Smoking Cessation in People with Serious Mental Illness

Tony P. George, M.D., FRCP (C)

Professor and Chair in Addiction Psychiatry,
University of Toronto, Faculty of Medicine
Centre for Addiction and Mental Health (CAMH)
Toronto, Ontario, Canada M5S 2S1

Adjunct Professor of Psychiatry,
Yale University School of Medicine
New Haven, Connecticut USA 06519

http://www.prism.yale.edu
Presentation Objectives

• To understand reasons for the high prevalence of tobacco use and dependence in smokers with serious mental illness.
• To become knowledgeable on the assessment of tobacco dependence in mentally ill smokers, and how to implement evidence-based pharmacological and behavioral treatments for tobacco dependence in these populations.
• To appreciate the barriers towards implementation of successful treatment programs in mental health and addictions settings.
“Quitting smoking is easy – I’ve done it several hundred times …”

- Mark Twain
## Prevalence of Tobacco Use in Canada

(CTUMS, 2005, Total Population Data, Ages 15-60)

<table>
<thead>
<tr>
<th>Province</th>
<th>Current Smokers (%)</th>
<th>Average CPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canada</td>
<td>19</td>
<td>15.7</td>
</tr>
<tr>
<td>NFLD</td>
<td>21</td>
<td>15.5</td>
</tr>
<tr>
<td>PEI</td>
<td>20</td>
<td>16.1</td>
</tr>
<tr>
<td>Nova Scotia</td>
<td>21</td>
<td>15.5</td>
</tr>
<tr>
<td>New Brunswick</td>
<td>22</td>
<td>16.9</td>
</tr>
<tr>
<td>Quebec</td>
<td>22</td>
<td>16.5</td>
</tr>
<tr>
<td>Ontario</td>
<td>16</td>
<td>15.6</td>
</tr>
<tr>
<td>Manitoba</td>
<td>22</td>
<td>14.1</td>
</tr>
<tr>
<td>Saskatchewan</td>
<td>22</td>
<td>14.1</td>
</tr>
<tr>
<td>Alberta</td>
<td>21</td>
<td>14.9</td>
</tr>
<tr>
<td>B.C.</td>
<td>15</td>
<td>15.7</td>
</tr>
</tbody>
</table>
Neurotransmitters: ACH, DA, NE, 5-HT, GLU

Nicotine Effects: From Cigarette to Receptor
**Nicotinic Receptor Composition**

Acetylcholine

Muscle type nAChR

Neuronal type nAChR

### Table 1: Smoking Status Among Respondents (n=4,411) in the National Co-Morbidity Survey (NCS) According to Report of Mental Illness in the Past Month

<table>
<thead>
<tr>
<th>Diagnosis in Past Month</th>
<th>% in US Population</th>
<th>% Current Smokers</th>
<th>Quit Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Mental Illness</td>
<td>50.7</td>
<td>22.5</td>
<td>42.5</td>
</tr>
<tr>
<td>Social Phobia</td>
<td>4.0</td>
<td>31.5</td>
<td>29.2</td>
</tr>
<tr>
<td>Panic Disorder</td>
<td>1.4</td>
<td>42.6</td>
<td>32.9</td>
</tr>
<tr>
<td><strong>Major Depression</strong></td>
<td><strong>4.9</strong></td>
<td><strong>44.7</strong></td>
<td><strong>26.0</strong></td>
</tr>
<tr>
<td>Non-Affective Psychosis</td>
<td>0.2</td>
<td>45.3</td>
<td>0.0</td>
</tr>
<tr>
<td>Bipolar Disorder</td>
<td>0.9</td>
<td>60.6</td>
<td>25.9</td>
</tr>
<tr>
<td>PTSD</td>
<td>2.3</td>
<td>44.6</td>
<td>23.2</td>
</tr>
<tr>
<td>ASPD</td>
<td>14.6</td>
<td>45.1</td>
<td>27.8</td>
</tr>
<tr>
<td>Alcoholism</td>
<td>2.6</td>
<td>56.1</td>
<td>16.9</td>
</tr>
<tr>
<td>Drug Addiction</td>
<td>1.0</td>
<td>67.9</td>
<td>22.4</td>
</tr>
</tbody>
</table>

