HIV and Co-morbidities:

Tackling depression and cardiovascular disease with an HIV Quit Smoking Pilot Study

Louise Balfour PhD
Paul MacPherson PhD, MD, FRCP
Division of Infectious Diseases
Ottawa Hospital
University of Ottawa, Ontario, Canada
HIV and Cardiovascular Health
New HIV Medications

- The new reality
- Normal or near-normal life expectancy
- For those diagnosed with HIV at age 20, life expectancy is now 65.8 years.

With longer life expectancy, we are starting to see new problems not previously in the HIV population: HIV co-morbidities

1. Cardiovascular disease

2. Cancers
Cardiovascular Disease and HIV

• HIV+ pts across all age groups are 2-4 times more likely to suffer an acute myocardial infarction (AMI).

• Rates of AMI ages 18 to 34 years:
  – HIV+: 4.65 per 1000 person years (RR: 5.3)
  – HIV-: 0.88 per 1000 person years
    » Triant et al., 2007

• DAD cohort: 41.3% of HIV+ pts are at high risk of cardiovascular disease.
Why?
Many Reasons Why ...

1. Traditional Cardiac risk factors:
   - PHAs are Aging, male, co-morbidities diabetes
2. HIV infection, inflammation, and immune dysregulation
3. Increased serum lipids among HIV+ pts
4. Many HIV patients smoke cigarettes
### Comparisons of Smoking Rates

<table>
<thead>
<tr>
<th>Population</th>
<th>Smoking Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>U.S. General</strong></td>
<td></td>
</tr>
<tr>
<td>Females</td>
<td>22 %</td>
</tr>
<tr>
<td>Males</td>
<td>20 %</td>
</tr>
<tr>
<td><strong>U.S. Medicaid patients</strong></td>
<td>36 %</td>
</tr>
<tr>
<td><strong>HIV+ National samples</strong></td>
<td>45-51 %</td>
</tr>
<tr>
<td><strong>HIV+ Outpatient clinics</strong></td>
<td>47-72 %</td>
</tr>
</tbody>
</table>

**Sources:** CDC, 2001; 2004; Collins et al., 2001; Turner et al., 2001; Gritz, et al., 2004; Mamary, et al., 2002; Niaura et al., 1999
Comparisons of Smoking Rates

<table>
<thead>
<tr>
<th>Population</th>
<th>Smoking Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canadian Adults</td>
<td>19 %</td>
</tr>
<tr>
<td>HIV+ pts Ontario (OHTN cohort)</td>
<td>54 %</td>
</tr>
<tr>
<td>HIV+ pts at Ottawa HIV clinic</td>
<td>43-49%</td>
</tr>
<tr>
<td>Ottawa population</td>
<td>12 %</td>
</tr>
</tbody>
</table>

Sources:
(Stein et al., 2008; Health Canada, 2007)
(Balfour et al., 2006)
4. Too many people living with HIV smoke

- **DAD cohort**: After pre-existing CVD, smoking was identified as the most significant predictor of CVD in the HIV+ population (RR: 2.92).
HIV and Cigarette Smoking

• Given the high rates of smoking among PHAs and the link between smoking and CVD, the issue of CVD in HIV clinical care is of great importance.

• Regular HIV clinical care would benefit from research on the effectiveness of HIV quit smoking interventions towards improving health outcomes such as:
  – Improved cardiovascular and lung health
  – Reduced rates of cancers
  – Improved mental and physical quality of life
However, there are unique considerations when looking at smoking cessation for PHAs
Potential Complications and issues: How do smoking cessation interventions interact with:

1. Immune suppression
2. Antiretroviral therapy and drug-drug interactions
3. Depression
Smoking and Depression and HIV

- Many people (60%) with depression smoke cigarettes.
- People who feel depressed may smoke to “self-medicate” with nicotine to “boost” their mood.
- Depressed smokers are less likely to successfully “stay quit”. They have high relapse rates.
- 40-60% of PHAs report symptoms of depression.
- 40-60% of PHAs smoke cigarettes.
Trying to quit smoking and “stay quit” …
Challenging Symptoms of Nicotine Withdrawal
Nicotine Withdrawal

- Nicotine withdrawal syndrome consists of both physical and affective symptoms

Withdrawal Syndrome

- Irritability, frustration, or anger
- Anxiety (may increase or decrease with quitting)
- Restlessness or impatience
- Difficulty concentrating
- Increased appetite or weight gain
- Dysphoric or depressed mood
- Insomnia/sleep disturbance

Quit Smoking: (Best to combine Counseling and Pharmacotherapy) Why?

