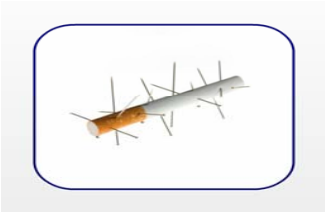
Smoking and pain



Alan Kaplan MD CCFP(EM) FCFP
Chair, Respiratory Medicine SIFP
Member, Chronic Pain SIFP

Objectives

- Review the epidemiology of pain and smoking
- Identify the relevant pharmacology of nicotine to pain
- Explain how nicotine exposure affects pain
- Hopefully, be able to integrate tobacco cessation strategies within patients suffering with pain in clinical practice

Faculty/Presenter Disclosure

- **Faculty:** Alan Kaplan MD CCFP(EM) FCFP
- Chair Family Physician Airways Group of Canada
- Chair of Special Interest Focused Practice, College of Family Physicians in Respiratory Medicine.
- Chronic pain consultant, Richmond Hill and Brampton Civic Hospital

- **Relationships with commercial interests:**
  - **Grants/Research Support:** none
  - **Speakers Bureau/Honoraria:** Astra Zeneca, Boehringer Ingelheim, Griffols, Pfizer, Purdue, Merck Frosst, Novartis, sanofi, Takeda.
  - **Consulting Fees:** Aerocrine, Novartis, Takeda, Purdue, Pfizer
  - **Other:**
    Member of Health Canada Section on Allergy and Respiratory Therapeutics.
    Member of Public Health Agency of Canada section on Respiratory Surveillance

Disclosure of Commercial Support

- **This program has received no financial support from .**
- **This program has received no other in-kind support**

  - **Potential for conflict(s) of interest:**
  - A) there are no organizations supporting this program
    B) The following companies make respiratory/pain products that I may mention in this talk including: Aerocrine, Astra Zeneca, Boehringer Ingelheim, Griffols, GSK, Merck Frosst, Pfizer, Purdue, Novartis, Sanofi, Takeda,
  - There are no organizations supporting a product that will be discussed in this program.

- **Mitigation of potential bias:**
  - **There is no bias other than being an anti-smoking activist!**

Overview of pain and smoking

- Chronic pain (APS, 2003; IASP, 2008; IOM, 2011)
  - Critical national health problem
  - 25-43% of U.S. adults (up to 116 M)
  - $125-635 B annual health care costs/lost productivity

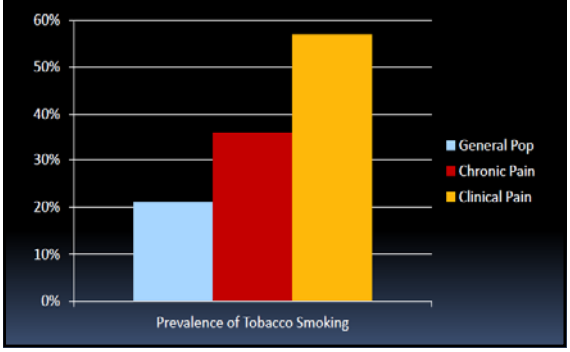
- Tobacco smoking (CDC, 2010)
  - 443,000 U.S. deaths annually
  - 21% of U.S. adults (46 M)
  - $193 B annual health care costs/lost productivity

Prevalence of smoking among persons in pain

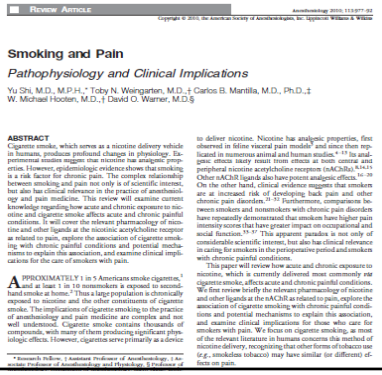
- Epidemiological data (e.g., Zvolensky et al., 2009)
  - 42% past year medically unexplained chronic pain
  - 30% past year or lifetime chronic neck or back pain
    - Up to twice rate observed in general population (21%)
      - After adjusting for sociodemographic, medical, and psychiatric features

