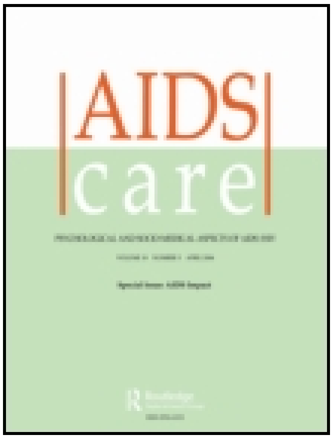

AIDS Care: Psychological and Socio-medical Aspects of AIDS/HIV
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/caic20

Effect of changing antiretroviral treatment eligibility criteria on patient load in Kampala, Uganda

Joseph Konde-Lule [a] , Fred Makumbi [a] , Nadine Pakker [b] , Asad Muyinda [c] , Mesach Mubiru [d] & Frank G.J. Cobelens [b]

[a] School of Public Health , Makerere University , Kampala, Uganda

[b] Department of Internal Medicine, Academic Medical Center , Center for Poverty-related Communicable Diseases and Amsterdam Institute of Global Health and Development , Amsterdam, The Netherlands

[c] Infectious Diseases Institute , Makerere University , Kampala, Uganda

[d] Kampala City Council, Health Department , Kampala, Uganda

Published online: 05 Oct 2010.

To cite this article: Joseph Konde-Lule , Fred Makumbi , Nadine Pakker , Asad Muyinda , Mesach Mubiru & Frank G.J. Cobelens (2011) Effect of changing antiretroviral treatment eligibility criteria on patient load in Kampala, Uganda, AIDS Care: Psychological and Socio-medical Aspects of AIDS/HIV, 23:1, 35-41, DOI: 10.1080/09540121.2010.498869

To link to this article: http://dx.doi.org/10.1080/09540121.2010.498869

AIDS Care
Vol. 23, No. 1, January 2011, 35–41

Effect of changing antiretroviral treatment eligibility criteria on patient load in Kampala, Uganda

Joseph Konde-Lule[a]*, Fred Makumbi[a], Nadine Pakker[b], Asad Muyinda[c], Mesach Mubiru[d] and Frank G.J. Cobelens[b]

[a]*School of Public Health, Makerere University, Kampala, Uganda;* [b]*Department of Internal Medicine, Academic Medical Center, Center for Poverty-related Communicable Diseases and Amsterdam Institute of Global Health and Development, Amsterdam, The Netherlands;* [c]*Infectious Diseases Institute, Makerere University, Kampala, Uganda;* [d]*Kampala City Council, Health Department, Kampala, Uganda*

(Received 1 December 2009; final version received 1 June 2010)

In many resource-poor countries, CD4 count thresholds of eligibility for antiretroviral treatment (ART) were initially low (<200 cells/mm^3) but are now being increased to improve patient survival and to reduce HIV transmission. There are few quantitative data on the effect of such increases on the demand for ART. The objective of this study was to measure HIV prevalence and the proportion of HIV-positives eligible for antiretroviral therapy at different CD4 cut-off levels among users of public health care services in Kampala, Uganda. We recruited 1200 adults from three primary care clinics in Kampala, including equal numbers of family planning (FP) clients, pregnant women, adult patients with any complaint, and persons seeking HIV counseling and testing. All participants were screened for HIV and those positive had a CD4 count done. HIV prevalence in all patients was 16.9% (203/1200). ART eligibility based on CD4 counts significantly increased from 36% at a 200 cells/mm^3 cut-off to 44% at 250 cells and to 57% at 350 cells cut-off (p for χ^2 trend <0.001). We concluded that changing cut-off levels to higher CD4 counts will significantly increase patient load in Kampala's primary care clinics, but a phased implementation should minimize negative effects on quality of care.