- Smokers who try to “quit on their own” have 6 month “still quit rate” of only 3-5% success
- In the general population, NRT patch compared to placebos increases 6 month success rate by 2 times
- In the general population, Champix compared to placebo increases success rate by 2.5-3 times
- Pharmacotherapy provides smokers with a relatively “withdrawal-free doorway” to quitting smoking and doubles or triples success rates
Quit Smoking Pharmacotherapy Options

- NRT (Nicotine Replacement Therapy) Patch
  - Long Acting
  - **Nicotine Replacement Patch** (“Nicoderm”, “Habitrol”)
  - Nicotine in the patch is absorbed into the bloodstream through the skin.
  - Peaks blood levels in 2 hours
  - Nicotine is released in a time-controlled manner (one patch is needed every 24 hours)
  - Available in three dose strengths - 21, 14, and 7mg
  - Dose depends on amount of cigarettes smoked prior to quit attempt
  - Average duration on NRT patch: 10-12 weeks
Pharmacotherapy Options

• NRT (Nicotine Replacement Therapy)
  – Short Acting
    • **Gum** (“Nicorette”)
      • Nicotine is absorbed into the bloodstream through the lining of the mouth.
      • Peak blood levels in 30 minutes
      • Eases cravings for a brief period.
      • Most people chew 10 pieces per day during the first week of quitting.
Pharmacotherapy Options

• NRT (Nicotine Replacement Therapy)
  – Short Acting

  • The **nicotine inhaler** (nicknamed "the puffer")

  • Thin, plastic cartridge that contains a porous nicotine plug in its base.

  • By puffing on the cartridge, nicotine vapor is extracted and absorbed through the lining of the mouth.

  • Peak blood levels in 10 minutes
Pharmacotherapy Options

• NRT (Nicotine Replacement Therapy)
  - **Short Acting**
    • **The nicotine lozenge**
      • Releases nicotine as it slowly dissolves in mouth.
      • Effects last 20-30 minutes
      • Must be careful not to eat/drink shortly before/after using the lozenge (like the gum, certain foods/drinks can alter the pH in the mouth which affects effectiveness of the product)

**Patch users are encouraged to carry the gum, inhaler, and/or lozenge in the event of increased cravings**
Pharmacotherapy Options

Oral Medication options

**Bupropion** (a.k.a. Wellbutrin, Zyban)
- Stimulates the areas of the brain involved in nicotine addiction
- Start 150 mg daily x 3 days then 150 mg BID
- Start one week before quit date
- Generally continue for 12 weeks
- Drug-drug interactions...Ritonavir may increase levels and thus there is risk of seizure.
Pharmacotherapy Options

Oral Medication options

**Varenicline** (a.k.a. Champix)

- Nicotine acetylcholine partial agonist and antagonist (prevents binding of nicotine but does stimulate partial release of dopamine)
- Titrate dose to reduce side-effects
- **Start one week before “quit date”**
- Continue for 12 weeks
- May exacerbate underlying psychiatric illness

http://www.champixinfo.co.uk/side-effects-contraindications.shtml
The First Ottawa Conference: State of the Art Clinical Approaches to Smoking Cessation, January 2009
There is a growing awareness that we need better options for HIV patients who want to Quit smoking...

- Unfortunately, very little research exists on smoking cessation interventions for PHAs;

- Tons of research publications reporting on the high rates of smoking among PHAs and how bad this is but...

- Until recently, there were no smoking cessation intervention studies conducted on PHAs
Responding to this need for HIV quit smoking interventions...what we did in Ottawa ...

- At The Ottawa Hospital, we obtained pilot funding for a small HIV quit smoking pilot project
- We approached Smoking cessation experts at Ottawa Heart Institute (Drs Pipe, Reid) to collaborate together
- No need to completely reinvent the Quit smoking wheel
- We could build from an established successful Quit Smoking program (i.e. The Ottawa Model for smoking cessation) and tailor and adapt the quit smoking program to the unique needs of PHAs.
Recent HIV Quit Smoking Studies

1. Champix HIV Quit Smoking Study, conducted in Hamilton, Ontario (Qu Cui et al Marek Smieja, in press) N = 36 HIV+ smokers, 32% quit rate at 6 months follow-up (depressed PHAs ?)