Reasons Why Individuals with PD and SUD May Have Higher Rates of Smoking

• The pathophysiology of these disorders increases vulnerability to nicotine dependence.
• Individuals with PD and SUD are self-medicating affective and cognitive symptoms associated with these disorders.
• Social factors (e.g., peer modeling, poverty, stress, availability)

Cigarette Smoking in Schizophrenia

• High prevalence of smoking (58-88%) and nicotine dependence in schizophrenia compared to general population [Kalman et al., 2005; de Leon and Diaz, 2005].

• These patients have great difficulty with smoking cessation [Lasser et al., 2000; Kalman et al., 2005, de Leon and Diaz, 2005], and appear to extract more nicotine from their cigarettes compared to non-psychiatric control smokers [Olincy et al., 1997; Sacco et al., 2005; Tidey et al., 2005; Williams et al., 2005].

• May be genetic factors which explain this co-morbidity (e.g. α7 nAChR, Freedman et al., 1997).

• Smoking is thought to precede the onset of psychotic symptoms (e.g., 1st psychotic break; McEvoy et al., 1999; Weiser et al., 2004; Riala et al., 2005)

• Higher rates of cardiovascular and lung disease are associated with schizophrenic disorders (but lower rates in 1st degree relatives) [Lichterman et al., 2001].
Dopamine (DA) Dysregulation in Schizophrenia

**Normal**

- **PFC** → **NAc** → **VTA** → **DA**
- Type of firing of VTA--PFC DA neurons: Regular basal firing
- Type of firing of VTA--NAc DA neurons: Burst firing

**Schizophrenia?**

- **PFC** → **NAc** → **VTA** → **DA**
- Type of firing of VTA--PFC DA neurons: Regular basal firing
- Type of firing of VTA--NAc DA neurons: Burst firing

**Mesocortical system**

**Dysfunctional mesocortical system**

**Mesolimbic system**

**Dysfunctional mesolimbic system**

**DA-mediated reward system functioning normally**

**DA-mediated reward-system deficiency**

Courtesy of Alan I. Green, M.D.
Nicotine Effects on DA Dysregulation in Schizophrenia

**Normal**

- **PFC** → **NAc**
- **VTA** → **DA**

**VTA--NAc DA neurons**
- Slow, irregular basal firing
- Burst firing

**VTA--PFC DA neurons**
- Regular basal firing
- Burst firing

**Mesocortical system**
- **Mesolimbic system**

**DA-mediated reward system functioning normally**

**Smoker with Schizophrenia?**

- **PFC** → **NAc**
- **VTA** → **DA**

**VTA--NAc DA neurons**
- Regular basal firing
- Burst firing

**VTA--PFC DA neurons**
- Regular basal firing
- Burst firing

**Dysfunctional mesocortical system**
- **Dysfunctional mesolimbic system**

**Nicotine improves DA-mediated reward-system deficiency**

Adapted from Alan I. Green, M.D.
Evidence for Potential Beneficial Effects of Nicotine/Smoking in Schizophrenia

• Reduce Antipsychotic Drug Side Effects (e.g. extrapyramidal symptoms, akathisia) [Dalack, Yassa, Pope, Yang]

• Alter Negative Symptoms of Schizophrenia [Goff, Ziedonis]

• Ameliorate Brain Psychophysiological Abnormalities (P50, SPEM, PPI) [Adler/Freedman/Olincy; Kumari and Sharma; Depatie, Avila, George]

• Improve Neuropsychological Deficits [Levin, George, Smith, Depatie, Sacco]
Visuospatial Working Memory (VSWM) Task

