

HIV/AIDS

Is smoking tobacco an independent risk factor for HIV infection and progression to AIDS? A systemic review

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Objectives: To systematically review the evidence of the relation between smoking tobacco and HIV seroconversion and progression to AIDS.

Methods: A systematic review was undertaken of studies to look at tobacco smoking as a risk factor for either HIV seroconversion or progression to AIDS.

Results: Six studies were identified with HIV seroconversion as an outcome measure. Five of these indicated that smoking tobacco was an independent risk factor after adjusting for important confounders with adjusted odds ratios ranging from 1.6 to 3.5. 10 studies were identified using progression to AIDS as an end point of which nine found no relation with tobacco smoking.

Conclusions: Tobacco smoking may be an independent risk factor for HIV infection although residual confounding is another possible explanation. Smoking did not appear to be related to progression to AIDS although this finding may not be true in developing countries or with the longer life expectancies seen with highly active antiretroviral therapy.

Tobacco and HIV/AIDS represent the only two major causes of death globally that continue to grow.¹ The intersection of these two epidemics represents an area of growing clinical and public health importance.

The global HIV epidemic largely affects developing countries. Of the world's 39.4 million people living with HIV/AIDS, 64% are in sub-Saharan Africa and 18% are from south and South East Asia.² Global tobacco related deaths are estimated to increase from 3.0 million in 1990 to 8.4 million in 2020. Tobacco use is projected to account for 9.0% of global disability adjusted life years (DALYs) by 2020, which would make it the world's single largest health problem.³

There is a growing recognition that cigarette smoking increases the risk of infection,⁴ including sexually transmitted infections.⁵ The possible mechanisms for this include structural modification in the lung and immunological changes. The latter include both cellular and humoral alteration such as decreasing the level of circulating immunoglobulins, the depression of antibody responses, a decrease in CD4 lymphocyte counts, an increase in CD8 lymphocyte counts, depressed phagocyte activity, and decreased release of proinflammatory cytokines.⁴ However it often remains unclear how these changes relate to clinical outcomes. The aim of this study was to systematically review the evidence on whether smoking tobacco is an independent risk factor for two clinically important outcomes for HIV infection—namely, seroconversion and progression to AIDS.

METHODS

Search strategy

In February 2005, we searched 13 bibliographic databases (Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, CINAHL, Database of Abstracts of Reviews of Effects (DARE), Embase, Health Management Information Consortium (HMIC), Medline, NHS HTA, PreMedline, PsychINFO, Science and Social Science Citation Indexes, the Current Controlled Trials database, and the UK National Research Register). We also conducted a search of abstract databases from three international AIDS conferences (2000, 2002, 2004), the World Health Organization website (www.who.int), and the Google search engine. Further unpublished reports were sought by contacting key experts and by a call for information through an email discussion group for tobacco control (Globalink). The reference lists from full papers were also checked. The searches were not limited by date.

Searches were performed using both free text and keywords. We used the following keywords and truncated free text terms: HIV, human immunodeficiency virus, human immune deficiency virus, HIV Infectio*, human immunodeficiency virus infection*, AIDS, acquired immunodeficiency syndrome, acquired immune deficiency syndrome, tobacco, smok*, nicotine*, cigarette smoking, and cigar*.

Inclusion criteria are listed in table 1. Exclusion criteria were studies concerned with paediatric HIV (for example, mother to child transmission), study participants who already had AIDS, and non-English language publications.

Analysis

Data were extracted independently by two researchers (AF and RM) using a standard proforma covering year of publication, setting/country, sample size, population characteristics, study design, outcome measures, findings, and study limitations. We extracted both adjusted and crude results where available. Where no effect size had been estimated we reviewed the

Abbreviations: CI, confidence interval; DALYs, disability adjusted life years; HAART, highly active antiretroviral therapy; OR, odds ratio; PCP, *Pneumocystis carinii* pneumonia; RH, relative hazard; RR, relative risk

Table 1 Inclusion criteria

Factor	Inclusion criteria
Population	Adults in populations exposed to HIV infection
Risk factor	Consumption of tobacco through smoking
Comparators	Equivalent population who have never smoked or who are not currently smoking
Outcome measures	Serologically confirmed HIV infection or progression to AIDS using standard definitions
Study type	All study types

available data to see if this could be calculated. We assessed study quality using the Newcastle-Ottawa Scale⁶ as recommended by the Cochrane Collaborative Review Group on HIV Infection and AIDS.⁷ Meta-analysis was not undertaken as the studies identified used such a variety of approaches that it was considered that pooled results would be potentially misleading.