2. Two USA based RCT on HIV smoking cessation intervention using NRT alone vs NRT & support
USA large HIV quit smoking RCT Study: (Lloyd-Richardson et al 2009)

**Objective:** To compare the efficacy of usual care (UC) smoking cessation treatment (e.g. NRT) vs NRT plus Motivational Enhancement (ME) among PHAs.

**Method:** 444 PHAs were enrolled and randomized into either the Usual Care group (i.e. NRT) or Motivational Enhancement plus NRT. Follow ups were conducted at the HIV clinic 6 months post enrolment.

**Results:** Smoke free rate at 6 month post quit date follow-up:
- Usual Care (and NRT) = 9 % smoke free at 6 month follow-up
- Motivational Enhancement (and NRT) = 10 % smoke free at 6 month follow-up

**Conclusion:** No difference between groups in quit rates at 6 months follow-up

**Overall Statement:** Modest quit rates of 9-10% for PHAs
USA large HIV quit smoking RCT Study: (Vidrine et al 2011)

**Objective:** To compare the efficacy of usual care (UC) smoking cessation treatment (e.g. NRT) vs NRT plus cell phone counselling

**Method:** 474 HIV pts were enrolled and randomized into either the Usual Care group (i.e. NRT) or NRT plus cell phone counselling

Follow ups were conducted at the HIV clinic 3 months post enrolment.

**Results:**
- Usual Care (and NRT) = 3.3% smoke free at 3 month follow-up
- Cell phone Counselling and NRT) = 11.9 % smoke free at 3 month follow-up

**Conclusion:** Cell phone counselling plus NRT patch was better than NRT patch alone

**Overall,** modestly successful quit rates for HIV+ pts (3-12% quit) (Vidrine et al., 2011)
HIV Quit Smoking Pilot Study

L Balfour, V Illing, D Sandre, C laPorte, E Lough, E. Bickerton, A Pipe, R Reid, D Aitken, K Corace, G Tasca, J Angel, G Garber, C Cooper, W Cameron, P Giguere, C Lee, and P MacPherson

1The University of Ottawa at The Ottawa Hospital, Ottawa, Ontario, Canada
2Ottawa Hospital Research Institute, Ottawa, Ontario, Canada
3University of Ottawa Heart Institute, Ottawa, Ontario, Canada
HIV Smoking Cessation Project

Goals of Pilot Project:

(1) To develop a brief HIV smoking cessation intervention tailored to the specific needs of PHAs (i.e. it would include Nicotine Replacement Therapy (NRT) patch, counseling support for coping with symptoms of withdrawal and depression, and address HIV specific concerns)

(2) To evaluate the short and long term physical and psychological outcomes of such an HIV Quit Smoking program.

Note: HIV Quit Smoking Pilot Study is approved by TOH’s Research Ethics Board
Pilot HIV Smoking Cessation Project

STUDY Goals:
From baseline to 6 month follow-up after quit date,
(1) Decreased smoking (expected 10-30% of HIV pts will stay quit at 6 months follow-up)

(2) PHAs who maintain a smoke-free status will also:
- (a) Experience a decrease in Nicotine Dependence
- (b) Report increased knowledge about NRT patch

(3) Both Depressed and Non-depressed smokers will have an equal chance of staying quit at 6 month follow-up (our HIV tailored quit smoking counselling intervention also helps patients cope with symptoms of depression)
Method:

Recruitment

- HIV patients were recruited during regular HIV clinic visits at The Ottawa Hospital-General campus
- Waiting Room Smoking Screening forms completed in order to identify current smokers interested in quitting in the next month
- HIV+ smokers eligible for the study were contacted by research coordinator, described the study, and interested participants completed consent forms
Study participants include N=50 HIV+ smokers

*Blood-work and Vital Stats
Metabolic, Lipid & CVD Parameters
Weight,
Waist circumference
Blood pressure
Hyperglycemia (HbA1C)
Serum lipids

*at Baseline, then at weeks 4, 12, and 24 Post Quit Date.

Smoking Status
- **Bedfont Smokerlyzer**
  (Smoke free = CO < 10 ppm)
- Self Report on Smoking status
1. The Center for Epidemiological Studies Depression Scale (CES-D):
   A 20-item widely used and psychometrically-validated self-report measure of depression where a score >16 is an indicator of depressive symptoms (Radloff, 1977; Schoevers et al., 2000).