Screen 1 (Cue)
- The dot is presented to the subject for 3 sec.
- Subject completes the tic-tac-toe during the “0”, 30 or 60 sec. delay.
- Mouse pointer is kept in the center of this box

Screen 2 (Delay)
- “Distractor Screen”

Screen 3 (Response)
- Subject has to click where the black dot was located in screen 1

(“0”, 30 or 60 Sec. Delay)
Effects of Smoking Abstinence on VSWM in Schizophrenics (n=23) versus Controls (n=29)

Cortical Dopamine Function and Spatial Working Memory

George, T.P. et al. (2003)
Prefrontal Cortex Neuropsychological Deficits are Associated with Smoking Cessation Failure in Schizophrenia


Smoking Abstinence and its Effects on VSWM Performance

Distance From Target (cm)

Study Group

Quit
Not Quit

p=0.052

Smoking Abstinence and its Effects on Perseverative and Non-Perseverative Errors

WCST Percentage Errors

Trial Endpoint Status

Quit
Not Quit

p<0.05

Smoking Abstinence and its Effects on Categories Completed in WCST

WCST Categories Completed

Study Group

Quit
Not Quit

p<0.05
Assessment of Tobacco Dependence in Mentally Ill Smokers

- Onset of tobacco use in relation to onset of mental illness or substance abuse
- Do smoking patterns change during periods of symptom remission versus exacerbation?
- Do symptoms change during attempts at cessation?
- Use of timeline follow-back methods
- Level of dependence? – Fagerstrom Test for Nicotine Dependence (FTND; Heatherton et al., 1991)
- Longest period of abstinence in past? – what factors were associated with successful quitting?
- Objective assessments of smoking and treatment response (carbon monoxide, cotinine, craving and withdrawal scales; good test-retest reliability and internal consistency in schizophrenic versus control smokers – Weinberger et al., 2007)
Contemplation Ladder

On the ladder below, each step represents the mindset of various smokers when they think about quitting. Circle the number that best indicates where you are now.

10: I have quit smoking and will never smoke again

9: I have quit smoking, but I still worry about slipping back, do I need to keep working on living smoke free

8: I still smoke, but I have begun to change, like cutting back on the number of cigarettes I smoke. I am ready to set a quit date.

7: I definitely plan to set a quit date within the next 30 days

6: I definitely plan to set a quit date within the next 6-months

5: I often think about quitting smoking, but I have no plans to quit

4: I sometimes think about quitting smoking, but I have no plans to quit

3: I rarely think about quitting smoking, and I have no plans to quit

2: I never think about quitting smoking, and I have no plans to quit

1: I enjoy smoking and have decided not to quit smoking for my lifetime. I have no interest in quitting.
Fagerstrom Test for Nicotine Dependence (FTND)

1) How soon after you wake up do you smoke your first cigarette?
   3 = Within 5 minutes.
   2 = 6 to 30 minutes.
   1 = 31 to 60 minutes.
   0 = After 60 minutes.

2) Do you find it difficult to refrain from smoking in places where it is forbidden?
   0 = No
   1 = Yes

3) Which cigarette would you hate most to give up?
   1 = The first one in the morning.
   0 = All others.

4) How many cigarettes per day do you smoke?
   3 = 31 or more.
   2 = 21 to 30
   1 = 11 to 20
   0 = 10 or fewer.

5) Do you smoke more frequently during the first hours after waking than during the rest of the day?
   0 = No
   1 = Yes

6) Do you smoke if you are so ill that you are in bed most of the day?
   0 = No
   1 = Yes

A score of 5 or higher is consistent with a moderate level of nicotine dependence
Barriers to Effective Treatment

• Access to cigarettes around mental health centers and in the community is high (Steinberg et al., 2005; Weinberger et al., 2007).
• Access to smoking cessation services is typically limited for the mentally ill, and there is a lack of specific services for these smokers.
• Mental health clinician who are smokers are less likely to encourage their clients to quit smoking (Weinberger et al., submitted)
• Insurance coverage of nicotine dependence treatment for mentally ill smokers is often limited or non-existent.
• Smoke-free community living environments are rare.
• A substantial portion of disability income (up to 25%) may be spent by heavily-dependent mentally ill smokers on tobacco products (Ziedonis et al., 2003).
Is it Safe to Get Mentally Ill Patients to Quit Smoking?