As the study represents secondary research, we did not seek ethics committee approval.

RESULTS

Numbers of studies

We identified 3718 studies from the searches. After removing duplicates using Reference Manager software this number fell to 2808. The titles of these papers were reviewed to remove obviously irrelevant studies producing 121 references for which abstracts were read. From these, 49 papers were obtained and read in full; 15 papers met the inclusion criteria and are summarised in tables 2 and 3. Nine of these studies used progression to AIDS as an outcome measure, five used HIV seroconversion, and one used both.

Smoking tobacco as an independent risk factor for HIV infection

Six papers assessed whether smoking was associated with an increased risk of acquiring HIV infection (table 2). Of these five found that it was and one that it was not. The study that did not find an association¹⁷ produced an adjusted odds ratio of 1.22 in favour of an association but the 95% confidence interval (0.99 to 1.50) was consistent with no association. The other studies produced adjusted odds ratios ranging from 1.6 to 3.5. Crude odds ratios where provided were all larger than the adjusted ratios and ranged from 2.4 to 4.7. One paper¹⁸ did not provide an estimate of effect size and it was not possible to calculate one from the data provided.

Smoking tobacco as an independent risk factor for progression to AIDS

Ten papers assessed whether smoking was associated with more rapid progression to AIDS (table 3). Of these nine found no association. The study that did find an association was one of the poorer quality studies.³⁰ Although not formally within the terms of this review, it is worth noting that two studies did note an association between smoking and the development of bacterial pneumonia.^{23, 25} One of these²⁵ also noted an association between smoking and increased risk of developing AIDS related dementia but a protective effect against Kaposi's sarcoma.

DISCUSSION

The studies identified in this systematic review indicate that while smoking might be independently associated with acquiring HIV infection, it does not appear to be related to progression to AIDS.

The consistency of the findings is striking and represents a major strength of this review. While the studies vary in quality, they include reports of high quality investigations using large sample sizes. However the methodology necessarily used (epidemiological, observational studies) is unable to demonstrate causal relations and is prone to confounding. Most of the studies assessing the association between smoking and HIV seroconversion were cross sectional. The only truly prospective study¹⁷ found no association. In contrast, all of the studies investigating the association between progression to AIDS and smoking were cohort studies and eight out of the 10 were prospective. Confounding is more likely to occur when exposure is measured at the same time as outcome (as in cross sectional studies) and this may well explain the paradoxical finding of an

association between smoking and HIV seroconversion but not with progression to AIDS.^{8, 9}

The measurement of the relevant risk factors including sexual behaviour and smoking status is difficult: these were mostly assessed from self reported data. Current smoking status is possible to verify biochemically but none of the studies did this. While the fundamental potential risk factor is past rather than current smoking status, validation of current smoking status might have gone some way to confirming self reported data. The studies included in this review classified ex-smokers as non-smokers in their analysis. This could cause possible misclassification bias. The effect of this would be to reduce any association between smoking and HIV seroconversion and progression to AIDS. Although attempts were made to identify unpublished studies, publication bias cannot be ruled out. Investigators who did not find an association between smoking and HIV seroconversion may not have tried or have been able to publish their findings. However publication bias is unlikely to be a factor for progression to AIDS, given the lack of association with smoking in published studies.

