

HIV and Co-morbidities:

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



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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.
 - May et al. (2010) Tenth International Congress on Drug Therapy in HIV Infection.

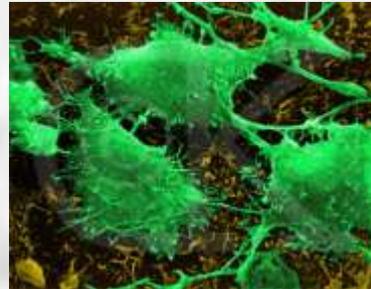


With longer life expectancy, we are starting to see new problems not previously in the HIV population: HIV co-morbidities

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

Population	Smoking Rate
U.S. General	22 %
Females	20 %
Males	24 %
U.S. Medicaid patients	36 %
HIV+ National samples	45-51%
HIV+ Outpatient clinics	47-72%

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

Population	Smoking Rate
Canadian Adults	19 %
HIV+ pts Ontario (OHTN cohort)	54 %
HIV+ pts at Ottawa HIV clinic	43-49%
Ottawa population	12 %

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:

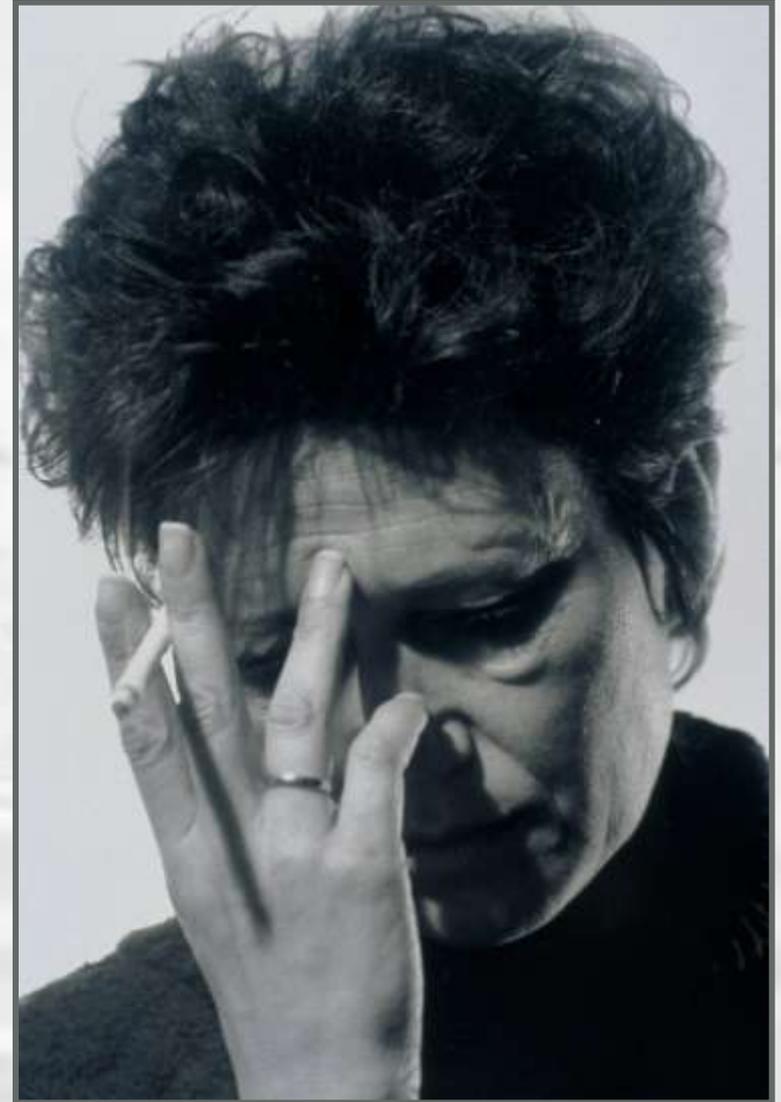
How do smoking cessation interventions interact with:

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

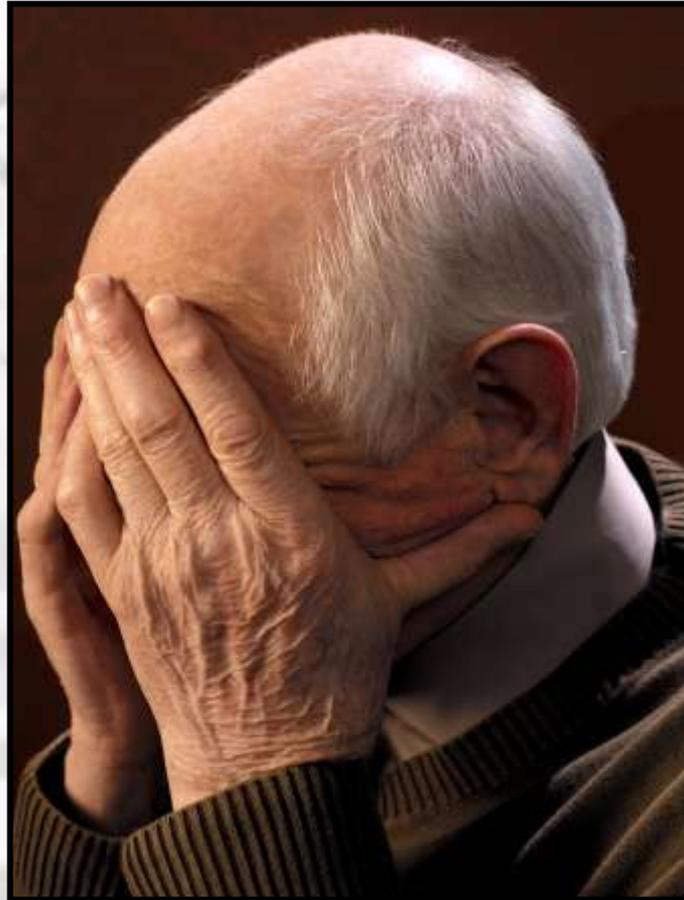


Smoking and Depression and HIV

- 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

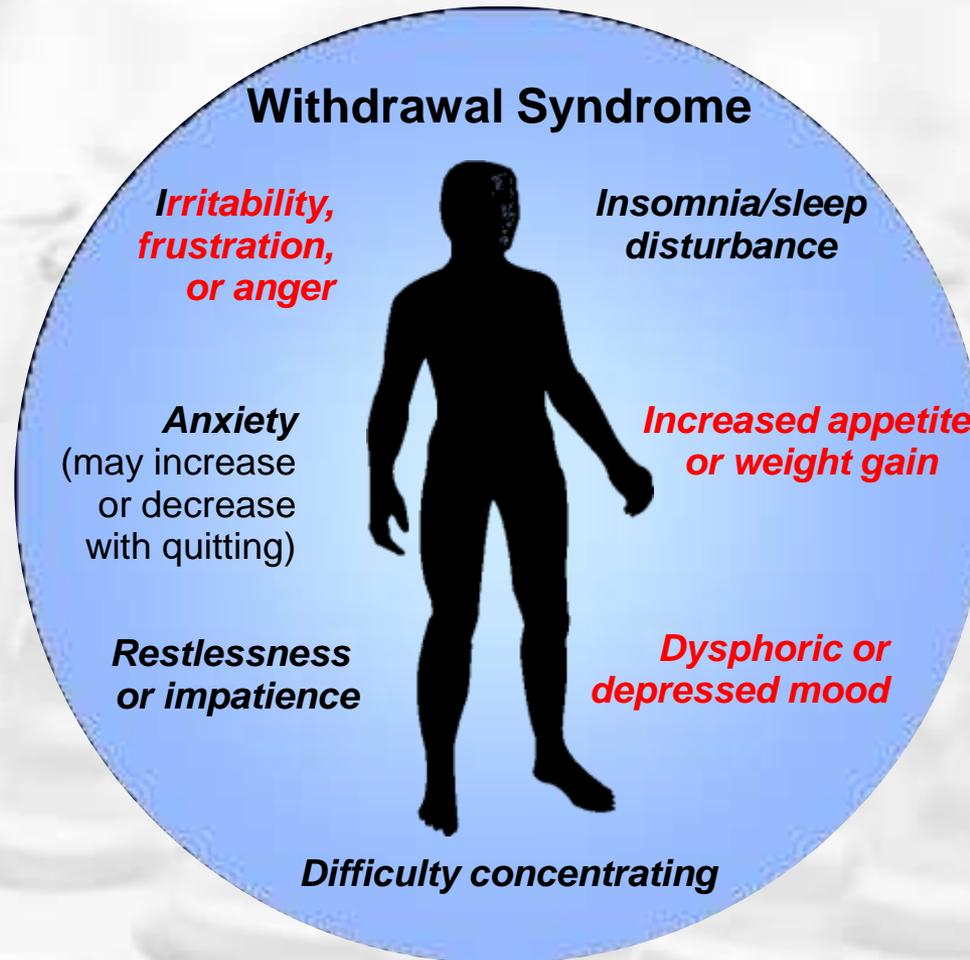


Trying to quit smoking and “stay quit” ... Challenging Symptoms of Nicotine Withdrawal



Nicotine Withdrawal

- **Nicotine withdrawal** syndrome consists of **both physical** and **affective symptoms**



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 quite 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