• **Short Answer:** Yes! But few studies have been conducted, and more research needs to be done.

• In schizophrenia, smoking cessation does not exacerbate psychotic or depressive symptoms (e.g. George et al., 2000; Evins et al., 2001; George et al., 2002; Evins et al., 2005).

• In major depression, some longitudinal studies by the Columbia group (Glassman et al., 1988; 1990) do suggest some increased risk of depression with smoking cessation, but several other studies have not supported this conclusion (Niaura et al., 2001; Thorsteinsson et al., 2001).

• In anxiety disorders, little evidence that cessation can exacerbate PTSD or GAD, and in fact severity and frequency of panic attacks in Panic Disorder may be higher in smokers versus non-smokers (Breslau and Klein, 1999).
Cigarette Smoking, Cytochrome P450 and Psychotropic Drug Plasma Levels

- Metabolized by CYP 1A2/3A4
  - Clozapine
  - Olanzapine
  - Haloperidol
  - Chlorpromazine
  - Caffeine

- Not Metabolized
  - Risperidone
  - Ziprasidone
  - Aripiprazole
  - Quetiapine
  - Bupropion

## Pharmacotherapies for Tobacco Dependence

<table>
<thead>
<tr>
<th>Medication Class</th>
<th>Examples</th>
<th>How used</th>
<th>Efficacy vs. PLO</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>NRT: Slow-acting</td>
<td>Nicotine Patch</td>
<td>Daily application</td>
<td>2-fold</td>
<td>Local irritation</td>
</tr>
<tr>
<td>NRT: Fast-acting</td>
<td>Gum, lozenge inhaler, nasal spray</td>
<td>Multiple uses as needed</td>
<td>1.5-2.5-fold</td>
<td>Oropharyngeal irritation</td>
</tr>
<tr>
<td>Antidepressant</td>
<td>Sustained-release (SR) Bupropion</td>
<td>150 mg po BID after induction</td>
<td>2.0-fold</td>
<td>Insomnia, activation, dry mouth</td>
</tr>
<tr>
<td>Nicotinic Partial Agonist</td>
<td>Varenicline</td>
<td>1 mg po BID after induction</td>
<td>3.0-fold (1.5-fold vs. Bupropion)</td>
<td>GI, Insomnia</td>
</tr>
<tr>
<td>Cannabinoid Antagonist</td>
<td>Rimonabant</td>
<td>Up to 20 mg daily (qd dosing)</td>
<td>1.5-2.0-fold</td>
<td>GI, Neuro</td>
</tr>
<tr>
<td>Monoamine Oxidase Inhibitor</td>
<td>Moclobemide/S elelgilene</td>
<td>BID dosing</td>
<td>2-4 fold</td>
<td>GI, Rare Cheese Reactions</td>
</tr>
</tbody>
</table>
Smoking Cessation Medication
Trials in Schizophrenia