Keywords: HIV antiretroviral therapy; eligibility criteria; Uganda; Africa

Introduction

HIV/AIDS remains a major public health challenge in the world and it is estimated that worldwide about 33 million people are infected with HIV, of whom 22 million (67%) are in sub-Saharan Africa (UNAIDS, 2008). The impact of the disease has been progressively mitigated by the increasing use of antiretroviral treatment (ART). As ART becomes increasingly accessible, however, the issue of when to initiate treatment in resource-limited settings, especially in asymptomatic patients, remains controversial. Whereas, many studies have continued to demonstrate that initiating ART early, before the CD4 count drops to 200 cells/µl, has got many benefits, including slowing progression to AIDS and death (Baker et al., 2008; Patel et al., 2008; Walensky et al., 2006), many countries in resource-poor settings still defer initiation of ART until the CD4 count has dropped to 200 cells/µl or lower. In resource-rich settings, the recommendation is to initiate ART at a CD4 count of 350 cells/µl or higher (Hammer et al., 2008). Studies have shown that risk of death increases significantly when the initiation of therapy is delayed until the CD4 count drops below 350 cells/µl (Kitahata et al., 2009). Other disadvantages of delaying initiation of ART include increased risk of tuberculosis (Edmonds et al., 2009) and patients remaining viremic for longer periods, thereby increasing the risk of HIV transmission in the population (Auvert et al., 2004). Because of its role in reducing viral load, ART is now believed to have population-wide preventive effects by reducing both vertical and horizontal transmission (De Cock, Crowley, Lo, Granich, & Williams, 2009). This is of high significance especially in countries with high HIV prevalence like in sub-Saharan Africa. From 2003 when the first Uganda ART guidelines were made, the practice in the country has been to initiate ART at a CD4 count of 200 cells/µl (Uganda, 2003). The cut-off point in the country has recently been raised to 250 cells/µl (Uganda, 2008), and it is expected that this will be raised further to 350 cells/µl as the cost of ART drops and HIV care becomes more accessible. The effect that such increases in treatment eligibility threshold will have on the need for ART is, however, unknown. To a large extent this will depend on the relative proportion of people newly identified with

*Corresponding author. Email: jkonde@musph.ac.ug

ISSN 0954-0121 print/ISSN 1360-0451 online

DOI: 10.1080/09540121.2010.498869
http://www.informaworld.com

HIV infection who have CD4 counts below the threshold. Knowledge of these proportions in various groups of health service users will therefore be important to inform planning for resources and services. We therefore did a survey to measure HIV prevalence among different user groups and proportions of HIV-positives eligible for antiretroviral therapy at different CD4 count cut-off levels in Kampala's primary health care facilities.

Methods

Kampala is the capital city of Uganda with a projected 2009 population of 1.5 million residents, and a daytime population of about three million people (Statistics, 2002). Primary health care services are provided by 10 public clinics operated by the Kampala City Council (KCC). The study was conducted at three of these 10 KCC clinics purposively selected to include clinics located in different population-density areas designated as high, medium, and low. The three clinics at health center (HC) level were Kisenyi HC located in the high density central division, Kiswa HC in a medium density industrial area and Kiruddu HC in a low density semi-rural area. The study population was all patients and clients at these clinics. The groups that we identified for study were pregnant women attending the antenatal clinic (ANC), clients seeking FP, patients attending the general outpatient department (OPD) for any complaint, and persons seeking voluntary HIV counseling and testing (VCT). The only exclusion criterion was being too sick to be interviewed.

Sample size

We estimated sample sizes assuming HIV prevalence levels between 8 and 15% in all the study groups, as based on a recently concluded national sero-survey that reported HIV prevalence in adults 15–49 years to be 8.5% for Kampala while it was 12% among women in urban areas (Macro, 2006). We assumed that sick persons would have slightly higher HIV prevalence up to about 15%. At the 5% level of significance and a precision of $\pm 5\%$, the sample size per category was determined to be 200 participants. The sample size was rounded upwards to 300 for each category to allow for multivariable analysis and within-strata comparisons of proportions of subjects with CD4 counts below the threshold level, making the four groups total recruitment 1200 subjects.

Recruitment procedure

Systematic sampling was done at each of the three clinics and this was based on the patient attendance register for the day, usually complete by 11.00 am. A sampling interval was determined to recruit 10 participants daily from one category. Each clinic recruited only one category a day during four work days a week. Recruitment days for each category were different in the clinics but were changed on rotational basis weekly in order to avoid selection bias. This translated into 40 participants from the four groups per clinic per week and recruitment was completed in 10 weeks. All patients provided a 4 ml blood sample drawn by the laboratory technician at the clinic with the help of the study nurse.

