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**Our Issues, Our Drugs,
Our Patients**

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SMOKING IN HIV



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- Smoking accounts for more life-years lost than HIV infection itself in areas with well-run HIV services
- Mortality rate per 100 person-years
 - HIV negative never smokers 1.76
 - HIV positive never smokers 2.45
 - HIV positive current smokers 5.48

SMOKING



COMMUNICABLE DISEASES

- Bacterial pneumonia
- Tuberculosis
- Pneumocystis pneumonia

NON-COMMUNICABLE DISEASES

- COPD
- Lung cancer
- Cardiovascular disease
- Oral thrush
- Oral hairy leukoplakia
- Cognitive and neurological effects, etc.

EFFECTS ON HIV INFECTION

- Faster progression to AIDS?
- Poorer response to ART?

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SMOKING CESSATION

COMMUNICABLE DISEASES

- Bacterial pneumonia
- Tuberculosis
- Pneumocystis pneumonia

BACTERIAL PNEUMONIA

- Increased risk for pneumonia at all levels of immunosuppression and despite ART

TABLE 3. BASELINE PREDICTORS FOR BACTERIAL PNEUMONIA BY STUDY ARMS—DRUG CONSERVATION AND VIRAL SUPPRESSION

Predictors	n (%)	Univariate Cox Regression*			Multivariate Cox Regression†		
		Hazard Ratio	95% CI	P Value	Hazard Ratio	95% CI	P Value
Treatment group							
DC	2720 (49.7)	1.55	1.07–2.25	0.02	1.55	1.07–2.25	0.02
VS	2752 (50.3)						
Cigarette smoking							
Current	2,215 (40.5)	2.19	1.34–3.60	0.002	1.82	1.09–3.04	0.02
Past	1,358 (24.8)	1.80	1.04–3.11	0.03	1.64	0.94–2.86	0.08
Never (ref)	1,899 (34.7)	1.00			1.00		

Cigarette smoking was the strongest predictor for development of pneumonia in the viral suppression arm.

TUBERCULOSIS

- “Syndemic” of HIV and TB
- Smoking associated with
 - Increased predisposition to TB infection and TB disease (despite ART)
 - More rapid disease progression of disease
 - Poorer response to treatment
 - Longer duration of infectivity
 - Higher likelihood of recurrence
 - Higher mortality despite appropriate TB treatment
- Estimated that 16% of TB cases preventable with elimination of smoking

TB OUTCOMES IN HIV SMOKERS

- Ever smokers 30% less likely to initiate ART (even though eligible)
- Ever smokers more likely than never smokers to have adverse TB Rx outcomes (lost to follow-up, death, Rx failure): HR 2.15
- Smokers for ≥ 10 years + initiated ART during TB Rx
 - More likely to be lost to follow-up (HR 5.11)
 - Higher mortality (HR 3.81)

PNEUMOCYSTIS JIROVECI PNEUMONIA

Increased risk of PCP in smokers

- 125 patients admitted with PCP
- 78% cigarette smokers
- CD4 < 200 x 10⁶/L: OR current vs non-smokers 2.7
- Dose-dependent relationship: 3% risk/cigarette/day
 - One pack/day: OR 1.8
 - Two packs/day: OR 3.35

COLONIZATION WITH PCP

TABLE 3 Risk factors for *Pneumocystis* colonization

Risk factor

Associated medical conditions

Chronic lung disease, especially COPD

Pregnancy

HIV infection

Autoimmune disease

Young children, especially during upper respiratory infections

Malignancy

Organ transplantation

Medications

Corticosteroids

TNF- α inhibitors

Other immunosuppressives

Clinical risk factors

Low CD4⁺ cell count

Cigarette smoking

Geographic location

History of recent PCP exposure

Lack of PCP prophylaxis

- Prevalence of colonization with PCP
 - Healthy subjects: up to 20%
 - HIV-infected subjects: 20–69%
- Risk of colonization amongst smokers: OR 2.9
- PCP prophylaxis does not reduce risk of colonization

NON-COMMUNICABLE DISEASES

- COPD
- Lung cancer

COPD

- HIV is independent risk factor for COPD
- Develops over much shorter period of time in HIV infected smokers than in HIV uninfected smokers
- Frequently unrecognized
 - Report of 338 HIV positive smokers (≥ 20 pack years)
 - Prevalence of COPD: 26%
 - Undiagnosed COPD: 74%
- Possible association with PCP

