Pre-Clinical Phase
Preventing Dementia: Smoking and Brain Health

Introduction
Brain health is essential to quality of life throughout the life course. There is a growing body of research evidence associating various activity lifestyle factors with the prevention of cognitive decline. Because most of these risk factors are self-manageable, health practitioners are being challenged to re-think a primary and secondary prevention approach to help client’s achieve and maintain cognitive vitality in later life.

This edition of “In Focus!” provides key pieces of research evidence that link smoking with the risk of cognitive impairment and dementia, and discusses the clinical issues of smoking behaviours and cessation efforts across the life course, particularly in the senior population.

Did you know…?
- Smoking is associated with greater cognitive decline from mid-life onwards than non-smoking, and heavy smoking is associated with an accelerated rate of cognitive decline;
- Mortality from dementia is greater among smokers than non-smokers;
- Smoking is a significant cardiovascular risk factor. Cardiovascular risk factors are dementia risk factors! Cardiovascular disease is preventable.
- Deaths from smoking result in, on average, 15 years' loss of expected life. Health Canada estimates that smoking will account for more than 50% of deaths before age 70 among today's 15-year-old smokers.
- Greater awareness needs to be developed in the seniors' population about the fact that quitting at any age leads to positive health benefits – it is never too late to stop smoking!

Key Clinical Messages:
- All health encounters should include screening to identify and document tobacco use status; If smoking is identified, the client should receive stop smoking and referral information
- It is never too late to stop smoking! There are benefits to quitting smoking at any age.
- Eliminating smoking can compress disability into a shorter period, and is associated with a longer life and years of disability-free living as compared to persistent life-time smokers.
- People with lower socio-economic status are more likely to start smoking, more likely to become regular smokers and less likely to quit.
- Older smokers are less likely than younger smokers to attempt quitting, but they are more likely to be successful in their attempts.
- Older people with lengthy smoking histories are likely to need additional or tailored assistance with cessation.
- More and more people are using assistance when they quit. (Assistance is defined as self-help materials, counseling, and/or nicotine replacement therapy.) Those who use assistance have higher quit rates. One fifth to one third of quit attempts are made with assistance.
1. Identifying the Relationship between Smoking and Cognition

Does smoking prevent dementia? Does it cause dementia? There has been conflicting evidence and much confusion about the relationship between smoking and dementia over the past 15 years. Some of this confusion is attributed to the earliest group of studies that were published in the early 1990s, which indicated that smokers were less likely to develop Alzheimer disease than non-smokers. These early studies even suggested that smoking has a protective effect for dementia. Despite the cautionary tone by researchers, these findings caused quite a stir in the public media, as conversely, messages about the ill effects of tobacco on lung cancer and heart disease, and the need to stop or reduce smoking were beginning to be heavily promoted. In an effort to find redemption from this negative public pressure, tobacco companies even began to sponsor conferences on dementia. The mixed messaging was confusing for both the public and health care professionals.

Since the late 1990s, two critical meta-analyses and several reviews of this research evidence have found these results to be spurious and unreliable due to study design and considerable methodology flaws. Most of these early case-control studies (level 2 and 3 evidence) were small, retrospective in design, and had significant selection and recall bias, creating misleading results. In the past 5-6 years, there has been increased interest in conducting epidemiological research of a prospective cohort (level 1 evidence) design, with reasonable follow-up and controls for confounding factors. The results of these more recent studies indicate that:

- **smoking, in a dose-dependent fashion, is associated with an increase in cognitive decline, which can begin in mid-life**;
- **smoking is significantly associated with various dementia types (Alzheimer, vascular, etc.) in later life**;
- **heavier smoking is associated with an accelerated rate of cognitive decline**;
- **mortality from dementia is greater among smokers than non-smokers**

**How does smoking affect cognition?**

a) Biological:

Smoking is thought to have a direct effect on the central nervous system. The early case control findings were considered biologically plausible because Alzheimer disease affects neurotransmitter systems, particularly the cholinergic system. Since nicotine is a cholinergic agonist, it was believed that smoking acted directly on the nicotine receptors in the brain. There are several studies which support this theory in relation to Parkinson’s disease. While this may indeed be an influence, it has a very short term physiological effect and evidence is inconclusive at this time.

**Did you know?** Nicotine is one of thousands of chemicals in tobacco products, but it is considered the primary compound that affects brain function. Nicotine deprivation can impair attention and cognition, and it can also reverse these withdrawal-induced deficits. Performance impairment has been observed within four hours of tobacco deprivation. Many studies describing nicotine's "enhancement" of attention and cognition only demonstrated that nicotine reversed withdrawal effects. Poor attention level and lowered cognition following a period of nicotine deprivation can be a strong motivating factor to smoke to reverse such deficits, thus maintaining nicotine addiction.