However, the consistent finding of an association between smoking and increased risk of becoming HIV seropositive could be a real effect. There is a theoretical basis for smoking being related to an increased risk of infection generally and an observed association in other infections, including sexually transmitted infections.^{4, 5} The size of the effect observed (adjusted odds ratios ranging from 1.6 to 3.5) in the studies would indicate a magnitude of public health importance. Likewise, the consistent finding of no association between smoking and progression to AIDS could represent the true picture. Most of the studies were done before the widespread use of antiretroviral therapy and were conducted over a relatively short period of time in industrialised countries. In these circumstances it may be the case that smoking contributes little to the risk of developing AIDS. This may be because the immune mechanisms that smoking affects are less relevant in progression to AIDS than in acquiring the infection in the first place.

Further research is also needed to investigate whether the association between smoking and HIV seroconversion is related to residual confounding. Such research would need to prospectively record more accurately HIV risk behaviours including sexual intercourse and injecting drug use. Given the sensitivity of these issues and the difficulty of getting accurate self reported information, it may be preferable to "piggyback" studies on smoking and HIV onto ongoing cohort studies in high prevalence countries. The fact that all the studies that examined progression to AIDS were set in developed countries is an important limitation. Given that highly active antiretroviral therapy (HAART) has dramatically increased life expectancy for people with HIV, it may now be the case that smoking causes intercurrent illness, which could contribute to general debilitation and progression to AIDS. In particular, in developing countries where bacterial pneumonia might be less well treated and tuberculosis is more prevalent,¹⁰ smoking might be an important risk factor. Data from the United States suggest that smokers taking HAART had more inter-current, non-AIDS defining illnesses than non-smokers.¹¹ The relation between long term treatment, dyslipidaemia, and the development of cardiovascular disease will also be of importance when considering the effects of smoking.¹²

Although most studies identified in this review were set in developed countries, future research must examine the effect of smoking of people living with HIV in developing countries where the AIDS epidemic has the greatest impact. Although we already know tobacco control and smoking cessation are important public health measures, such research might add

Table 2 Papers using HIV seroconversion as the outcome measure ranked by study quality (best quality study first)