- Acute exacerbations of COPD
 - Rate higher in HIV-infected vs HIV-uninfected (IRR 1.54)
 - HIV-related risk factors
 - Lower CD4 count
 - HIV RNA levels > 500 copies/ml
 - Not on ART
 - Alcohol-related conditions (even after controlling for smoking)

LUNG CANCER

- Increased susceptibility (lower pack-year history)
- Earlier age at presentation
- More advanced disease at presentation
- Worse outcome

- Possible mechanisms
 - High smoking rates in HIV population
 - Decreased immunovigilance (despite ART)
 - Chronic lung damage from infections
 - Enhanced inflammation
 - Increased lifespan due to ART and better healthcare

Table 2. Crude Cancer Type-Specific Incidence Rates and All-Cause Death Rates, by HIV Infection Status, NA-ACCORD, 1996-2009

Event	Persons With HIV		Uninfected Persons	
	Persons, <i>n</i>	Incidence Rate per 100 000 Person-Years	Persons, <i>n</i>	Incidence Rate per 100 000 Person-Years
Kaposi sarcoma	612	130.4	3	0.2
Non-Hodgkin lymphoma	725	153.5	233	12.6
Lung cancer	614	129.3	839	45.4
Anal cancer	285	60.1	22	1.2
Colorectal cancer	173	36.4	510	27.7
Liver cancer	220	46.3	201	10.9
Hodgkin lymphoma	159	33.5	36	1.9
Melanoma	78	16.4	268	14.5
Oral cavity/pharyngeal cancer	163	34.3	340	18.4
Death	17 534	3686.0	15 400	833.0

NA-ACCORD = North American AIDS Cohort Collaboration on Research and Design.

SCREENING FOR LUNG CANCER IN HIV INFECTED POPULATION

- 442 patients underwent LDCT scans
 - Prevalence of lung cancer 2.03%
 - Positive images in 21%
 - 8 cancers occurred in patients < 55 years
- Possible concerns
 - Higher number of false positives due to previous lung infections?
 - Need to lower age at which screening should be performed?

EFFECTS OF SMOKING ON HIV INFECTION

- Faster progression to AIDS?
- Poorer response to ART?

EFFECT OF SMOKING ON HIV

- ? Adverse effect on HIV disease progression
 - Conflicting studies

Table 1 Sociodemographic and clinical characteristic differences between PLWH receiving Ryan White Part A services in the New York Eligible Metropolitan Area with and without recent tobacco smoking (N = 14,713)