More recent studies theorize that the negative effect of smoking on the brain results from vascular damage and tobacco-induced oxidative stress (free radical activity). The vascular damage results from a long term decline in cerebral perfusion, and is associated with cerebral atrophy.

Another possible mechanism is through the role of inadequate nutrition combined with an increase in free radical production and antioxidant depletion from nicotine. Smokers’ diets have been found to have a lower intake of antioxidant vitamins, higher levels of triglycerides and serum cholesterol, compared with non-smokers. In a small diagnostic cohort study (level 2 evidence), Polidori et al. (2003) studied the plasma levels of several antioxidant micronutrients and resistance to oxidative challenge. They found that four weeks following cessation of cigarette smoking there was a marked increase in plasma antioxidant concentrations, and a significant lowering of malondialdehyde (MDA) levels, which is a biomarker for free radical activity associated with ischemic stroke and congested heart failure. Investigation into the mechanisms between smoking and brain health continue.

b) Sociological:
Smoking is also a complex social behaviour. A discussion on the mechanisms of action for smoking and brain health requires a population level look into the social determinants that result in smoking behaviours in the first place. Extensive epidemiological investigations have looked at who smokes, why people smoke and what influences the health behaviour choices that they make. These factors make up the ‘smoking gradient’.

One of these factors, lower socio-economic status (SES) significantly influences smoking behaviours across the life-course. Although cigarette smoking has been declining in recent decades, socio-economic inequalities in smoking persist and appear to be widening. People of lower SES are more likely to start smoking, more likely to be regular smokers, and less likely to quit. Therefore, addressing the socio-economic inequalities in smoking is important to reducing smoking at a population level.

Three key factors are thought to influence how health behaviours develop:
- the health locus of control (beliefs that personal well-being is dependent on personal health behaviours rather than chance or luck);
- future salience of health (how a state of health relates to one’s future);
- health consciousness (self-awareness of the influence of lifestyle choices on personal health).

In a recent cross-sectional national survey (level 2 evidence), Wardle and Steptoe (2003) investigated whether attitudes could mediate socioeconomic differences in healthy lifestyle, smoking being one of four health variables studied. They found that individuals that smoked tended to have a high “chance” health locus of control (good health is a result of good luck rather than personal choices), a lack of future salience (did not think about their short-term or long-term health), and lacked awareness of the influence that their smoking behaviours have on their personal state of health. These findings have implications for evaluating the relevance and effectiveness of some traditional tobacco cessation programs – is the message correctly targeted? Is it getting through to vulnerable populations?
2. Key Summaries of Smoking and Dementia Evidence

The process of creating Clinical Practice Recommendations is described in the Dementia Project Website at [http://inside.interiorhealth.ca/NR/rdonlyres/4BAD12CF-0150-486D-8B48-2261BBF7869A/15864/HowareClinicalPracticeRecommendationsCreated.pdf](http://inside.interiorhealth.ca/NR/rdonlyres/4BAD12CF-0150-486D-8B48-2261BBF7869A/15864/HowareClinicalPracticeRecommendationsCreated.pdf). The key research evidence that has been reviewed and used to create the Practice Recommendations in this document is summarized below.

1) In a prospective birth cohort (1959) study (level 1 evidence), Gilman et al\(^9\) (2003) investigated the association between multiple indicators of SES over the life course and three stages of cigarette use: initiation, regular use, and cessation. They found that people from lower socio-economic backgrounds are at significantly increased risk of smoking initiation. Low SES in childhood also increased the risk for progression to regular smoking and was associated with a reduced likelihood of smoking cessation. Progression to regular smoking and smoking persistence were also associated with lower adult SES. These researchers concluded that SES over the life course accumulates to produce increased rates of smoking uptake and reduced rates of smoking cessation among lower SES people.

2) In a large multi-center prospective cohort study (EURODEM) (level 1 evidence), Ott et al\(^4\) (2004) investigated the effect of smoking on cognition in over 17,610 persons over the age of 65 and followed up for over an average of 2.3 years. They found that after adjusting for age, sex, baseline MMSE, education, type of residence and history of MI or stroke, that smoking and the amount smoked was associated with cognitive decline. Higher cigarette pack-year exposure was correlated with a significantly higher rate of cognitive decline. They concluded that smoking may accelerate cognitive decline in the non-demented elderly.