Ranking from quality assessment	Reference (date of publication) Setting/country	Design, population, and sample size	Relevant outcome measures	Findings	Quality assessment: study strengths	Quality assessment: study weaknesses
1	Halsey <i>et al</i> (1992) ¹⁴ Primary healthcare clinic in Cité Soleil, Haiti	Nested case-control study of 41 HIV positive women and 373 HIV negative women who had all participated while 6–7 months pregnant in a survey assessing HIV risk factors	HIV-1 serostatus	After adjustment for factors associated with HIV-1 infection and smoking in regression analysis, smoking was independently associated with HIV-1 infection (adjusted OR = 3.4, 95% CI = 1.6 to 7.5, crude OR = 4.7, 95% CI = 2.0 to 10.9) OR for HIV-1 seropositivity in smokers against non-smokers after adjusting for factors listed in next cell OR = 1.6 (95% CI = 1.1 to 2.4). The unadjusted OR = 2.4 (95% CI = 1.7 to 3.2)	Investigators blinded and important confounders taken into account (marital status, number of non-marital unions, visits to folk healers, religion, age at first intercourse, number of lifetime sexual partners, socioeconomic status as indicated by floor type in home) Interviewer-blinded, important confounders taken into account (history of sexually transmitted disease, number of sexual partners, maternal age, education, marital status, income, age at first pregnancy, parity, oral contraceptive use, partner circumcised, had sex to support herself)	Smoking status not biochemically validated
=2	Chao <i>et al</i> (1994) ¹⁵ Antenatal clinic serving a semirural population in Butare region, Rwanda	Cross sectional survey of 5690 pregnant women attending an antenatal clinic	HIV-1 antibody serology	Adjusted OR for HIV-1 seropositivity in smokers against non-smokers = 1.6 (95% CI 1.1 to 2.4). Dose-response effect noted between number of cigarettes smoked and risk of HIV-1 seropositivity. Crude OR not provided	Accounted for important confounders (marital status, age, previous pregnancy, number of sexual partners, positive VDRL (test for syphilis))	Recruitment method unclear (may not have been consecutive patients)
=2	Boulos <i>et al</i> (1990) ¹⁶ Outpatient clinics operated by a philanthropic organisation in a periurban slum in Port-au-Prince, Haiti	Cross sectional survey of 4485 pregnant women (6–7 months gestation) attending a well child clinic and also participating in a measles vaccine study	HIV-1 antibody serology	Smoking was not associated with HIV-1 seroconversion (adjusted OR = 1.22, 95% CI = 0.99 to 1.50, crude OR not provided)	Accounted for appropriate confounders (number of sexual partners, number of anonymous partners, condom use, CD4+ lymphocyte count, age, education, ethnic origin, alcohol use, and recreational drug use)	Recruitment method not adequately described, no biochemical validation of smoking status, assessors not blinded
=2	Penkower <i>et al</i> (1991) ¹⁷ Baltimore, Chicago, Los Angeles, and Pittsburgh, United States	A nested case-control study of 644 bisexual and homosexual men practising receptive anal intercourse drawn from a prospective cohort study (Multicentre AIDS Cohort Study). Seroincident men were matched with men who remained HIV negative throughout the study period (1984–7)	HIV-1 seroconversion	Participants who were initially HIV-1 seronegative were more likely to become seropositive if they smoked (p = 0.03). No difference between smokers and non-smokers in progression to AIDS (p = 0.31) or development of PCP. Insufficient data provided to calculate OR	Appropriate selection and comparability of exposed and non-exposed cohorts, good assessment of key confounders (number of partners, frequency of receptive anal intercourse, percentage of CD4+ and CD8+ lymphocytes)	No biochemical validation of smoking status, assessors not blinded
5	Burns <i>et al</i> (1991) ¹⁸ Primary care setting in Washington DC and New York, United States	Prospective cohort study of 202 homosexual men consecutively enrolled with three primary care physicians. Analysis included all those found to be HIV-1 antibody positive during enrolment (n = 84) and those who seroconverted (n = 47) during the observation period (1982–8). Control group were those who remained HIV-1 antibody negative at the end of the study period (n = 71)	HIV-1 antibody seroconversion, diagnosis of AIDS by CDC definition (1987)	In multivariate analysis, smoking was associated with HIV seropositivity (adjusted OR = 3.5, 95% CI = 1.2 to 10.5, crude OR = 3.7, 95% CI = 1.3 to 11.0)	Accounted for appropriate confounders (age, educational attainment, marital status, frequency of sex with a commercial sex worker, history of sexually transmitted infection)	Smoking status self reported and not biochemically validated. Assessors not reported as being blind to study hypothesis or outcomes. Unclear how key confounders were used in the analysis
6	Sirapapastiri <i>et al</i> (1996) ¹⁹ Sexually transmitted diseases clinic in Chiang Mai, Thailand	Cross sectional study of men attending the clinic. 124 men who were HIV negative and 26 who were HIV positive on recruitment were included	HIV serostatus			Recruitment methods unclear, no biochemical validation of smoking status, assessors not blinded

CI, confidence interval; OR, odds ratio; PCP, *Pneumocystis carinii* pneumonia; RH, relative hazard; RR, relative risk.

Table 3 Papers using progression to AIDS as the outcome measure ranked by study quality (best quality study first)

