolled in a pre-operative smoking cessation intervention programme liked the offer and suggested that all smokers should have the same opportunity. The patients said that free nicotine replacement therapy, smoke-free surroundings, and an empathic and competent expert were important for quitting the use of cigarettes. This attitude was seen among patients who managed to stop smoking and among patients who did not manage. The patients experienced increased motivation from the fact that they were able to influence their outcome in a positive direction. Furthermore, one-third had reduced their alcohol intake when admitted to hospital. Patients undergoing acute surgery are motivated to change lifestyle behaviour regarding smoking and hazardous drinking. This period has been described as a window of opportunity.

Clinical expertise
Risk reduction including preoperative smoking and alcohol cessation intervention programmes requires competent and dedicated health professionals. They have been shown to increase the patients’ acceptance for motivational counselling up to 50%. Interestingly, our own lifestyle seems to influence the involvement in patients’ lifestyle, that is, staff who smoke are more likely to forget to inform smoking patients about the risk of smoking and intervention programmes compared with non-smoking staff. If this is also the case with alcohol, this may be a previously overlooked barrier, but it has not yet been investigated.

Quality management
Preoperative smoking or hazardous drinking cessation programmes should be integrated into the quality management at the hospital or department and, therefore, included in local audit and the relevant clinical databases for surgery and anaesthesia. Documentation of the activities in the medical records can follow the simple model evaluated recently. The preoperative smoking cessation intervention programme has been found economical and cost-effective in relation to the operation the patient initially presented for. The effect of the smoking cessation intervention at an individual level can be followed up and compared with others by using the Smoking Cessation Database, a non-profit quality improvement database established by the Danish Ministry of Health. It was originally a Danish database, but it is now open to all organizations and professionals offering face-to-face smoking cessation intervention.

Implications for research
Several of the studies described have been performed in non-surgical patients. We urgently need research on the pathophysiological mechanisms related to smoking and the surgical processes. Research should also focus on timing of preoperative interventions for both smoking and hazardous drinking. There are only a few intervention studies and the results of these need to be confirmed in future randomized trials.

Conclusion
Smoking and alcohol are important risk factors for perioperative morbidity in all elective and emergency surgery
in both males and females. Intervention programmes starting 3–8 weeks before surgery will significantly reduce the incidence of several serious postoperative complications, such as wound and cardiopulmonary complications and infections. All patients presenting for surgery should be questioned regarding smoking and hazardous drinking, and interventions appropriate for the surgical setting applied. Interventions must be intensive to obtain sufficient effect on surgical complications.

Funding
The work was supported by grants from the ‘IMK Almene Fond’. The funding source was not involved in any stage of the work.

References
1. Amer Psychiatric Pr. Diagnostic and Statistical Manual of Mental Disorders DSM-IV. 1994
77 Whiteford L. Nicotine, CO and HCN: the detrimental effects of smoking on wound healing. Br J Community Nurs 2003; 8: S22–6
82 World Health Organization. WHO Lexicon of Alcohol and Drug Terms. 2000