3) In a large prospective birth cohort (1946) study (level 1 evidence), Richards et al\(^11\) (2003) investigated the effects of cigarette smoking on midlife cognition performance. This British cohort was followed up 21 times between birth and age 53. The researchers found that smoking was associated with faster declines in verbal memory and slower visual search speeds. The effects were largely accounted for by individuals who smoked > 20 cigarettes/day, and were independent of sex, SES, previous (adolescent) cognitive abilities, and a range of other health indices. These researchers concluded that heavy smoking is associated with cognitive impairment and decline in midlife (Note: The link between this study and dementia is that other research evidence indicates that significant cognitive losses across the life course (eg, head injury, Down’s syndrome, severe lead exposure in childhood) are associated with an increased risk of dementia in later life).

Discussion Point:

What is exciting about the Richards study is the possibility of a mid-life window for preventative action. The association between smoking and memory was not observed at age 43, but emerged as a change in function between ages 43 and 53. Furthermore, the association between smoking and memory observed at age 53 was far stronger than that observed at age 43, suggesting that a further 10 years of persistent heavy smoking exposure resulted in this change.

4) In a large prospective cohort study (level 1 evidence) of British male doctors followed up since 1951, Doll et al\(^12\) (2000) found that the relative risk of all types of dementia was increased for smokers as compared to non-smokers (RR 0.96, 95% CI 0.78-1.18) and for probable or definite Alzheimer disease (RR 0.82, 95% CI 0.68-1.00).
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disease, the relative risk was 0.99 (95%CI, 0.78-1.25). The limitation of this study includes the underestimation of cases of vascular dementia due to categorization methodology.

5) In a large meta-analyses (pooled GLOBE and LSOA studies) of Dutch citizen aged 30-74 years, Nusselder et al13 (2000) examined whether eliminating smoking would lead to a reduction in the number of years lived with disability. These researchers found that non-smokers spend fewer years (2.5 years less for men, and 1.9 years less for women) with disability, and have lower mortality risks than smoking groups. The authors concluded that eliminating smoking will not only extend life and result in an increase in years lived without disability, but will compress disability into a shorter period. They recommended that discouragement of smoking should receive high priority.

3. Clinical Practice Considerations
I thought less people were smoking. What is happening with seniors?
While the number of Canadians who have quit smoking is now higher than the number of current smokers, there are still about 5.4 million smokers in Canada14. There are favourable trends in the prevalence of smoking among seniors. Health Canada15 reports that the daily smoking rate of adults 65 years and older has declined from approximately 18% in 1965 to 12% by 1994. In 1996-97, 36% of all seniors were former smokers and overall quit rates are higher among older people than for younger people. However, mid-life and life-long smoking leaves a legacy well into old age, even after people quit. For example, despite the general decline in smoking prevalence among women since the late 1970s, the number of smoking-related deaths for females 65 years and older continues to grow. This is believed to be a cohort effect of the growth in the popularity of smoking among younger women in the late 1940s and 1950s.

Isn’t it too late to benefit from quitting smoking in older age?
Research has shown that it is beneficial to quit smoking at any age! While it is true that the health risks from smoking persist into old age, so do the benefits of smoking cessation. Cessation of smoking exerts a protective action that increases with the number of years since stopping. Among older smokers, the benefits of cessation include rapid improvements in circulation and pulmonary perfusion (both necessary for good brain health!), with most of the improvement occurring in the first year.

How ready to quit are older smokers?
Older smokers tend to have attitudes which are less favourable to stopping smoking than younger people. There is research evidence that smoker attitude, knowledge and the length of addiction are influencing factors. First, older smokers are far less likely than younger people to accept the health risks associated with smoking18. Second, older smokers frequently view smoking as a beneficial coping and weight control strategy, and may also doubt that quitting this late in life will reap any benefits. Finally, those who still smoke are likely to be highly dependent on nicotine.

There is some evidence that effectiveness of smoking cessation programs might be improved by matching interventions to a smoker's age and stage in the smoking cessation process16. Among smokers 50 years of age or older, those with a realistic understanding of the health consequences of smoking and those who perceive smoking as addictive were more likely to be ready to quit17. Older smokers are less likely than younger smokers to attempt quitting, but they are more likely to be successful in their attempts18. This evidence suggests that older people with lengthy smoking histories are likely to need additional or tailored assistance with cessation.

What are the most effective tobacco intervention for older smokers?
Cessation remains the most effective way of altering smoking-induced disease at all ages, including those 65 years of age or over\textsuperscript{15}. Research has shown that older smokers are highly responsive to targeted smoking cessation programs, and that they are at least as likely as younger smokers, if not more, to succeed in quitting either on their own or with the aid of self-help and counseling with or without pharmacological aids\textsuperscript{16}. More and more people are using assistance when they quit. There is evidence that those who use assistance have higher quit rates. One fifth to one third of quit attempts are made with assistance. Assistance is defined as self-help materials, counseling, and/or nicotine replacement therapy.