- **Ziedonis and George, 1997.** Schizophr. Bull. – Open-label NRT + MET in n=24 SZ smokers.
- **George et al. (2000).** Am. J. Psychiatry – open-label TNP in n=45 SZ smokers. Subjects on atypical vs. typical antipsychotics had best outcomes in short long-term (55 vs. 22%), but low long-term abstinence rates (~16%).
- **Evins et al. (2001).** Nicotine Tob. Res. PLO-controlled trial of bupropion in n=18 SZ smokers at 150 mg/day. Evidence for reduction but only ~10% quit at trial endpoint.
- **George et al. (2002).** Biol. Psychiatry. PLO-controlled trial of bupropion SR at 300 mg/day in n=32 SZ smokers. Higher rates of quitting in active group (~50%), but low long-term abstinence rates (<15%).
- **Chou, K.-R. et al. (2004).** Int. J. Nurs Stud. Controlled trial of TNP+group therapy versus group alone in 68 schizophrenic smokers. EOT abstinence rate (Week 8) was 26.9% in experimental group and 0% in control group.
- **Evins et al. (2005).** J. Psychopharmacol. PLO-controlled trial of bupropion SR (300 mg/day) in n=56 SZ smokers. ~22% vs. 5% abstinence rates in active vs. PLO groups.
- **Williams et al. (2005).** Compared low (21 mg) vs. high (42 mg) TNP in SZ smokers. No differences in overall quit rates, but greater reduction in tobacco withdrawal and craving in the high dose TNP group.

**Bottom Line:** FDA-approved medications seem to work in the short-term, but success rates are low, and long-term success rates are low!
Smoking Cessation in Schizophrenia: What Works?

- High motivation to quit and lower levels of tobacco dependence at baseline [Addington et al., 1998a/b; George et al., 2000]

- Ability to quit smoking in first week of the trial predicts success at trial endpoint and 6-month follow-up [George et al., 2000; 2002]

- Behavioral treatment that is tolerable and motivationally-based, with CBT modified to account for cognitive dysfunction [Ziedonis and George, 1997; Addington et al., 1998; George et al., 2000; Evins et al., 2001]

- Lack of prefrontal cortex-related neuropsychological deficits [Dolan, Sacco et al., 2004]

- Treatment with atypical antipsychotic medications [George et al., 2000; 2002]
Schizophrenia Cessation Studies – Common Design For Three Sequential Trials

**Weekly Group Therapy**

- **Week 1**: Baseline Assessments (including cognitive testing and genetics)
- **Week 2**: (Start Study Medication - #2/3)
- **Week 3**: “Target Quit Date” [Start TNP (Studies#1/3), then Continue TNP x 8 weeks]
- **Week 10**: NTP/BUP (#2/3), D/C Study Medication

**6-month Follow-up**

- **Study 1**: TNP alone
- **Study 2**: BUP vs. PLO
- **Study 3**: TNP + BUP vs. PLO
Components of Yale Modified Group Therapy for Smokers with Schizophrenia

- Emphasis on motivational enhancement therapies (MET)
- Psychoeducational approach
- Modified CBT emphasizing small amounts of material at each session with frequent repetition to accommodate cognitive deficits so common in this population.
- Focus on building social skills
- 10 weekly sessions of group smoking cessation counseling.
- Quit date set in 3rd week, but will frequently reset a quit date if unsuccessful on initial attempt.
Atypical Versus Typical Antipsychotic Drugs and Nicotine Patch for Smoking Cessation in Schizophrenia (n=45)

Smoking Abstinence Rate (%)

- Endpoint
- Last Four Weeks
- 6-Month F/U


*p<0.05 vs. Typical
Bupropion for Nicotine Dependence in Schizophrenia

- **Bupropion is a weak catecholamine reuptake inhibitor** [Ascher et al., 1995].
- **Recent data suggests that it is a non-competitive ion channel site antagonist of the high-affinity nAChR** [Fryer and Lukas, 1999; Slemmer et al., 2000].
- **May be helpful for smoking cessation in schizophrenia since it may:**
  1) block the drive to smoke mediated by mesolimbic DA systems;
  2) augment hypofunctional cortical DA systems associated with schizophrenia.
Effects of Bupropion on Smoking Cessation Rates in Patients with Schizophrenia (n=32)


* p<0.05 vs. Placebo
Bupropion versus Placebo: Effects on Positive and Negative Symptoms

**Positive Symptoms**
- PANSS Positive Score
- Quit Date

**Negative Symptoms**
- PANSS Negative Symptom Score

**F = 4.32, df = 1,15, p < 0.05**

![Chart showing PANSS Positive and Negative Scores](chart.png)
Combination with Atypical Antipsychotic Drugs Predicts Anti-Smoking Responses to Bupropion