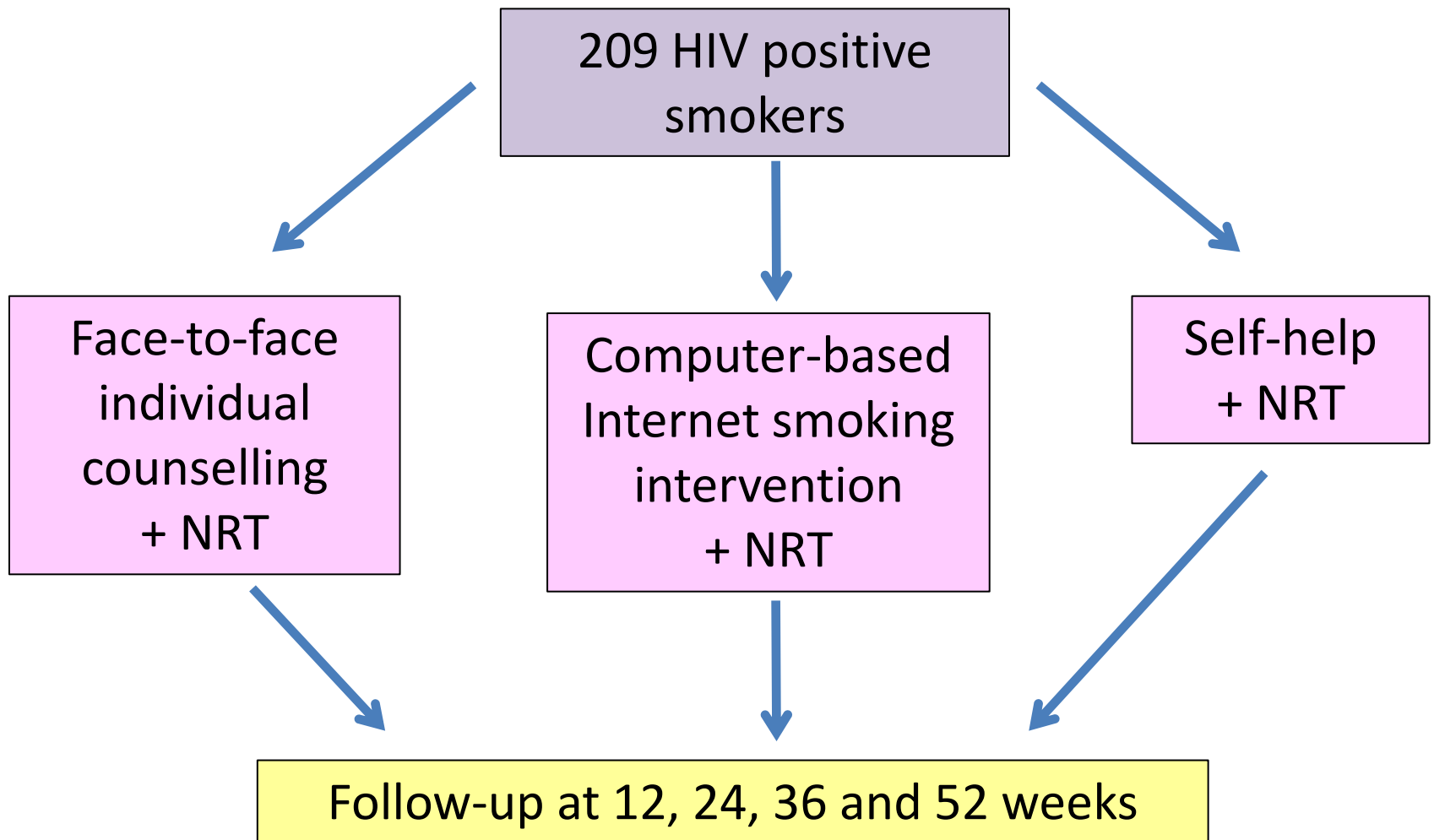
Characteristic ^a	Recent tobacco smoking N = 5942 (40 %) n (col %)	No recent tobacco smoking N = 8771 (60 %) n (col %)	P value
Low CD4 cell counts ^c	1321 (23.4 %)	1506 (18.1 %)	<.001
Unsuppressed viral load ^d	2658 (46.4 %)	2688 (31.8 %)	<.001

Largest study sample to date examining relationship between smoking and biomarkers of HIV disease progression

- Smokers have poorer response to ART than non-smokers
 - Surrogate marker for non-adherence
 - More side-effects to drugs in smokers
 - Activation of genes by cigarette smoke which promote HIV replication
 - Altered pharmacokinetics

SMOKING CESSATION

- Counselling
- Cognitive therapy (adjustment skills)
- Pharmacotherapy
 - Nicotine replacement therapy
 - Bupropion
 - Varenicline



- No significant difference between 3 groups (abstinence 15-29%)
- Factors associated with achieving abstinence: employment, greater desire to quit, lower mood disturbance score

VARENICLINE

- Adherence: only 58% at 1 month
- Safety: no difference in adverse effects in patients on ART vs no ART
- Efficacy: OR of abstinence at 3 months for Varenicline vs NRT: 2.75
- Adverse effects: not increased compared to HIV neg
 - Most common adverse effects: nausea, abnormal dreams, change in affect, insomnia
 - No effect on CD4 count or viral load

Shelley D et al. Nicotine & Tobacco Research 2015
Ferketich AK et al. Nicotine & Tobacco Research 2013
Cui Q et al. AIDS Patient Care and STDs 2012



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BARRIERS TO SMOKING CESSATION IN HIV PERSONS

- Failure of healthcare providers to
 - screen for smoking
 - promote smoking cessation
- Availability and cost of pharmacological therapy for smoking cessation
- Associated depression in smokers
- High rate of other substance abuse, e.g. alcohol
- Poor social support networks
- Use of tobacco as coping mechanism for HIV-related issues
- Perceived competence

THE WAY FORWARD

- Prioritization and integration of smoking cessation programmes into HIV/TB care programmes
 - Inexpensive
 - Sharing of resources
 - Holistic care