- Clinical data (e.g., Hooten et al., 2011)
  - 49-68% of treatment-seeking pain patients
    - Greater with more severe pain/functional impairment
      - Smokers: greater pain/emotional distress and decreased activity

Prevalence of smoking among persons in pain



Resource article of use:



Review Article

Smoking and Pain

Pathophysiology and Clinical Implications

Yu Shi, M.D., M.P.H.,* Toby N. Weingarten, M.D.,† Carlos B. Mantilla, M.D., Ph.D.,‡ W. Michael Hooten, M.D.,† David O. Warner, M.D.§

ABSTRACT

Cigarette smoke, which serves as a nicotine delivery vehicle in humans, produces profound changes in physiology. Experimental studies suggest that nicotine has analgesic properties. However, epidemiologic evidence shows that smoking is a risk factor for chronic pain. The complex relationship between smoking and pain not only is of scientific interest, but also has clinical relevance in the practice of anesthesiology and pain medicine. This review will examine current knowledge regarding how acute and chronic exposure to nicotine and cigarette smoke affects acute and chronic painful conditions. It will cover the relevant pharmacology of nicotine and other ligands at the nicotinic acetylcholine receptor as related to pain, explore the association of cigarette smoking with chronic painful conditions and potential mechanisms to explain this association, and examine clinical implications for the care of smokers with pain.

APPROXIMATELY 1 in 5 Americans smoke cigarettes,[1] and at least 1 in 10 nonsmokers is exposed to secondhand smoke at home.[2] Thus a large population is chronically exposed to nicotine and the other constituents of cigarette smoke. The implications of cigarette smoking to the practice of anesthesiology and pain medicine are complex and not well understood. Cigarette smoke contains thousands of compounds, with many of them producing significant physiologic effects. However, cigarettes serve primarily as a device to deliver nicotine. Nicotine has analgesic properties, first observed in feline visceral pain models[3] and since then replicated in numerous animal and human studies.[4–13] Its analgesic effects likely result from effects at both central and peripheral nicotine acetylcholine receptors (nAChRs).[8,14,15] Other nAChR ligands also have potent analgesic effects.[16–20] On the other hand, clinical evidence suggests that smokers are at increased risk of developing back pain and other chronic pain disorders.[21–25] Furthermore, comparisons between smokers and nonsmokers with chronic pain disorders have repeatedly demonstrated that smokers have higher pain intensity scores that have greater impact on occupational and social function.[26–37] This apparent paradox is not only of considerable scientific interest, but also has clinical relevance in caring for smokers in the perioperative period and smokers with chronic painful conditions.

This paper will review how acute and chronic exposure to nicotine, which is currently delivered most commonly via cigarette smoke, affects acute and chronic painful conditions. We first review briefly the relevant pharmacology of nicotine and other ligands at the nAChR as related to pain, explore the association of cigarette smoking with chronic painful conditions and potential mechanisms to explain this association, and examine clinical implications for those who care for smokers with pain. We focus on cigarette smoking, as most of the relevant literature in humans concerns this method of nicotine delivery, recognizing that other forms of tobacco use (e.g., smokeless tobacco) may have similar (or different) effects on pain.

* Research Fellow, † Assistant Professor of Anesthesiology, ‡ Associate Professor of Anesthesiology and Physiology, § Professor of

Smoking as a Risk Factor for Chronic Pain:

Prospective Cohort Studies (Longitudinal)

Study & Year	Duration of Study	Smoking Status	Results
Mikkonen et al., 2008	2 years	Smoking	Increased risk of persistent low back pain
Mattila et al., 2008	11 years	Smoking	Increased risk of low back pain hospitalization
Eriksen et al., 1999	4 years	Smoking	Increased risk of moderate to severe back pain
Hestbaek et al., 2006	8 years	Smoking	Increased risk of low back pain
Miranda et al., 2008	15 years +	Smoking	Increased risk of incidental sciatic pain
Kaila-Kangas et al., 2003	37 years	Smoking	Increased risk of hospitalization for intervertebral disc disorder
Power et al., 2001	33 years	Smoking	Increased risk of low back pain