Ranking from quality assessment	Reference (date of publication) Setting/country	Design, population and sample size	Relevant outcome measures	Findings	Quality assessment: study strengths	Quality assessment: study weaknesses
= 1	Webber <i>et al</i> (1999) ²⁰ Hospital affiliated methadone maintenance programme with on-site primary care in New York City, United States	Prospective cohort study of 524 HIV positive people who attended the methadone programme	Time to AIDS defining condition (by CDC 1993 definition ²¹ but excluding CD4+ cell count $\leq 200 \times 10^6/l$) and death	Cigarette smoking did not add information to a model controlling for CD4+ cell counts, constitutional symptoms, crack cocaine use, zidovudine use, type and route of drug use, sexual risk factors, and age (hazard ratios not provided and data insufficient to calculate)	Wide range of confounders taken into account (age, sex, CD4+ cell counts, constitutional symptoms, crack cocaine use, zidovudine use, type and route of drug use, sexual risk factors, and sociodemographic variables)	Investigators not blinded and smoking status not biochemically validated
= 1	Stephenson <i>et al</i> (1999) ²² 15 genitourinary medicine clinics in Britain and Ireland	Prospective observational cohort study of 385 women aged over 18 years with a positive HIV antibody test who progressed to AIDS	Incidence of AIDS (criteria for AIDS or AIDS defining condition not stated)	In multivariate analysis, rate of progression to AIDS and mortality were not affected by smoking status. Adjusted hazard ratio for smokers versus non-smokers for progression to AIDS was 1.36 (95% CI 0.75 to 2.45) Crude hazard ratio not provide and data insufficient to calculate	Wide range of confounders taken into account (CD4+ lymphocyte count, antiretroviral drug use, <i>Pneumocystis carinii</i> prophylaxis, age, ethnic origin, number of sexual partners, occupational status, marital status, alcohol use, and use of oral contraception)	Date of HIV seroconversion was unknown but CD4+ lymphocyte count was fitted as a fixed variable to adjust for illness on entry to study. Investigators not blinded and no biochemical validation of smoking status
= 1	Conley <i>et al</i> (1996) ²³ San Francisco, Denver, and Chicago, United States	Prospective and retrospective cohort study of 237 HIV infected homosexual and bisexual men previously enrolled for a hepatitis B study. Participants classified as either smokers (n = 106) or non-smokers (n = 126)	Included diagnosis of AIDS by CDC definition (1987) ²⁶	Neither univariate analysis nor Kaplan-Meier survival analysis found any association between cigarette smoking and the development of AIDS (univariate RR = 1.0, 95% CI = 0.8 to 1.3). PCP (univariate RR = 0.9, 95% CI = 0.5 to 1.6), or Kaposi's sarcoma (univariate RR = 0.6, 95% CI = 0.3 to 1.1)	Adequate assessment of baseline characteristics including date of seroconversion	Assessors not blinded, smoking status not biochemically assessed
= 4	Coates <i>et al</i> (1990) ²⁴ Toronto, Canada	Prospective cohort study of 159 apparently healthy homosexual or bisexual male contacts of other men known to have AIDS with follow up for 4.5 years	Diagnosis of AIDS by CDC definition (1985) ³¹	Cox regression models showed no relation between smoking status and progression to AIDS (hazard ratio not provided or raw data to calculate)	Interviewer administered questionnaire of exposure (smoking status) and complete follow up of eligible participants. Confounders taken into account were age, alcohol consumption, recreational drug use, sexually transmitted infections, and intestinal parasites	Smoking status not biochemically confirmed. Disease progression for 143 participants who were HIV seropositive on enrolment assessed by estimated length of HIV infection (rather than known dates or proxy measure such as CD4+ cell count). Assessors not blinded
= 4	Burns <i>et al</i> (1996) ³⁵ 17 community based clinical centres in 13 cities in the United States	Prospective cohort study of 3221 HIV-1 seropositive men and women with median follow up of 36 months for current smokers and never smokers and 37 months for former smokers	Participants classified as never (n = 760), former (n = 618), or current (n = 1843) smokers on the basis of an enrolment questionnaire (not biochemically validated). Outcome measures were HIV related diagnoses similar to CDC list of AIDS defining illnesses (1987) ³⁵	After adjustment for confounders, there was no difference between current and never smokers for overall risk of opportunistic diseases (adjusted RH = 1.05, 95% CI = 0.9 to 1.23) or death (adjusted RH = 1.00, 95% CI = 0.86 to 1.18). However current smokers were at greater risk than non-smokers of developing bacterial pneumonia (adjusted RH = 1.57, 95% CI = 1.14 to 2.15) and AIDS dementia complex (adjusted RH = 1.80, 95% CI = 1.11 to 2.90). Current smokers were less likely than never smokers to develop Kaposi's sarcoma (adjusted RH = 0.58, 95% CI = 0.39 to 0.88). Crude RH not provided and data insufficient to calculate	Selection criteria clear and appropriate with important confounders taken into account (age, gender, race/ethnicity, HIV-1 risk behaviour, previous disease progression, baseline CD4+ lymphocyte count, Karnofsky score, use of antiretroviral therapy, use of <i>Pneumocystis carinii</i> prophylaxis, alcohol use, and "street" drug use)	Assessors not blinded, smoking status not biochemically verified