Laboratory testing

Blood samples were screened for HIV by the laboratory technicians at the three respective HCs using three sequential rapid HIV tests as is recommended by the Uganda Ministry of Health series algorithm for rapid HIV testing. We used Determine™ (Abbott Laboratories by Abbott Japan CO. LTD, Minato-Ku, Tokyo, Japan), HIV1/2 Stat-Pak (Chembio Diagnostics Systems, 3661 Horseblock Road, Med Ford, NY 11763, USA), and Unigold™ (Trinity Biotech PLC, IDA Business Park, Bray, Cowicklow, Ireland) testing kits. Specimens that were negative on Determine™ HIV1/2 were considered negative and specimens that were found positive on Determine™ HIV1/2 and HIV1/2 Stat-Pak were considered positive. Specimens with discordant results on Determine™ HIV1/2 and HIV1/2 Stat-Pak were retested on Unigold™ as a tie-breaker. Specimens negative on the tie-breaker were considered negative while specimens positive on the tie-breaker were considered positive. Samples found positive at the HC were transported to the core laboratory at Mulago Hospital for HIV confirmatory testing and a CD4 cell count by flow cytometry technique using Becton-Dickinson (BD) FACS calibur.

Data management and analysis

The completed laboratory request forms were checked daily by the nursing officer in charge of the unit for completeness. Those found with errors were referred to the respective data collectors for correction. The corrected data were double entered into a custom-programmed database using ASP.NET and stored in Microsoft SQL Server Express Edition database (Microsoft Software, Seattle, WA, USA), and discrepancies were checked against the raw data. This was followed by cleaning and analysis using Stata 10 (Stata Corp, College Station, TX, USA).

We estimated the HIV prevalence as the number of HIV-positive subjects divided by the total number of subjects. We used prevalence risk ratios (PRR) as a measure of association, with their 95% confidence intervals (CI) to ascertain factors associated with HIV prevalence. The log-binomial model, other than the logistic model, was used because the outcome (HIV prevalence) was not rare (>10%; Zou, 2004). In the multivariable analysis, we included factors significant at $p < 0.15$ from the bivariable analysis or potential confounders. Eligibility for ART based on CD4 count (cells/µl) was grouped as ≤200 cells/µl, ≤250 cells/µl, and ≤350 cells/µl. Proportions eligible for ART were then estimated as the number of HIV-positive clients who attained these CD4 levels divided by total number of clients, and trends in the proportion eligible across the changing CD4 levels were obtained using Chi-square for trends analysis. All these analyses were done by category of sex, age, type of care sought for, and primary HC where services were sought.

Ethical considerations

Ethical clearance to conduct the study was sought and obtained from the Higher Degrees, Research and Ethics Committee of Makerere University School of Public Health, as well as from the Uganda National Council for Science and Technology. Permission and letters of introduction to the health units and to the local leaders were obtained from the District Health Officer of Kampala. To obtain informed consent, the purpose, benefits, and risks of the study were explained to the participants with assurance of confidentiality. All participants who were found to be HIV-positive were referred to the counseling section of the clinic where they were counseled and then notified of their results. ART was initiated according to government guidelines and at the time of the survey the threshold was 250 cells/µl.

Results

In all the four service categories no individual was excluded because of being too ill to participate. The study participants were largely in the age range of 18–45 years. The exception was the antenatal and FP groups that had 17 and 6 persons, respectively, aged <18 years.

HIV prevalence

The overall HIV prevalence was 16.9% (203/1200; 95% CI 14.8–19.2%) from Table 1. There was no significant difference in HIV prevalence by sex, although after multivariable adjustment for age, type of care sought, and HC, women had a 1.55 times higher risk of HIV infection than men.

HIV prevalence was lowest in the youngest age group (15–19 years) at 5.1% and rose with age until it was 29.2% in the 30+ year age group. The linear trend of rising HIV prevalence with age was statistically significant ($p < 0.001$, Chi square linear trend). This trend of rising HIV prevalence with higher age persisted even after stratifying by type of service sought (Table 2).

Looking at HIV infection by type of service, prevalence was 22.0% (66/300) in the VCT group, 20.0% (60/300) in general OPD adults, 13.0% (39/300) in FP, and 12.7% (38/300) in ANC (Table 1). These differences were maintained after multivariable adjustment, be it less pronounced and short of statistical significance. Among VCT participants, HIV prevalence was significantly lower among men (15.7%; 19/121) than among women, (26.3%; 47/179, $p = 0.030$). However, no gender differentials in HIV prevalence were observed in the OPD category; prevalence among men was 18.8% (21/112) compared to 20.7% (39/188) among women. Clinic HIV prevalence was highest at Kisenyi clinic located in the high-population density area and much lower at the other two clinics (Table 1).