2. Fagerstrom Test for Nicotine Dependence (FTND):
   A 6-item questionnaire that measures participants’ extent of dependence on nicotine (Heatherton et al, 1991; Pomerleau et al, 1994; Lloyd-Richardson et al, 2008).
HIV Quit Smoking Intervention Components

Smoking cessation program includes meeting with a trained smoking cessation counselor:

The counselor helps with:

(1) Developing a **Personalized Quit Smoking Plan** (e.g. prepare and plan for a “quit date” within 1 month)
(2) **Nicotine Replacement Therapy (NRT)** – free Nicotine patches (dose adjusted) for 10 weeks
(3) **Ongoing individual counseling support sessions** (Using our HIV quit smoking Treatment Manual) Addresses coping with withdrawal, urges, depression
(4) **Additional telephone support** (Interactive Voice Response (IVR)-Ottawa Model-Heart Institute)
### Participant Characteristics (N=50)

<table>
<thead>
<tr>
<th>Age (mean yrs ± SD)</th>
<th>Concurrent Substance Users</th>
</tr>
</thead>
<tbody>
<tr>
<td>45 ± 9</td>
<td>Cigarettes smoked/day (mean ± SD)</td>
</tr>
<tr>
<td>Male</td>
<td>Caffeine (4+ servings/day)</td>
</tr>
<tr>
<td>Caucasian</td>
<td>Alcohol (&gt;1-2 times/week)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sexual Orientation¹</th>
<th>Daily Marijuana Users</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heterosexual</td>
<td>88 %</td>
</tr>
<tr>
<td>Gay/Lesbian</td>
<td>97 %</td>
</tr>
<tr>
<td>Other</td>
<td>40 %</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Level of Education¹</th>
<th>Employment Status⁵</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grades 1-8</td>
<td>Employed Full/Part time</td>
</tr>
<tr>
<td>High School</td>
<td>Unemployed</td>
</tr>
<tr>
<td>Some College</td>
<td>Disability</td>
</tr>
<tr>
<td>University Degree</td>
<td>Other (e.g. Student, Homemaker)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Live with Smoker</th>
<th>Depression CES-D Score of &gt;16</th>
</tr>
</thead>
<tbody>
<tr>
<td>54 %</td>
<td>48 %</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CD4 count</th>
<th>Viral Load &lt; 50 copies</th>
</tr>
</thead>
<tbody>
<tr>
<td>540 ± 262</td>
<td>77 %</td>
</tr>
</tbody>
</table>

**NOTE:** Percentages may not sum to 100 due to rounding errors.
<table>
<thead>
<tr>
<th>Study Visit</th>
<th>Number of Participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>50</td>
</tr>
<tr>
<td>Quit Date</td>
<td>50</td>
</tr>
<tr>
<td>4 week follow up</td>
<td>33</td>
</tr>
<tr>
<td>3 months follow up</td>
<td>24</td>
</tr>
<tr>
<td>6 months follow up</td>
<td>17</td>
</tr>
</tbody>
</table>
Main Study Results: Smoking Quit Rates

- 27% of PHAs in our pilot HIV Quit Smoking Study had completely stopped smoking and were still smoke free at 6 months follow-up

Note: Data from a previous cohort of HIV+ patients who were smokers at the Ottawa Hospital, we found that there was a 0% spontaneous quit rate in HIV+ smokers followed over a 6 month period
## Objective CO level Quit Smoking Data

| CO Levels (ppm) (mean±SD) | Quit Date: 18.3 ± 9.84 | 6 Month follow-up 7.7 ±11.8 *** |

CO Levels: <10 ppm is considered smoke-free status (***p<0.001)
## Nicotine Dependence: Baseline to 6 mts (N=17)

<table>
<thead>
<tr>
<th>Overall Score: Fagerstrom Test of Nicotine Dependence (FTND)</th>
<th>Quit Date</th>
<th>Week 4</th>
<th>Week 24</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.5 ± 0.9</td>
<td>2.6 ± 3.3</td>
<td>2.2 ± 3.2</td>
<td></td>
</tr>
</tbody>
</table>

### Items from the Fagerstorm Test of Nicotine Dependence Questionnaire

1. **How soon after you wake up do you smoke your first cigarette?**
   - <5 min (3); 6-30 min (2); 31-60 min (1); >60 min (0)