Provides further evidence for a relationship between smoking and chronic pain

Yu Shi et al., 2010

Smoking as a Risk Factor for Chronic Pain:

People who smoke tend to experience:

- Greater pain intensity
- Increased number of painful sites.
- Persistent pain
- Greater long-term disability

Yu Shi et al., 2010

Smoking and Pain: A Paradox

- Nicotine has analgesic properties likely resulting from effects at both central and peripheral incotine acetylcholine receptors (nAChRs)

BUT....

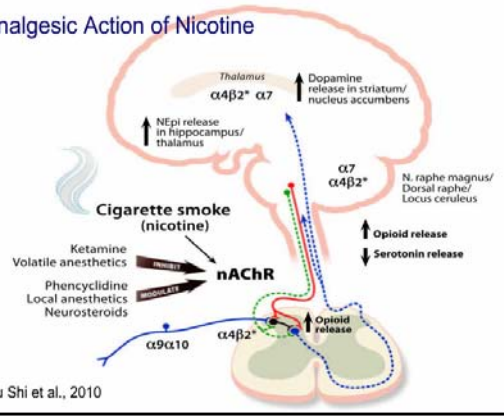
- Smoking is a risk factor for chronic pain
  - Numerous studies demonstrate evidence of covariation between smoking and the prevalence of a variety of chronically painful conditions
  - Recent meta-analytic support for smoking as a **causal** factor in the development of chronic LBP & RA (Shiri et al., 2010; Sugiyama et al., 2010)

Pharmcotherapy of Nicotine Acetylcholine Receptors NAChR's

- Shows a wide distribution in the central and peripheral nervous system
- Involved in sleep, arousal, anxiety, cognition and pain
- Activation can trigger the release of neurostransmittors such as GABA, glutamate, serotonin, histamine, and norepinephrine

Tally et al, 2009
Gotti et al, 2004

Analgesic Action of Nicotine



Yu Shi et al., 2010

Nicotine and Experimental Pain

- Nicotine produces analgesia in human models of experimental pain.
- Nicotine administration via nasal spray or transdermal patches reduces pain sensitivity in both smokers and non-smokers
- Smoking a cigarette decreases awareness of and increases tolerance to some experimental pain stimuli.

→ These effects may involve additional substances in cigarette smoke, as they are attenuated when nicotine-depleted cigarettes are smoked.

Jammer et al., 1998 Kanarek et al. 2004
Perkins et al., 1994 Pomerleau et al., 1984
Walter et al., 1983 Ferlig et al. 1986

Nicotine and Experimental Pain

- Nicotine effects on pain responses may represent treatment of nicotine withdrawal rather than direct analgesic effects in studies examining smokers deprived of nicotine.
- Nicotine administration in cigarette smoke may also confound interpretation of analgesic effects.
  - i.e. smoking increases blood pressure and heart rate which can reduce pain sensitivity

Schachter et al., 1978
Yu Shi et al., 2010

Nicotine and Postoperative Pain (1)

Study & Year	Smoking Status	Sex	Surgery	Nicotine Delivery & Application	Results
Flood et al. 2004	Non-smoking	Female	Uterine, low transverse incision	3 mg nasal spray before emergence from general anesthesia	Reported improved analgesia and reduced opioid consumption
Cheng et al. 2008	Non-smoking	Female	Uterine, open incision	3 mg intranasal	Did not report improved analgesia or reduced opioid consumption post-op.
Hong et al. 2008	Non-smoking	Male & Female	Abdominal and pelvic procedures	Transdermal patch preoperative application	Reported improved analgesia and reduced opioid consumption
Habib et al. 2008	Non-smoking	Male	Retropubic prostatectomy	7 mg/24 h transdermal patch preoperative application	Reported improved analgesia and reduced opioid consumption
Turan et al. 2008	61% smoking	Females	Abdominal hysterectomy	21 mg/24 h transdermal patch preoperative application	Did not report improved analgesia or reduced opioid consumption post-op.
Olson et al. 2009	Smoking	Male & Female	Abdominal and pelvic procedures	5 to 15 mg/24 h transdermal patch preoperative application	Did not report improved analgesia or reduced opioid consumption post-op.