There are many published clinical guidelines for the treatment of tobacco dependence\textsuperscript{19,20,21,22}. These guidelines provide an evidence base for the types of interventions that should be used by health care professionals to assist smokers to quit. Brief advice by medical providers to quit smoking is minimally effective\textsuperscript{19}. This includes brief interventions in primary care settings\textsuperscript{20} and combining quitting advice with nicotine replacement therapy. The challenge will be to incorporate smoking behaviour monitoring and smoking cessation interventions as part of standard practice, so that all patients are given an opportunity to be asked about their tobacco use and to be given advice and/or counseling to quit along with reinforcement and follow-up\textsuperscript{20}. More intensive interventions (i.e. individual, group or telephone counseling\textsuperscript{21}) that provide social support and training in problem solving are even more effective\textsuperscript{22}.

The presence of regular physician and/or dentist support is considered a critical factor for older adults to quit smoking\textsuperscript{23}. Older patients are open to physician advice to quit and say that their quitting decisions and confidence in quitting are influenced positively by this advice. Physicians are more likely to advise patients with commonly recognized smoking-related diseases, such as cardiovascular, cerebrovascular or respiratory diseases. Unfortunately, despite the fact that older adults see their doctors more often than younger age groups, 36% percent of older smokers say that their physician never advised them to quit\textsuperscript{15}, and fewer than half (49.4\%) of physicians say that they ask their patients about tobacco use\textsuperscript{24}.

Dentists also have a unique opportunity to discuss tobacco use and options to quit. In a very recent survey\textsuperscript{25} researchers examined tobacco cessation knowledge, attitudes, and behaviors of dentists. The survey revealed that dentists do not routinely incorporate tobacco cessation into their practices. Only 28\% of dentists reporting that they asked their patients about tobacco or recorded tobacco use in their patients’ charts at least 41\% of the time, and approximately half of the dentists advised tobacco-using patients to quit at least 41\% of the time. However, there is a growing evidence base supporting an increased primary and preventive care role for dentists regarding tobacco cessation. Such a role could afford dentists opportunities to expand the bounds of dental practice, improve therapeutic outcomes and promote patients' overall health.

The evidence is strong and consistent that pharmacologic treatments for smoking cessation (specifically, nicotine replacement therapy and bupropion) can help people quit smoking. All of the commercially available forms of NRT (gum, transdermal patch, nasal spray, inhaler and sublingual tablets/lozenges) are effective as part of a strategy to promote smoking cessation. They increase the odds of quitting approximately 1.5 to 2 fold regardless of setting\textsuperscript{26}. Pharmacotherapies are effective even when they are used without behavioural support. Studies show that the effectiveness of NRT appears to be largely independent of the intensity of additional support provided to the smoker.
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4. Summary and Conclusions about Smoking and Dementia
In summary, there is a small but growing data base of level 1 evidence to conclude that heavy smoking is associated with cognitive impairment and dementia. There is also a growing amount of research and guideline information on cessation and tobacco intervention strategies for older adults. This topic area remains to be a developing and dynamic field of research.

5. Clinical Practice Recommendations
Clinical practice recommendations are directed at an agency level for planning and management purposes, as well as at an individual client care level. The Strength of Recommendations (A, B, C) concerning smoking and dementia are noted following each recommendation.

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<th>Strength of Recommendations Taxonomy</th>
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<td>A = consistent and good quality client-oriented evidence;</td>
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<td>C = evidence lacking, more research needed; based on expert</td>
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The SORT research grading tool emphasizes patient-oriented outcomes – outcomes that matter to patients and help them live longer or better lives, including reduced morbidity, mortality or symptoms, improved quality of life and lower cost of health care services. Levels of evidence are ranked 1-3 based on the validity (quality) of the study design. Strengths of recommendations (A to C) are based on grading the quantity and consistency of the studies and their findings. Ratings are listed following each recommendation or group of recommendations as needed.