Eligibility for antiretroviral treatment (ART)

ART eligibility by type of service sought and by CD4 cut-off is summarized in Table 3. Four samples did not have a CD4 count, reducing the number of HIV-positive patients with data available on CD4 count to 199.

At a cut-off of 200 cells/µl, the proportion eligible for ART was 35.7% (71/199, 95% CI 29.0–42.8%). At this cut-off, ART eligibility was significantly lower in the age group 15–24 years compared to all other age groups combined ($P = 0.012$), but not associated with sex, service category, or HC. At a cut-off of 250 cells/µl, the proportion eligible increases to 43.7% (87/199, 95% CI 36.7–50.9%), corresponding to a 23% increase, taking the proportion eligible at the cut-off of 200 cells/µl as 100%. At a cut-off of 350 cells/µl, the proportion eligible rises to 56.8% (113/199; 95% CI 49.6–63.8%), corresponding to a 59% increase. The rising trend of a higher proportion being eligible for ART at a higher CD4 cut-off is statistically significant (p for linear trend <0.0001). This significant increase in proportion eligible by higher CD4 count was most noted among clients aged 25+ years, being 41.3, 51.1, and 63.1% ($P = 0.001$), but not by type of service sought, sex, or HC. On the other hand, the relative increase was most pronounced in the age group 15–24 years old (by 84.6% when shifting the cut-off from 200 to 350 cells).

Table 1. Prevalence of HIV by sex, age, service sought, and clinic.

Category	HIV+/ total	Prevalence (%)	Unadjusted RR (95% CI)	Adjusted RR (95% CI)
Sex				
Male	40/233	17.2	1.0	**1.0**
Female	163/967	16.9	0.98 (0.69, 1.39)	**1.55 (1.06, 2.26)**
Age (years)				
15–19	9/175	5.1	1.0	1.0
20–24	49/404	12.1	**2.4 (1.18, 4.70)**	**2.6 (1.25, 5.24)**
25–29	49/292	16.8	**3.3 (1.64, 6.48)**	**3.5 (1.69, 7.09)**
30+	96/329	29.2	**5.7 (2.94, 10.96)**	**5.6 (2.75, 11.21)**
Service sought				
ANC	38/300	12.7	1.0	1.0
FP	39/300	13.0	1.0 (0.66, 1.60)	0.8 (0.50, 1.25)
OPD	60/300	20.0	**1.6 (1.05, 2.37)**	1.2 (0.79, 1.90)
VCT	66/300	22.0	**1.7 (1.17, 2.59)**	1.4 (0.88, 2.10)
Health center				
Kiruddu	60/400	15.0	1.0	1.0
Kisenyi	90/400	22.5	**1.5 (1.08, 2.08)**	**1.5 (1.09, 2.12)**
Kiswa	53/400	13.3	0.88 (0.61, 1.28)	0.9 (0.64, 1.34)
Overall	203/1200	16.9		

Note: Bold indicates statistically significant result.

Discussion

Eligibility for antiretroviral treatment (ART)

Of the 199 HIV-positive persons with data available on CD4 count 35.7% qualified for ART on the basis of a CD4 cell count of 200 cells/μl or less. The proportion eligible rises to 56.8% at a cut-off of 350 CD4 cells/μl, i.e., 59% more than the number of people requiring treatment with the eligibility threshold as it existed just before this study. Although estimated with less precision due to smaller numbers, this increase was 85% among people aged 15–24 years. This means that if a cut-off of 350 cells was to be adopted immediately, the demand on resources could increase by about 60%. The decision to first change to a cut-off of 250 CD4 cells when only 43.7% of HIV-positive clients qualify for treatment (i.e., an overall increase of 23%) before adopting 350 cells should enable the health system to adjust and avoid being overwhelmed by patient numbers. Differential elevation of CD4 thresholds is another option for preventing health system overload. The 2008 Uganda ART guidelines, for example, allow a cut-off point of 350 cells/μl among persons co-infected with TB, those with WHO stage III disease, and women who are pregnant. In addition to these groups elevation of CD4 thresholds could be considered for all women of

Table 2. HIV prevalence by age and service group.