B=21.1, SE=1.0, Wald Statistic=445.1, df=1, p<0.001
Patch and Bupropion in Smokers with Schizophrenia (PABS)

• Funded by NIDA (5R01-DA-13672; 9/1/01-11/30/06)
• A randomized, placebo-controlled trial of open-label transdermal nicotine patch (TNP; 21 mg/24h) + bupropion SR (300 mg/d) or placebo (0 mg/d) + SZ Behavioral Therapy in cigarette smokers with schizophrenia or schizoaffective disorder.
• Block randomization on the basis of treatment with atypical versus typical antipsychotic drugs.
• N=289 subjects screened; N=63 eligible; N=59 subjects randomized to date, N=55 completers.
• Enrollment will be completed (as of December, 2006), and final data analyses will begin after completion of all 6-month follow-up assessments in May, 2007.
# Demographic Characteristics: PABS Trial (n=54)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Bupropion SR +TNP (n=27)</th>
<th>Placebo + TNP (N=27)</th>
<th>Significance Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>41.5 ± 8.4</td>
<td>39.1 ± 6.8</td>
<td>p = 0.27</td>
</tr>
<tr>
<td>Race</td>
<td>12 C/ 13 AA/ 2H</td>
<td>13 C/ 12 AA/ 2H</td>
<td>p = 0.83</td>
</tr>
<tr>
<td>Sex</td>
<td>165 M/ 11F</td>
<td>17 M/ 10F</td>
<td>p = 0.57</td>
</tr>
<tr>
<td>Education (years)</td>
<td>11.8 ± 2.0</td>
<td>11.2 ± 2.1</td>
<td>p = 0.28</td>
</tr>
<tr>
<td>Cigarettes Per Day</td>
<td>24.3 ± 10.1</td>
<td>23.9 ± 1.6</td>
<td>p = 0.88</td>
</tr>
<tr>
<td>FTND</td>
<td>6.5 ± 1.7</td>
<td>6.8 ± 1.6</td>
<td>p = 0.51</td>
</tr>
<tr>
<td>Plasma Cotinine (ng/ml)</td>
<td>452 ± 273</td>
<td>442 ± 176</td>
<td>p = 0.89</td>
</tr>
<tr>
<td>Expired Breath CO (ppm)</td>
<td>24.8 ± 13.4</td>
<td>28.0 ± 13.8</td>
<td>p = 0.40</td>
</tr>
<tr>
<td>HDRS 17-item scale</td>
<td>5.0 ± 3.8</td>
<td>5.4 ± 3.5</td>
<td>p = 0.74</td>
</tr>
<tr>
<td>PANSS-Positive Score</td>
<td>14.8 ± 2.9</td>
<td>14.5 ± 2.6</td>
<td>p = 0.74</td>
</tr>
<tr>
<td>PANSS-Negative Score</td>
<td>13.9 ± 2.4</td>
<td>14.9 ± 3.5</td>
<td>p = 0.25</td>
</tr>
<tr>
<td>PANSS-Total Score</td>
<td>58.3 ± 7.4</td>
<td>60.0 ± 9.9</td>
<td>p = 0.50</td>
</tr>
<tr>
<td>Antipsychotic Class</td>
<td>22 ATP/ 5 TYP</td>
<td>22 ATP/ 5 TYP</td>
<td>p = 1.00</td>
</tr>
<tr>
<td>CPZ Equivalents (mg/day)</td>
<td>477 ± 323</td>
<td>594 ± 464</td>
<td>p = 0.30</td>
</tr>
</tbody>
</table>
Smoking Abstinence Rates in Bupropion SR (BUP)+TNP and Placebo+TNP Groups During 10-week Trial and Six Month Follow-up Assessment