Nicotine and Postoperative Pain (2)

- **People who *do not* smoke**: Nicotine can produce an analgesic effect in a clinical setting
- **People who *do* smoke**: Receptor desensitization and/or withdrawal effects may limit any analgesic effects of perioperative nicotine administration

Yu Shi et al., 2010

Smoking and pain intensity

Smokers report greater pain and functional impairment than nonsmokers (Weingarten et al., 2008)

Smokers use substantially more analgesic medication (e.g., opioids) than nonsmokers (Broekmans et al., 2010, Woodside, 2000)

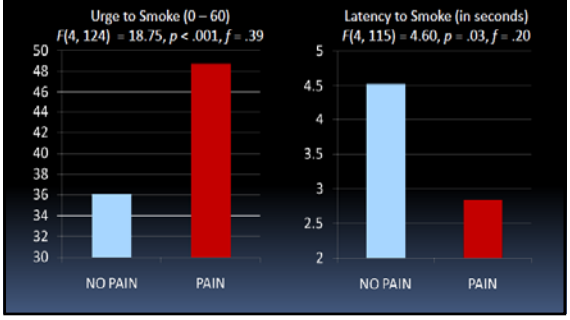
Effects of pain on smoking: Pain as a motivator of smoking

- Cross-sectional & qualitative evidence (pain patients):
- Reported increased smoking in response to pain
- Endorsed pain-induce desire to smoke (Hooten et al., 2011) "My smoking is extremely related to my pain…instead of rubbing my knee I'll go smoke a cigarette"; "If I have a flare-up…I'll…go for a cigarette"
- Endorsed smoking for pain-coping (e.g., via distraction) "I'm thinking of the cigarette…puffing it, and lighting it, and holding it…so it diverts me away from the pain"; "Smoking is a great distraction tool"
- Reported that opioid use increased urge to smoke "When I was on…opioids it would make me a chain smoker"

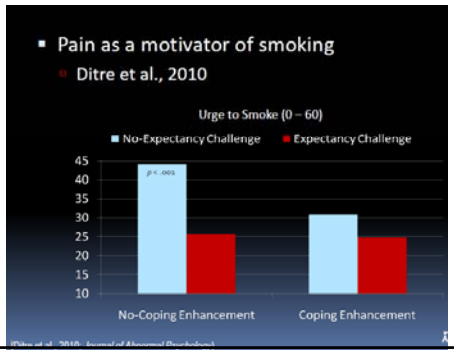
Jamison et al., 1991

Effects of pain on smoking

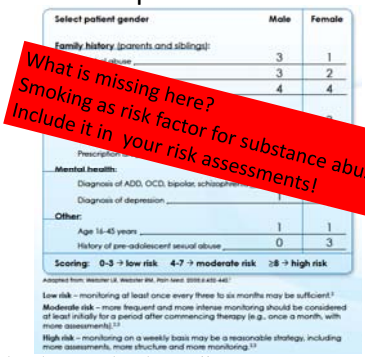
- Pain as a motivator of smoking



Smoking is a method of coping….