Table 3 Continued

Ranking from quality assessment	Reference (date of publication) Setting/country	Design, population and sample size	Relevant outcome measures	Findings	Quality assessment: study strengths	Quality assessment: study weaknesses
= 4	Eskild <i>et al</i> (1994) ²⁷ A health clinic for homosexual and bisexual men in Oslo, Norway	Prospective cohort study of 78 HIV infected homosexual and bisexual clinic clients classified as either non-smokers (n = 31), smoking 1–20 cigarettes a day (n = 26) or more than 20 cigarettes daily (n = 21)	Diagnosis of AIDS by CDC definition (1987) ²⁶	No association found between cigarette smoking and progression to AIDS (adjusted relative risk of developing AIDS in smokers versus non-smokers for 1–20 cigarettes per day was 0.4 [95% CI 0.1 to 1.2] and for > 20 cigarettes per day was 1.1 [95% CI 0.4 to 2.7]. Crude relative risks were 0.4 [95% CI = 0.2 to 1.2] and 1.1 [95% CI = 0.5 to 2.7], respectively.	Important confounders assessed by interview (age, year of HIV diagnosis, number of male lifetime partners, frequency of receptive and intercourse, alcohol consumption). Small loss to follow up (2.5%).	Disease progression only accounted for reported year of HIV diagnosis. Smoking status not biochemically verified. Assessors not blinded. No statistically significant association found between known risk factors (number of male lifetime partners, frequency of receptive and intercourse) and progression to AIDS suggesting study may have been underpowered
= 4	Galai <i>et al</i> (1997) ²⁸ Baltimore, Chicago, Los Angeles, and Pittsburgh, United States	Prospective cohort study (part of Multicentre AIDS Cohort Study) of 2420 men with HIV	Included diagnosis of AIDS by CDC definition (1987), ²⁶ PCP	No association found in Kaplan-Meier or multivariate Cox regression analyses between smoking and AIDS (adjusted hazard ratio 0.96, p = 0.7, CI not provided or data available to calculate) or PCP	Large cohort with important confounders assessed (date of seroconversion, CD4+ lymphocyte count, antiretroviral and anti-PCP therapy)	Smoking status assessed only by participant completed questionnaire and not biochemically verified. Assessors not blinded
= 8	Burns <i>et al</i> (1991) ¹⁸ See table 2	See table 2	HIV-1 antibody seroconversion, diagnosis of AIDS by CDC definition (1987) ²⁶	Participants who were initially HIV-1 seronegative were more likely to become seropositive if they smoked (p = 0.03). No difference between smokers and non-smokers in progression to AIDS (p = 0.31) or development of PCP. Insufficient data provided to calculate relative risk	See table 2	See table 2
= 8	Craib <i>et al</i> (1992) ²⁹ Two general practices in Vancouver, Canada	122 seroincident homosexual men classified as either smokers (n = 74) or non-smokers (n = 48) followed up for 3 years	HIV-1 antibody seroconversion, diagnosis of AIDS by CDC definition (1987) ²⁶	No effect of smoking on progression to AIDS (p = 0.829) or diagnosis of PCP (p = 0.894). Insufficient data provided to calculate relative risk	Representative sample with adequate assessment of disease stage at enrolment (measured by CD4+ and CD8+ lymphocyte counts and date of seroconversion). However use of log rank test meant analysis did not adjust for these confounders	Other potential confounders apart from age and disease progression not assessed. Assessors not blind to smoking status. Unclear why only 122 participants included in analysis
= 8	Nieman <i>et al</i> (1993) ³⁰ Genitourinary medicine outpatient department in London, UK	82 men with AIDS (CDC definition), ³¹ of whom 43 were classified as smokers and 41 as non-smokers (never smoked or stopped more than 12 months ago)	Diagnosis of AIDS by CDC definition (1986) ³¹	Median time to AIDS (all diagnoses) was 8.17 months for smokers and 14.50 months for non-smokers (p = 0.003). Median time to PCP was 9.0 months for smokers and 16.0 months for non-smokers (p = 0.002). No difference was noted between smokers and non-smokers on the development of non-PCP AIDS	Complete follow up and adequate assessment of disease stage at enrolment (CDC stages were not significantly different between smokers and non-smokers at initial assessment)	Other important confounders (eg, CD4+ cell counts and continued risk behaviours) not measured. Smoking status not biochemically verified. Assessors not blinded to smoking status