2. **Do you find it difficult to refrain from smoking in places where it is forbidden?**
   - Yes(1); No (0)

3. **Which cigarette would you hate to give up most?**
   - The first in the morning (1); Any other (0)

4. **How many cigarettes do you smoke per day?**
   - <10 (0); 11-20(1); 21-30 (2); >30 (3)

5. **Do you smoke more frequently during the first hours after waking than during the rest of the day?**
   - Yes(1); No (0)

6. **Do you smoke even if you are so ill that you are in bed most of the day?**
   - Yes(1); No (0)

### Nicotine Dependence Score Legend:
- 0-2 = very low nicotine dependence
- 3-4 = Low Dependence
- 5 = medium Dependence
- 6-7 = High Dependence
- 8-10 = Very High Dependence

(** p<0.001, *p<0.05; significant from Baseline Scores)**
Summary of Results

(1) 27 % quit rates at 6 month follow-up (objectively verified by CO levels)

(2) Reduced nicotine dependence levels for those who stayed quit at 6 months follow-up

(3) Both depressed and non-depressed HIV pts had an equal chance of staying quit at 6 months follow-up
Next Steps

GREAT follow-up news:
We obtained CIHR funding for a 1 year for a CIHR catalyst grant to expand our HIV quit smoking program

Title: The HIV quit smoking program: Tackling the co-morbidities of cardiovascular disease and depression

Goals of CIHR Catalyst Grant:
(1) To create new multi-d partnerships to assess and address the problem of smoking in HIV+ pts across Canada
   - To raise awareness of the links between HIV smoking, depression, and CVD among Health Care providers
   - (conduct KT workshops at HIV clinics across Canada, stimulate new CTN site partnerships for larger RCT)
Next Steps

Goals of CIHR Catalyst Grant:

(2) To assess the feasibility of conducting an RCT of the HIV quit smoking intervention at Partnering HIV clinic sites by assessing the:

(i) rates of smoking among PHAs at each site
(ii) the interest among PHAs in quitting smoking at each site
(iii) the available infrastructure at each site (e.g. CTN research coordinator, nurses, psycho-social support) and staffing needs to conduct the HIV quit smoking program at each site
Next Steps

Goals of Catalyst Grant:

(3) To update the content of our pilot HIV quit smoking intervention manual and design a multi-site RCT for the HIV quit smoking intervention Program

- To organize national meetings between partnering sites (e.g. with CTN) to collaborate with other smoking cessation experts in Canada (e.g. Marek, Hamilton) in the design of the RCT.

- We used the data from the two Canadian quit smoking pilot studies to inform the sample size calculations of the RCT
Next Steps

Final Goal of CIHR Catalyst Grant:

We submitted our comprehensive, Canadian multi-site RCT on HIV quit smoking intervention to CIHR’s 2011 competition
STUDY Proposal:
Canadian HIV Quit Smoking Trial

4 Groups – Randomized Controlled Trial (N=256)

(1) CHAMPIX (& Usual Care)
(2) CHAMPIX (& HIV Quit Smoking Counselling)
(3) NRT Patch (& Usual Care)
(4) NRT Patch (& HIV Quit Smoking Counselling)
<table>
<thead>
<tr>
<th>Drug Type</th>
<th>CHAMPIX (&amp; Usual Care) N=64</th>
<th>CHAMPIX (&amp; HIV Quit Smoking Counselling) N=64</th>
</tr>
</thead>
<tbody>
<tr>
<td>NRT Patch &amp; Usual Care</td>
<td>N=64</td>
<td>N=64</td>
</tr>
<tr>
<td>NRT Patch &amp; HIV Quit Smoking Counselling</td>
<td>N=64</td>
<td>N=64</td>
</tr>
</tbody>
</table>

(Total N=256)
Thank you!!

- Garcías “CORPORACIÓN DE LUCHA CONTRA EL SIDA”
- Research Supported by:
  - University of Ottawa Dept of Medicine
  - Canadian Foundation for AIDS Research (CANFAR)
  - Bristol-Myers Squibb, Janssen
  - CIHR

Collaborators:

- The University of Ottawa Heart Institute
- The Division of Infectious Diseases at The Ottawa Hospital
- PHA study participants

This study was also supported by the Canadian HIV Trials Network (CTN 008).
Thank You !  Gracias !

Strength in Team Work