The Dementia Clinical Practice Working Group advises the following clinical practice recommendations concerning smoking and dementia:

At a Health Authority Level:
- Current tobacco cessation programs in IHA need to be made aware of the level of evidence currently available concerning smoking and dementia. (C)
- Current tobacco cessation programs in the IH need to be evaluated for evidence of a life-course approach and multi-stage strategies to smoking cessation. (C)
- Strategies within tobacco cessation programs need to target the smoking gradient for vulnerable clients (i.e., lower SES across the life-course) (A)
- Strategies within tobacco cessation programs need to use sociological knowledge about locus of control for client health beliefs, future salience and health consciousness in order to develop and target meaningful and effective intervention strategies. (A)
- Primary and secondary strategies across the life-course are important. The “teachable moment” in secondary interventions may be equally or more effective in changing behaviour than primary prevention strategies. (A)
- The IH needs to integrate tobacco cessation knowledge and messaging into everyday clinical practice for all health professionals. (A)

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* Strength of Recommendations are made from conclusions about the amount and quality of level of evidence evaluated using the SORT tool. See IH Dementia website for further details: [http://inside.interiorhealth.ca/Health+Delivery/Home+Community/Planning+Development/Dementia+Care+Strategy/](http://inside.interiorhealth.ca/Health+Delivery/Home+Community/Planning+Development/Dementia+Care+Strategy/), under “Project Tools”
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- The IH needs to support physicians and dentists with academic detailing regarding current research and guidelines on tobacco cessation strategies, including counseling. (B)

At a Client Care Level:
- All health encounters need to include screening to identify & document tobacco use status. (A)
- If smoking is identified, the client should receive stop smoking & referral information. (A)
- Nurses and other frontline Primary Health Care staff are in effective positions to provide community clients with assessment, education and counseling regarding tobacco cessation. They may need education and support to fulfill this role. (C)
- Health care staff need to use the knowledge that older people with lengthy smoking histories are likely to need additional or tailored assistance with cessation into their care plans. (B)
- For health staff who are involved in counseling and patient education, tobacco cessation strategies need to include, but not be limited to:
  - “5-A” behavioural counseling framework (ask, advise, assess, assist and arrange); (A)
  - “5-R” framework to treat tobacco use (relevance, risk, rewards, roadblocks, repetition) (A)
  - Quit smoking telephone support lines; (B)
  - Tailored counseling and education for vulnerable clients, e.g., pregnancy, older adult (A)
  - Access to current and accurate self-help materials specific for this health authority are made available on-line and in prominent health resource centers; (C)
  - Self-help material is not a stand alone strategy (has minimal effect), but part of a comprehensive, multi-strategic approach to cessation counseling; (A)
- Access to pharmacotherapy options, including:
  - nicotine replacement therapy (NRT), e.g., gum, patch, nasal spray); (A)
  - sustained-release bupropion; (A)

6. Quality Practice Indicators for smoking and dementia may include:
- Abstinence rates across the life-course, including seniors;
- Quit rates for seniors >65 years
- Presence of brain health rationale in tobacco cessation programs in IH

7. Clinical Tool Kit for Smoking and Dementia
- Information on Canada’s national smoking policy can be accessed through the following link:
  [http://www.phac-aspc.gc.ca/seniors-aines/pubs/workshop_healthyaging/tobacco/tobacco1_e.htm](http://www.phac-aspc.gc.ca/seniors-aines/pubs/workshop_healthyaging/tobacco/tobacco1_e.htm)
- Health Canada has greatly expanded and enhanced its web site to provide Canadians of all ages with access to:
  - interactive, self-help cessation support based on the stages of change;
  - referral to cessation programs across the country;
  - e-quit messages to motivate and support smokers to quit;
  - information on the adverse health impacts of smoking;
  - information on best practices in cessation;
  - statistics on cessation in Canada;
  - resources for service providers.
- Here are some of the federal support services:
  - Health Canada’s "[www.gosmokefree.ca](http://www.gosmokefree.ca)" web site is a free e-Quit subscription program where clients can sign up for a 30-day series of free e-mail messages to help them through the cessation process. To date, subscribers have found
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the e-mail messages to be both supportive and effective. In fact, of 300 "graduates" surveyed at the end of their 30-day program, 74% had stopped smoking.

- "On the Road to Quitting" is another interactive self-help web-based resource that motivates and supports smokers who want to quit. The program helps people to deal with temptations, withdrawal symptoms and relapse. It answers questions about nicotine replacement therapies and other stop-smoking strategies. Access to the booklet is available by calling 1 800 O-Canada toll-free phone line and also via "www.gosmokefree.ca" web site.

- B.C. Ministry of Health has a tobacco control strategy. Further information about the BC provincial resources and approach can be gained via http://www.healthservices.gov.bc.ca/tobacco/

- Interior Health participates in the provincial tobacco strategy and has several tobacco cessation programs and strategies. Information can be accessed at http://www.interiorhealth.ca/Choose+Health/Tobacco+Cessation/

References


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