Category	ANC HIV+/ total	ANC Percentage (%)	FP HIV+/ total	FP Percentage (%)	OPD HIV+/ total	OPD Percentage (%)	VCT HIV+/ total	VCT Percentage (%)
Age group (years)								
15–19	4/85	4.7	3/37	8.1	1/26	3.8	1/27	3.7
20–24	15/124	12.1	9/109	8.3	8/81	9.9	17/90	18.9
25–29	13/66	19.7	11/93	11.8	12/71	16.9	13/62	21.0
30+	6/25	24.0	16/61	26.2	39/122	32.0	35/121	28.9
p-Value	0.013		0.006		<0.001		0.027	
Totals	38/300	12.7	39/300	13.0	60/300	20.0	66/300	22.0

Note: Patient/client categories: ANC, antenatal care; FP, family planning; OPD, outpatient department (any presentation); VCT, voluntary counselling and HIV testing; HIV+, positive HIV-1/2 antibody test; *p*-Value for association with age (Chi-square linear trend test).

Table 3. Proportions of HIV - positives eligible for ART at different CD4 cut-off levels.

	CD4 count cut-off (cells/μl)							
	<200		<250			<350		
	Eligible/ total	Eligible (%)	Eligible/ total	Eligible (%)	Ratio eligible prop. 250/200 cells ratio (95% CI)	Eligible/ total	Eligible (%)	Ratio eligible prop. 350/200 cells ratio (95% CI)
Age (years)*								
15–24	13/58	22.4	15/58	25.9	1.15 (0.6, 2.2)	24/58	41.4	**1.85 (1.1, 3.3)**
25+	58/141	41.3	72/141	51.1	**1.24 (1.0, 1.6)**	89/141	63.1	**1.53 (1.2, 1.9)**
Sex								
Female	56/159	35.2	69/159	43.4	1.23 (0.9, 1.6)	91/159	57.2	**1.63 (1.3, 2.1)**
Male	15/40	37.5	18/40	45.0	1.20 (0.7, 2.0)	22/40	55.0	1.47 (0.9, 2.4)
Service								
VCT	27/66	40.9	32/66	48.5	1.19 (0.8, 1.7)	43/66	65.2	**1.59 (1.1, 2.2)**
FP	13/38	34.2	15/38	39.5	1.15 (0.6, 2.1)	17/38	44.7	1.31 (0.7, 2.3)
ANC	11/38	30.0	14/38	36.8	1.27 (0.7, 2.4)	22/38	57.9	**2.00 (1.1, 3.5)**
OPD	20/57	35.1	26/57	45.6	1.30 (0.8, 2.0)	31/57	54.4	**1.55 (1.0, 2.4)**
Health centre								
Kiruddu	16/60	26.7	21/60	35.0	1.31 (0.8, 2.3)	32/60	53.3	**1.52 (1.0, 2.3)**
Kisenyi	34/86	39.5	39/86	45.4	1.15 (0.8, 1.6)	49/86	57.0	**1.44 (1.1, 2.0)**
Kiswa	21/53	39.6	27/53	50.9	1.29 (0.8, 2.0)	32/53	60.4	**1.52 (1.0, 2.3)**
Overall	71/199	35.7	87/199	43.7	**1.23 (1.0, 1.6)**	113/199	56.8	**1.59 (1.3, 2.0)**

*p-Value for difference between categories <0.05.

Note: Ratio eligible prop. provides the percentage increase in number of ART eligible patients compared to the baseline value (CD4 200 cells/μl). For example, the overall increase is 23% for an eligibility cut-off CD4 <250 cells /μl, and 59% for CD4 <350 cells/μl; 95% CI, 95% confidence interval; bold indicates statistically significant results.

child bearing age (to further reduce vertical transmission) and for young adults in general to maximize the gain in life years. Reports that many Ugandans, especially males, the older age groups, and the less educated seek hospital care late (Kigozi et al., 2009) could mean that the effect of raising CD4 cut-off levels on numbers of patients at health facilities may be cushioned by the common practice of seeking health care late. Between the different categories, eligibility for ART among HIV-positives was highest in the VCT group (be it not significant: $P=0.223$), pointing to the possibility that many of them sought VCT after getting HIV/AIDS related symptoms. The proportion eligible for ART among persons aged 25 years or more was significantly higher than in the age group 15–24 years at all the cut-off levels, probably indicating that the older group had been with HIV infection for a longer period than the younger group. Also, this finding may suggest that older people progress to ART eligibility earlier than younger people. Follow up studies have shown that older people progress to AIDS more rapidly than the young, in both men and women (Chow, And, Verghesse, Chwe, & Leo, 2005; Pezzotti et al., 1996).