* All p’s < 0.05

George, T.P. et al. (2007)
Conclusions – PABS Trial

- The combination of TNP+Bupropion SR is superior to TNP alone for both short- and long-term cessation outcomes in schizophrenia.
- Possible agonist-antagonist effects of this combination, given that bupropion is a potent nAChR antagonist.
- Future studies will examine effects of other nAChR agents including the $\alpha_4\beta_2$ nAChR partial agonist Varenicline (Chantix®, Champix®)
Smoking Cessation Trials in Other Psychiatric Disorders

- **Chengappa et al. (2001)** – demonstrated that open-label bupropion SR (300 mg/day) was well-tolerated and led to a 30% abstinence rate in smokers with MDD treated with SSRIs.

- **Hertzberg et al. (2001)** - showed that bupropion was safe in smokers with PTSD, and led to 60% endpoint cessation rate with active bupropion compared to placebo (0%).

- **McFall et al. (2005)** - demonstrated that integrated treatment of nicotine dependence and PSTD in the same clinic lead to the best smoking cessation outcomes.

- **George et al. (2006), in progress.** Double-blind, placebo controlled trial of bupropion SR in smokers with Bipolar I Disorder. Still blinded but overall 33% quit rate, and bupropion does not lead to emergence of mania/hypomania in outpatients stabilized on mood stabilizers.

- Documentation of Risks and Benefits: No 30%
- Coding of Nicotine Dependence on Admission: No 100%
- Inclusion of Nicotine Dependence in Master Treatment Plan: No 100%
- Coding of Nicotine Dependence at Discharge: No 100%
- Inclusion of Tobacco Use in Discharge Planning: No 100%

Hackney, Potenza, DiGiorgio and George, 2006
Reduced Smoking – A Viable Target or Not?

- Many smokers especially those with SMI’s are simply unable to quit smoking.
- Should sustained reductions in smoking been considered a goal of tobacco treatment or should reduction be a transitional goal towards eventual smoking abstinence (Hughes, 2002; George and Vessicchio, 2002; McChargue et al., 2002)?
- But, the question of whether sustained reductions in smoking consumption can accrue health benefits has not been proven, in fact a recent study suggests that sustained smoking reductions do not reduce cancer or cardiac disease risk (Tverdall and Bjartveit, 2006).
Figure 1  Deaths from (A) all causes, (B) cardiovascular disease and (C) smoking-related cancer, as cumulative proportions of male and female participants in each category, by time of death. Nelson-Aalen cumulative hazard estimates. The x axis shows the observation years and the y axis shows the cumulative proportions.
## Recommendations for the Treatment of Nicotine Dependence in Psychiatric and Substance Use Disorders

<table>
<thead>
<tr>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>● Identification of cigarette smoking at each clinic visit</td>
</tr>
<tr>
<td>● Assessment of motivation to quit smoking</td>
</tr>
<tr>
<td>● Focus on motivating smokers to quit, and teaching basic smoking cessation</td>
</tr>
<tr>
<td>counseling skills to the smoker *(e.g., motivational interventions, stimulus</td>
</tr>
<tr>
<td>control and relapse-prevention skills)*</td>
</tr>
<tr>
<td>● Adjunctive use of combination treatments *(e.g. NRT plus sustained-release</td>
</tr>
<tr>
<td>bupropion)* in refractory cases of nicotine dependence</td>
</tr>
<tr>
<td>● Aggressive treatment of PD and/or SUD first, then treatment of nicotine</td>
</tr>
<tr>
<td>dependence <em>(sequential treatment)</em></td>
</tr>
<tr>
<td>● Use of pharmacotherapies which target the underlying pathophysiology of the</td>
</tr>
<tr>
<td>PD/SUD that constitutes a vulnerability factor for cigarette smoking *(e.g.,</td>
</tr>
<tr>
<td>atypical antipsychotics in schizophrenia, antidepressants in major depression,</td>
</tr>
<tr>
<td>naltrexone for alcoholism)*</td>
</tr>
</tbody>
</table>