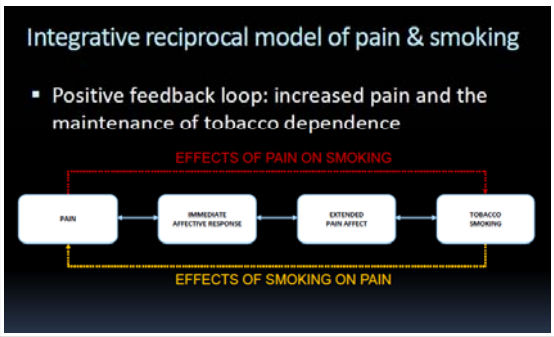
Opioid Risk Tool



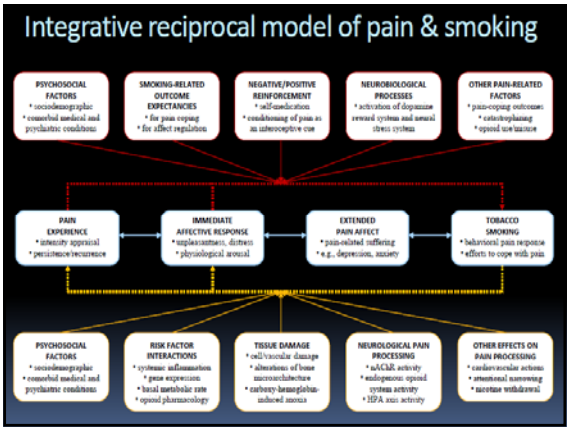
What is missing here?
Smoking as risk factor for substance abuse!
Include it in your risk assessments!

1. Webster LR, et al. *Pain Med.* 2005;6:432-442. 2. Chou R, et al. *J Pain.* 2009;10(2):113-130.
3. Jovey RD, ed. *Managing Pain – The Canadian Healthcare Professional's Reference.* 2008.

It goes both ways..



Integrative reciprocal model of pain & smoking



Pain as a barrier to **smoking cessation**

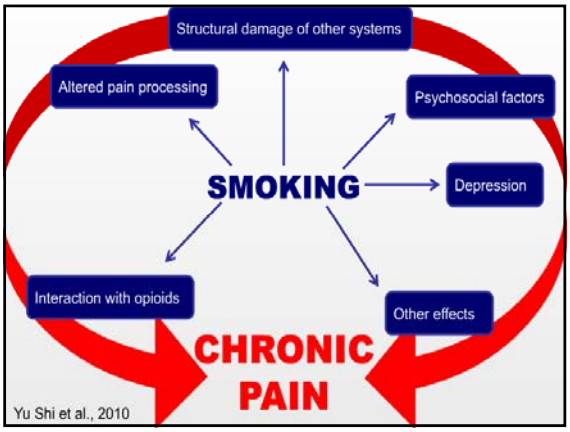
- Smokers in pain report greater difficulty and less confidence in quitting (e.g., Waldie et al., 2008; Hooten et al., 2011)
- Pain may precipitate relapse to smoking
  - Smoking-related outcome expectancies (pain/mood coping)
  - Negative reinforcement (smoking for stress-coping/self-medication) Conditioning of pain as a smoking cue
  - Positive reinforcement (unemployment, loneliness, low social support) Smoking to maintain stable rates of positive reinforcement when other environmental reinforcers have been removed
  - Neurobiological processes Pain may activate overlapping neural substrates (i.e., reward and stress systems) that act synergistically to motivate smoking