HIV prevalence

The overall adult HIV sero-prevalence of 16.9% at the three KCC Clinics was much higher than the 8.5% prevalence of Kampala district adults reflected in the national sero-survey (Macro, 2006). We attribute this to the fact that many of our study participants were patients, whose prevalence is expected to be higher than that of the general population. HIV prevalence was highest in the VCT category and this could probably be attributed to individuals seeking HIV testing after suspecting that they might have been exposed to HIV. The FP and ANC groups were two groups that attended the clinics as clients for specific services rather than for illness. The overall HIV prevalence for FP was 13.0% while the prevalence for ANC was 12.7%. These prevalence levels are very similar to the HIV prevalence of 12.8% that was obtained for the women aged 15–49 years in urban areas during the Uganda national sero-behavioral survey of 2004/2005 (Macro, 2006). Our study population being urban, these findings are consistent with the national sero-survey finding. Higher HIV infection prevalence was recorded among women compared to men in the categories that had both sexes (OPD adults and VCT). This is the expected finding, which has been reported in many previous population-based surveys in the country that have shown women HIV prevalence to be 20–40% higher than the men prevalence (Macro, 2006). In our OPD adults group the difference in prevalence between men and women is much smaller and this could reflect differences in health seeking behavior between the sexes in the city population. Kisenyi clinic, located in a high population-density area, had a significantly higher HIV prevalence (22.5%) than Kiruddu (15.0%) and Kiswa (13.3%) clinics. This could be attributed to the high mobility of the population in this area, a demographic feature that has been linked with higher HIV prevalence (Garcia-Calleja, Gouws, & Ghys, 2006; Kishamawe et al., 2006; Lydie et al., 2004).

Limitations

The main limitation of our study is that we did purposeful rather than random sampling of study clinics. This limits the representativeness of our findings for the Kampala population accessing health services. However, the similarity of the HIV prevalence estimates from our study with those of other surveys suggests that selection bias due to our sampling method is not substantial. Furthermore, selection bias is expected to affect the proportions of study subjects who are eligible for ART at different CD4 cut-offs largely to similar extent. Therefore, the effect of selection bias on the observed increases in ART eligibility with increasing eligibility thresholds will be limited.

Conclusions

Changing the CD4 count cut-off level for ART eligibility upwards will considerably increase the load of patients in this urban setting. Although there has been some concern about the health system getting overwhelmed by patient numbers, a phased increase in the cut-off level for ART eligibility will most likely prevent this.

Acknowledgements

We wish to acknowledge all our collaborators in this study including Makerere University School of Public Health, the INTERACT Project, Kampala City Health Department, and the health units where the study was based. We are also grateful to all the individuals who participated in the study. This study was done as part of the INTERACT Program and funded by the European Union (SANTE/2006/105-316).

References

Auvert, B., Males, S., Puren, A., Taljaard, D., Carael, M., & Williams, B. (2004). Can highly active antiretroviral therapy reduce the spread of HIV? A study in a township of South Africa. *Journal of Acquired Immune Deficiency Syndromes*, *36*(1), 613–621.

Baker, J.V., Peng, G., Rapkin, J., Abrams, D.I., Silverberg, M.J., MacArthur, R.D., … Terry Beirn Community Programs for Clinical Research on AIDS (CPCRA). (2008). CD4+ count and risk of non-AIDS diseases following initial treatment for HIV infection. *AIDS*, *22*(7), 841–848.

Chow, K.Y., And, L.W., Verghesse, I., Chwe, S.K., & Leo, Y.S. (2005). Measurable predictive factors for progression to AIDS among HIV infected patients in Singapore. *Annals Academy of Medicine Singapore*, *34*, 84–89.