CI, confidence interval; OR, odds ratio; PCP, *Pneumocystis carinii* pneumonia; RH, relative hazard; RR, relative risk.

Key messages

- Smoking tobacco is known to be associated with immunological changes and an increased risk for certain infections
- Studies identified in this systematic review indicated that smoking was associated with an increased risk of HIV seroconversion but no increased risk of progressing to AIDS
- Tobacco control and smoking cessation as well as being essential public health measures, may also contribute to the effectiveness of HIV/AIDS programmes
- Further research is required to understand the effect of smoking since the introduction of HAART and on the health of people living with HIV in developing countries

evidence to inform decisions at population and individual levels. The public health message on smoking remains clear—tobacco is not good for health. Smoking prevalence is high among groups who are also vulnerable to HIV infection, including sex workers and men who have sex with men. In developing countries these groups are especially marginalised and providing any sort of support, let alone smoking cessation services, is difficult. Research is required into the best approaches for these groups.¹³

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CONTRIBUTORS

The study was conceived by AF and the protocol was developed by all the authors; CC developed and performed the literature searches; AF and RM extracted the data; AF wrote the first draft with all authors contributing to later drafts; AF is the guarantor.

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REFERENCES

- 1 Asma S, Pederson L. Tobacco control in Africa: opportunities for prevention. *Tobacco Control* 1999;**8**:353-4.
- 2 UNAIDS. *AIDS epidemic update*. Geneva: UNAIDS, 2004. Available from www.unaids.org/wad2004/report.html, accessed 14 September, 2005.
- 3 Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990-2020: Global Burden of Disease Study. *Lancet* 1997;**349**:1498-504.
- 4 Arcavi L, Benowitz NL. Cigarette smoking and infection. *Arch Intern Med* 2004;**164**:2206-16.
- 5 Wolf R, Freedman D. Cigarette smoking, sexually transmitted diseases, and HIV/AIDS. *Int J Dermatol* 2000;**39**:1-9.
- 6 Wells GA, Shea B, O'Connell D, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Available from www.ohri.ca/programs/clinical_epidemiology/oxford.htm, accessed 14 September, 2005.
- 7 The Cochrane Collaborative Review Group on HIV Infection and AIDS. *Editorial policy: inclusion and appraisal of experimental and non-experimental (observational) studies*, (undated) www.igh.org/Cochrane/pdfs/EP_inclusionquality.pdf, accessed 14 September, 2005.
- 8 Phillips AN, Smith GD. HIV infection and smoking behavior. *JAMA* 1992;**268**:1539-40.
- 9 Phillips AN, Davey Smith G. Cigarette smoking as a potential cause of cervical cancer: has confounding been controlled. *Int J Epidemiol* 1994;**23**:42-9.
- 10 Bothamley GH. Smoking and tuberculosis: a chance or causal association? *Thorax* 2005;**60**:527-8.
- 11 Crothers K, Griffith TA, McGinnis KA, et al. The impact of cigarette smoking on mortality, quality of life, and comorbid illness among HIV-positive veterans. *J Gen Intern Med* 2005;**20**:1142-5.
- 12 Sax PE. Strategies for management and treatment of dyslipidaemia in HIV/AIDS. *AIDS Care* 2006;**18**:149-57.