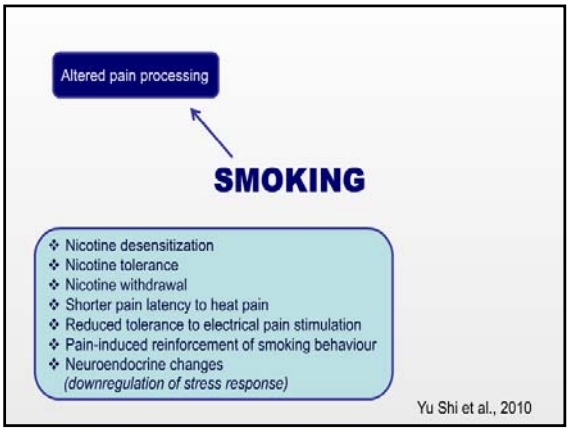
Pain as a barrier to smoking cessation

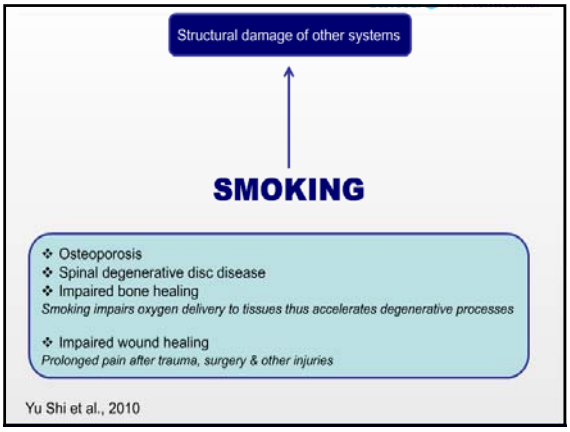
Novel treatment considerations:

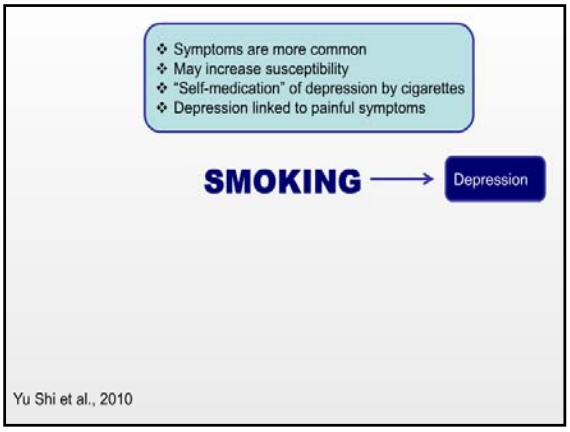
- Pain factors (pain severity, functional impairment, disability status, pain-coping outcomes)
- Psychiatric comorbidity (depression/anxiety, substance use, personality disorders)
- Medication interactions (effects of increasing/decreasing opioid use)
- Pain-induced relapse (painful stressors can reinstate extinguished drug-seeking)
- Smoking abstinence-induced hyperalgesia

"I'd be afraid of the pain getting worse if I quit smoking" (Hooten et al., 2011)









SMOKING

Interaction with opioids

- Increased opioid use
- Use of illicit substances
- Cross-tolerance between nicotine and opioids
- Altered opioid pharmacokinetics

(downregulation of stress response)

Yu Shi et al., 2010

SMOKING

- Chronic exposure to carbon monoxide increases the level of heme oxygenase (may contribute to the development of neuropathic pain)

Other effects

Yu Shi et al., 2010

Clinical Implications

Outcomes of Chronic Pain Therapy

- Factors affecting the outcomes of chronic pain treatment:
  - Depression
  - Substance use
  - Unemployment (more persistent disability)

Yu Shi et al., 2010

Smoking Cessation Interventions for Chronic Pain Patients

- Motivation and intent to quit smoking is very high
- Quitting smoking would dramatically improve long-term health

Yu Shi et al., 2010
Hahn et al., 2006

Smoking Cessation Outcomes

Short Term Abstinence	Long Term Abstinence
May worsen painful symptoms and complicate concurrent efforts to treat pain	Recovery from the long-term effects of exposure to nicotine may improve chronic pain
Take away their primary coping mechanism to control stress and anxiety	Adoption of new coping strategies may improve adaptive responses to persistent pain and improve functional status

Yu Shi et al., 2010

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Take away their primary coping mechanism to control stress and anxiety	Adoption of new coping strategies may improve adaptive responses to persistent pain and improve functional status

Future research should explore:

1. **How tobacco abstinence affects chronic pain**
2. **The development of effective methods to help people with chronic pain quit smoking**

Yu Shi et al., 2010

How about comorbid psychiatric illness and smoking cessation: Does that make it worse?