De Cock, K.M., Crowley, S.P., Lo, Y-R., Granich, R.M., & Williams, B.G. (2009). Preventing HIV transmission with antiretrovirals. *Bulletin of the World Health Organization*, *87*, 488–488A. doi: 10.2471/BLT.09.067330

Edmonds, A., Lusiama, J., Napravnik, S., Kitetele, F., Van Rie, A., & Behets, F. (2009). Anti-retroviral therapy reduces incident tuberculosis in HIV-infected children. *International Journal of Epidemiology*, *38*(6), 1612–1621.

Garcia-Calleja, J.M., Gouws, E., & Ghys, P.D. (2006). National population based HIV prevalence surveys in sub-Saharan Africa: Results and implications for HIV and AIDS estimates. *Sexually Transmitted Infections*, *82*(Suppl. 3), iii64–iii70.

Hammer, S.M., Eron, Jr., J.J., Reiss, P., Schooley, R.T., Thompson, M.A., Walmsley, S., … Volberding, P.A. (2008). Antiretroviral treatment of adult HIV infection: 2008 recommendations of the International AIDS Society – USA panel. *JAMA*, *300*(5), 555–570.

Kigozi, I.M., Dobkin, L.M., Martin, J.N., Geng, E.H., Muyindike, W., Emenyonu, N.I., … Hahn, J.A. (2009). Late-disease stage at presentation to an HIV clinic in the era of free antiretroviral therapy in sub-Saharan Africa. *Journal of Acquired Immune Deficiency Syndromes*, *52*(2), 280–289.

Kishamawe, C., Vissers, D.C., Urassa, M., Isingo, R., Mwaluko, G., Borsboom, G.J., … de Vlas, S.J. (2006). Mobility and HIV in Tanzanian couples: Both mobile persons and their partners show increased risk. *AIDS*, *20*(4), 601–608.

Kitahata, M.M., Gange, S.J., Abraham, A.G., Merriman, B., Saag, M.S., Justice, A.C., … Moore, R.D. (2009). Effect of early versus deferred antiretroviral therapy for HIV on survival. *New England Journal of Medicine*, *360*(18), 1815–1826.

Lydie, N., Robinson, N.J., Ferry, B., Akam, E., De Loenzien, M., & Abega, S. (2004). Mobility, sexual behavior, and HIV infection in an urban population in Cameroon. *Journal of Acquired Immune Deficiency Syndromes*, *35*(1), 67–74.

Macro, U.M.o.H. (2006). *Uganda HIV/AIDS Sero-behavioral Survey 2004–2005*. Claverton, MD: Ministry of Health in Uganda, Kampala, Uganda and ORC Macro.

Patel, K., Hernan, M.A., Williams, P.L., Seeger, J.D., McIntosh, K., Van Dyke, R.B., & Seage III, G.R. (2008). Long-term effectiveness of highly active antiretroviral therapy on the survival of children and adolescents with HIV infection: A 10-year follow-up study. *Clinical Infectious Diseases*, *46*(4), 507–515.

Pezzotti, P., Phillips, A.N., Dorrucci, M., Lepri, A.C., Galai, N., Vlahov, D., & Rezza, G. (1996). Category of exposure to HIV and age in the progression to AIDS: Longitudinal study of 1199 people with known dates of seroconversion. *BMJ*, *313*, 583–586.

Statistics, U.B.o. (2002). *The 2002 Uganda population and housing census, population size and distribution*. Entebbe, Uganda: National census office, Uganda Bureau of Statistics.

Uganda, M.o.H. (2003). *National antiretroviral treatment and care guidelines for adults and children* (1st ed.). Kampala, Uganda: Ministry of Health in Uganda.

Uganda, M.o.H. (2008). *National antiretroviral treatment and care guidelines for adults and children* (2nd ed.). Kampala, Uganda: Ministry of Health in Uganda.

UNAIDS (2008). *Report on global AIDS epidemic*. Geneva, Switzerland: WHO/UNAIDS.

Walensky, R.P., Paltiel, A.D., Losina, E., Mercincavage, L.M., Schackman, B.R., Sax, P.E., … Freedberg, K.A. (2006). The survival benefits of AIDS treatment in the United States. *Journal of Infectious Diseases*, *194*(1), 11–19.

Zou, G. (2004). A modified poisson regression approach to prospective studies with binary data. *American Journal of Epidemiology*, *159*(7), 702–706.