- 13 Niaura R, Shadel WG, Morrow K, et al. Human immunodeficiency virus infection, AIDS, and smoking cessation: the time is now. *Clin Infect Dis* 2000;**31**:808-12.
- 14 Halsey NA, Coberly JS, Holt E, et al. Sexual behaviour, smoking, and HIV-1 infection in Haitian women. *JAMA* 1992;**267**:2062-6.
- 15 Chao A, Bulterys M, Musanganire F, et al. Risk factors associated with prevalent HIV-1 infection among pregnant women in Rwanda. *Int J Epidemiol* 1994;**23**:371-80.
- 16 Boulos R, Halsey NA, Holt E, et al. HIV-1 in Haitian women 1982-1988. *J AIDS* 1990;**3**:721-8.
- 17 Penkower L, Dew MA, Kingsley L, et al. Behavioral, health and psychosocial factors and risk for HIV infection among sexually active homosexual men: the Multicenter AIDS Cohort Study. *Am J Public Health* 1991;**81**:194-6.
- 18 Burns DN, Kramer A, Frances Y, et al. Cigarette smoking: a modifier of human immunodeficiency virus type 1 infection? *J AIDS* 1991;**4**:76-83.
- 19 Siraprasitri T, Foy HM, Kreiss JK, et al. Frequency and risk of HIV infection among men attending a clinic for STD in Chiang Mai, Thailand. *Southeast Asian J Trop Med Public Health* 1996;**27**:96-101.
- 20 Webber PM, Schoenbaum EE, Gourevitch MN, et al. A prospective study of HIV disease progression in female and male drug users. *AIDS* 1999;**13**:257-262.
- 21 Centers for Disease Control. 1993 revised classification system for HIV infection and expanded surveillance case definition for AIDS amongst adolescents and adults. *Morb Mort Wkly Rep* 1992;**41**:1-19.
- 22 Stephenson JM, Griffioen A, Woronowski H, et al. Survival and progression of HIV disease in women attending GUM/HIV clinics in Britain and Ireland. *Sex Transm Infect* 1999;**75**:247-52.
- 23 Conley LJ, Bush TJ, Buchbinder SP, et al. The association between cigarette smoking and selected HIV-related medical conditions. *AIDS* 1996;**10**:1121-6.
- 24 Coates RA, Farewell VT, Raboud J, et al. Cofactors of progression to acquired immunodeficiency syndrome in a cohort of male sexual contacts of men with human immunodeficiency virus disease. *Am J Epidemiol* 1990;**132**:717-22.
- 25 Burns DN, Hillman D, Neaton JD, et al. Cigarette smoking, bacterial pneumonia, and other clinical outcomes in HIV-1 infection. *J Acquir Immune Defic Syndr Hum Retrovir* 1996;**13**:374-83.
- 26 Centers for Disease Control. Revision of the CDC surveillance case definition for acquired immunodeficiency syndrome. *Morb Mort Wkly Rep* 1987;**36**:1-155.
- 27 Eskild A, Petersen G. Cigarette smoking and drinking alcohol are not associated with rapid progression to acquired immunodeficiency syndrome among homosexual men in Norway. *Scand J Soc Med* 1994;**3**:209-12.
- 28 Galai N, Park LP, Wesch J, et al. Effect of smoking on the clinical progression of HIV-1 infection. *J Acquir Immune Defic Syndr Hum Retrovir* 1997;**14**:451-8.
- 29 Craib KJP, Schechter MT, Montaner JSG, et al. The effect of cigarette smoking on lymphocyte subsets and progression to AIDS in a cohort of homosexual men. *Clin Invest Med* 1992;**15**:301-8.
- 30 Nieman RB, Fleming J, Coker RJ, et al. The effect of cigarette smoking on the development of AIDS in HIV-1-seropositive individuals. *AIDS* 1993;**7**:705-10.
- 31 Centers for Disease Control. Classification system for HIV infections. *Morb Mort Wkly Rep* 1986;**35**:334-9.