Psychiatric hospitals:

- One of last healthcare facilities to ban smoking
- Assumption that abstinence would worsen mental health outcomes - - FALSE
- Tobacco interventions are now targeted to patients with mental health issues

Fishbain et al., 2008
Hooten et al., 2009

Management of Postoperative Pain

- Few studies exist of how smoking status affects acutely painful conditions in postoperative pain
  - Studies that do exist have poor methodology
- Based on limited evidence, increased postoperative analgesic requirements may be anticipated in people who smoke

Warner et al., 2004
Yu Shi et al., 2010

Management of Postoperative Pain (2)

Can Nicotine Replacement Therapy (NRT) contribute to postoperative analgesia in people who smoke?

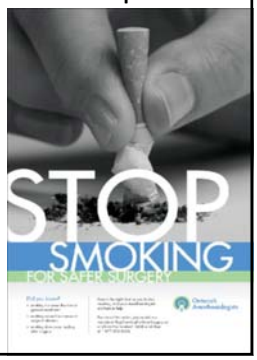
- Several placebo-controlled trials indicate that NRT:
  - Did not improve postoperative analgesia
  - Did not improve withdrawal symptoms

BUT/AND! *For many people, NRT can be efficacious in helping patients maintain postoperative abstinence after hospital discharge*

Warner et al., 2005
Turan et al., 2008
Olson et al., 2009

When is the best time to quit?

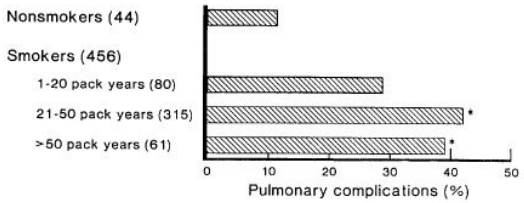
- At least pre-operatively!



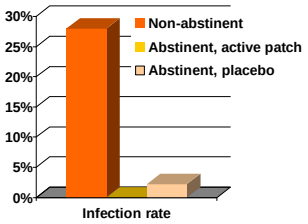
Anesthesiology
60:380–383, 1984

Preoperative Cessation of Smoking and Pulmonary Complications in Coronary Artery Bypass Patients

MARK A. WARNER, M.D.,* MATTHEW B. DIVERTIE, M.D.,† JOHN H. TINKER, M.D.‡



Nicotine Replacement Therapy and Wound Healing



- 48 smokers randomized to continuous smoking or abstinence, with or without nicotine replacement
- Standardized surgical wounds over a 12 week period

43 Sorensen et al, Ann Surg 238:1, 2003

Smokers do less well postoperatively

Short Term

- Worse wound healing (Mastectomy flap necrosis 18.9% v 9.0 in NS) (DW Chang Plastic & Reconstr Surg. 2000 p2374)
- More infections (12% in smokers, v 2% NS) (Sorensen, Ann Surg, 2003)

Long Term

- Worse outcome (more pain, poorer function) one year after ACL repair (Karim, JBJS, 2006)

"We found that smoking was the single most important risk factor for the development of postoperative complications"

(Moller JBJS 2002)

The Lancet, Volume 359, Issue 9301, Pages 114 - 117, 12 January 2002
doi:10.1016/S0140-6736(02)07369-5 Cite or Link Using DOI

< Previous Article | Next A

Effect of preoperative smoking intervention on postoperative complications: a randomised clinical trial

Dr Ann M Møller MD a, Nete Villebro RN a, Tom Pedersen MD a, Hanne Tønnesen MD b

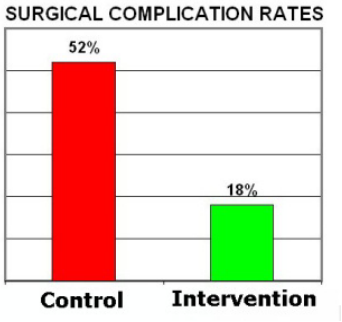
120 patients for elective joint replacement
Randomised to control or smoking cessation intervention:

Control	Routine preoperative preparation 4 stopped smoking anyway
Intervention	Routine preoperative preparation plus weekly meetings with nurse, NRT therapy 36 stopped smoking, 14 reduced, 6 continued

Results

	Control	Intervention
Wound problems:	31%	5%
CV Insufficiency	10%	0%
Avg. days in hospital	13	11
Total days in ICU	32	2

Stopping smoking reduces risk:



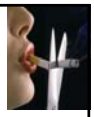
When to stop?