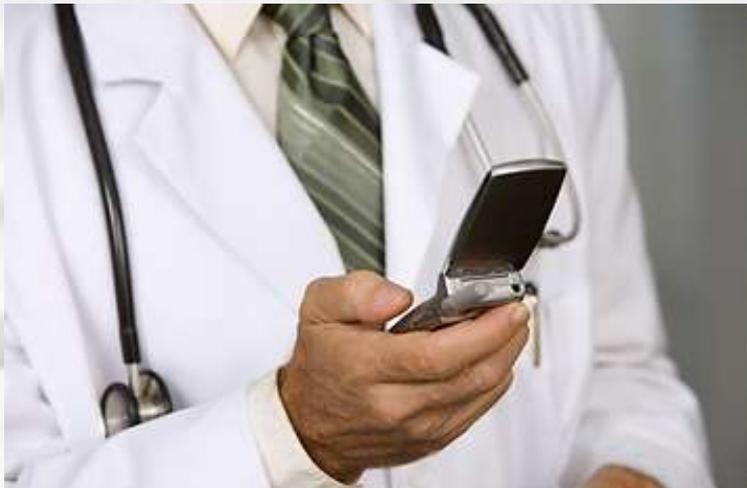
Responding to this need for HIV quit smoking interventions...what we did in Ottawa ...

- 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)



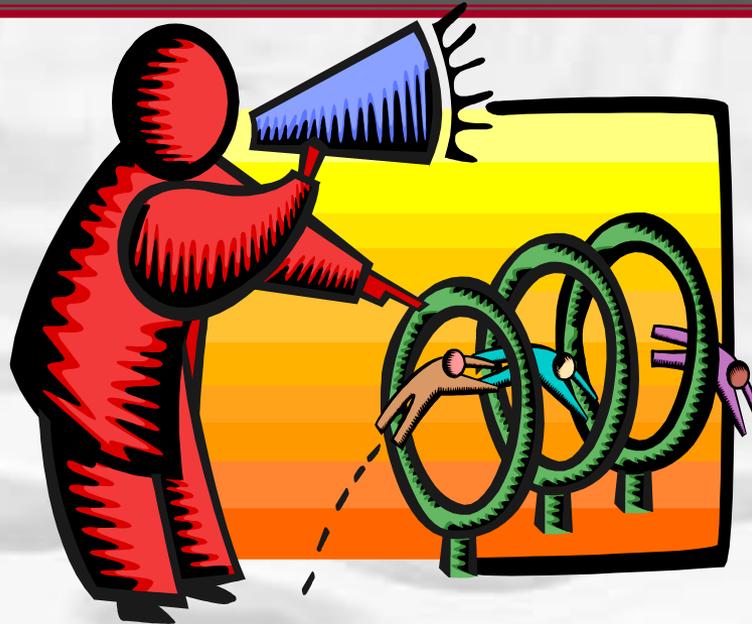
HIV Quit Smoking Pilot Study

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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



METHOD - STUDY MEASURES

- 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



Psychological Questionnaires:

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)

Age (mean yrs \pm SD)	45 \pm 9	Concurrent Substance Users	
		Cigarettes smoked/day (mean \pm SD)	18 \pm 8
Male	88 %	Caffeine (4+ servings/day)	24 %
Caucasian	97 %	Alcohol (>1-2 times/week) ¹	16 %
Sexual Orientation¹		Daily Marijuana Users	26 %
Heterosexual	40 %	Employment Status⁵	
Gay/Lesbian	52 %	Employed Full/Part time	34 %
Other	6 %	Unemployed	8 %
Level of Education¹		Disability	44 %
Grades 1-8	8 %	Other (e.g. Student, Homemaker)	3 %
High School	28 %	Live with Smoker	54 %
Some College	40 %	Depression CES-D Score of >16	48 %
University Degree	22 %	CD4 count	540 \pm 262
		Viral Load < 50 copies	77 %

NOTE: Percentages may not sum to 100 due to rounding errors.



Number of Participants at Each Study Time Point

Study Visit	Number of Participants
Baseline	50
Quit Date	50
4 week follow up	33
3 months follow up	24
6 months follow up	17



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



Quit Date:

6 Month follow-up

CO Levels
(ppm)
(mean \pm SD)

18.3 \pm 9.84

7.7 \pm 11.8 ***

CO Levels: **<10 ppm** is considered smoke-free status (**p<0.001)



Nicotine Dependence: Baseline to 6 mts (N=17)

	Quit Date	Week 4	Week 24
Overall Score:	6.5 ± 0.9	2.6 ± 3.3	2.2 ± 3.2
Fagerstorm Test of Nicotine Dependence (FTND)			

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)



Counselling

**Drug
Type**

CHAMPIX (& Usual Care) N=64	CHAMPIX (& HIV Quit Smoking Counselling) N=64
NRT Patch (& Usual Care) N=64	NRT Patch (& HIV Quit Smoking Counselling) N=64

(Total N=256)



Thank you!!

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 - CIHR

Collaborators:

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

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Thank You ! Gracias !



Strength in Team Work