- Ideally 6 – 8 weeks or longer
- Definite advantage of 4 weeks
- For carbon monoxide elimination, 4 -8 hours
  - "No smoking after midnight"?
  - Risk of stopping shortly before surgery?
- Postoperative quitting aids wound healing

Case study

- Wanda is a 62 year old married pharmacist
- Wanda wants to quit smoking, but is asking for your help
- Started smoking at age 15, quit at 32 with birth of her child, but restarted at age 40 when diagnosed with Crohn's disease and reactive arthritis.
- Smoked to help deal with stress of illness and raising three kids, but has found that when she stopped smoking in past quit attempts, her pain worsened.
- On Arthrotec for arthritis pain and Oxycocet for her abdominal pain.
- Needs a bowel resection for active Crohns segment with obstruction despite optimal therapy
- 40 lb overweight and restricted in activities d/t pain.
- On waiting list for biologic therapies……..which I agree would help!!

Case study: Questions



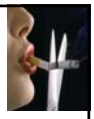
1) What are the central issues in this case?
2) What are the patient's barriers to change
   Chronic pain and smoking
3) Where would YOU start if you were seeing Sue?
   Smoking may well have some benefits in patients with IBD
   Smoking helps her stress and potentially her mood
4) What interventions would you perform in addressing smoking cessation recognizing the other co-existing risk factors/issues?
   Surgical outcomes in smokers much worse
   Analgesic needs pre and post op

Case study: Questions

1) What are the central issues in this case?
2) What are the patient's barriers to change
3) Where would YOU start if you were seeing Sue?
4) What interventions would you perform in addressing smoking cessation recognizing the other co-existing risk factors/issues?

   Pain
   Stress
   Anxiety re surgery
   Coping mechanisms
   Surgical outcomes
   Long term benefits

Case study: Questions



1) What are the central issues in this case?
2) What are the patient's barriers to change
3) Where would YOU start if you were seeing Sue?
4) What interventions would you perform in addressing smoking cessation recognizing the other co-existing risk factors/issues?

   Explanation of issues so she is prepared
   Smoking cessation strategies that she can work with
   Multimodal, eg NRT + Buproprion(anxiety and mood?)
   E cig etc for coping skills?
   Analgesics available for worsening pain?
   NRT post-op aggressively

Pain in patients with COPD…another issue!

SciVerse ScienceDirect

Pain in people with chronic obstructive pulmonary disease (COPD)

Bahareh HajGhanbari [a,*], Lilisa Holsti [b], Jeremy D. Road [c], W. Darlene Reid [a]

KEYWORDS
Pain;
Chronic obstructive pulmonary disease;
Physical exertion;
Exercise

Summary

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We do need more research..

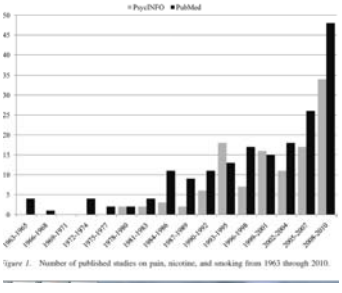

Figure 1. Number of published studies on pain, nicotine, and smoking from 1963 through 2010.

Psychological Bulletin
Pain, Nicotine, and Smoking: Research Findings and Mechanistic Considerations
Joseph W. Ditre, Thomas H. Brandon, Emily L. Zale, and Mary M. Meagher Online First Publication, October 3, 2011. doi: 10.1037/a0025544

Summary

- Pathophysiologic reasons for why smoking helps pain
- Smoking does worsen conditions and cause pain
- Does it induce pain sensitivity, like opioids do?
- Clinically pain may be worse if smoking stopped in short term
- Outcomes undoubtedly better in long term
- When is the best time?
- Especially if they are preop!