TITLE

HIV incidence among older adults in a rural South African setting: 2010-2015

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INTRODUCTION

HIV research, treatment and prevention has mainly focused on populations under 50 years of age, with only a few studies highlighting the importance of the HIV epidemic in older age groups (1-3). Evidence shows that there is high prevalence in older people (4, 5) stressing the importance of quantifying HIV transmission in older adults.

It has been shown that sexual behaviour among older adults in rural African settings is consistent with high acquisition and transmission risk (6). South Africa is home to the largest HIV epidemic worldwide and a robust ART program (7). Increases in life expectancy due to ART uptake are expected to result in increases in prevalence due to longer survival of those infected. In this context, it is crucial to understand when new infections are occurring among older age groups to inform policy makers of the importance of including older populations in the implementation of HIV prevention policies (8). However, there is a paucity of longitudinal studies on HIV negative, older populations that would allow direct measurement of HIV incidence. In most cases, methods to estimate HIV incidence have used changes in prevalence (9) or detection of recent infections through specific tests like BED IgG-Capture Enzyme Immunoassay (10).

This study uses a cohort of adults in rural South Africa who tested negative for HIV at age 40 years or older in 2011 and were retested in 2016 to estimate HIV incidence over an approximately five-year period.

METHODS

HIV cohort creation: surveys and sample

We calculated incidence established on laboratory-based HIV testing sampled in the same participants at two time points collected at the MRC/Wits Rural Public Health and Health Transitions Research Unit, where the Agincourt Health and Demographic Surveillance System(11). The baseline study (4), the Ha Nakekela HIV and Non-communicable Disease Study, ran from August 2010 to June 2011 and included

a random selection of 7,662 men and women ages 15 and over from the 2009 census, stratified by age and sex. Participants in this study were asked to respond to a sexual behaviour questionnaire. We took anthropometric measurements, point of care blood test for diabetes (Caresense^{TM}) and lipid profile (Cardiocheck^{TM}) and dried blood spot for HIV test and viral load. HIV dried blood spot testing was performed using screening assay Vironostika Uniform 11 (Biomeriuex, France). All positives were confirmed by the SD Bioline HIV ELISA test (SD; Standard Diagnostics Inc, Korea). Positive samples were also tested for HIV viral load using the Biomeriuex NucliSens (Biomeriuex, France) viral load assay.

The first follow up round, the Health and Aging in Africa: A Longitudinal Study of an INDEPTH Community in South Africa (HAALSI) study, ran from November 2014 to November 2015, with a sample of 6,281 women and men over 40 years of age. The HAALSI sample included all participants from the 2010 survey ages 40 and over at the time of follow-up sampling, and was complemented with a random sample selected from the Agincourt HDSS 2013 census round(12). In the HAALSI study, we conducted interviews to collect household and individual data that included socioeconomic data, self-reported health on specific diseases, anthropometric measurements, blood pressure, and point-of-care blood tests that included glucose, lipid profiles and HIV-status.

Ethics clearance for the HDSS and for the surveys was obtained from the University of the Witwatersrand Human Research Ethics Committee (Medical) and the Mpumalanga Provincial Research and Ethics Committee. The HAALSI study received ethical approval from Harvard TH Chan School of Public Health, Office of Human Research Administration.

Figure 1 shows the final cohort used to calculate HIV incidence rates. In the first round, 2050 individuals consented for HIV testing: 433 (21%) were HIV-positive. The remaining 1617 HIV-negative individuals were then invited to be part of the second round; among these, 1275 (79%) individuals consented to be tested.

Statistical analysis

We calculated HIV prevalence for the population aged 40 years and older for both surveys. We calculated crude HIV incidence over five years of follow up overall and by age group, gender and other key socio-demographic characteristics. We used Poisson regression to measure the association of HIV seroconversion with demographic and behavioural covariates using the original sample weights. We assumed the time of infection to be midway between the two surveys. Those who aged to 40 during the follow up time only contributed exposure time in the period where they were 40 years or older.

RESULTS

HIV prevalence in those 40 years and older at baseline was 21% increasing to 23% five years later in the follow-up survey. Overall, 33 individuals seroconverted from the 1275 HIV negative at baseline who consented to be tested in the follow up round (total of 5295 person-years). The overall HIV incidence rate was 0.6 per 100 person-years (95% CI 0.4 – 0.9); 0.4 (95% CI 0.2 - 0.8) for men and 0.8 (95% CI 0.5 - 1.1) for women.

Table 1 shows the crude Incidence Rate and the Incidence Rate Ration of the Poisson regression of the association between incident HIV infection and key demographic variables. Women presented two times higher risk than men to seroconvert (IRR=2.1, 95%CI 0.9 – 5.0, p-value=0.073), older people have significantly lower risk of HIV seroconversion compared to those aged 40-49 (60-69 IRR=0.2, 95%CI 0.1-0.6; and 70-79 IRR=0.1, 95%CI 0.03-0.6), and those with some primary (IRR=1.6, 95%CI 0.7 – 3.5) or secondary education (IRR=2.1, 95%CI 0.8 – 5.3) were at higher risk of infection than those with no education although these results were not significant. Also, household structure and employment status were not associated with the risk of new infection.

DISCUSSION

To the best of our knowledge this is the first study reporting an estimate of population-based HIV incidence in a cohort of people 40 years and older in rural Africa. These results add to the existing evidence that older HIV negative adults are at risk for acquiring HIV(6). Other studies have reported HIV incidence in younger age groups (13-16), repeated measures in a voluntary counselling and testing (VCT) context (17-19), using mathematical models to estimate incidence from prevalence studies (9, 20, 21) or using the BED capture enzyme immunoassay (10). Our results show HIV seroconversion is still high even for those in their 50s and 60s, and disease acquisition only seems to slow over the age of 80. Our data corroborates a study from Kwa Zulu Natal, South Africa showing that women are at higher risk of HIV seroconversion (16), as we observed that women have higher levels of HIV infection in their 50s and 60s than their male counterparts. However, our data seems to contradict the finding that those with greater formal education have lower risk of HIV seroconversion (22).

Due to the low number of individuals who seroconverted (n=33) in the 5 years of follow up, our power to show significant associations between incident HIV and sociodemographic factors was limited and many of these estimates were measured imprecisely with wide confidence intervals.

It is important to consider death as a competing event for incident HIV infection. We identified 55 HIV negative participants from the 2010 study who died during the follow up period so were not available in 2015. We do not expect AIDS-related deaths among those who tested negative in 2010 because the period between the two studies was only 5 years while the life expectancy of those newly infected has been estimated to be between 8-10 years. However, we might expect that those who died would have been less likely to seroconvert during follow-up (due to age or infirmity) had they not died. If this scenario held, the HIV incidence we observed would slightly overestimate the true HIV incidence.

This study is among the first to show HIV incidence directly measured at the population level from an older population cohort. Our findings also highlight the importance of taking into consideration the older population in preventive HIV campaigns.

REFERENCES

1. Bendavid E, Ford N, Mills EJ. HIV and Africa's elderly: the problems and possibilities. AIDS. 2012;26 Suppl 1:S85-91.
2. Negin J, Barnighausen T, Lundgren JD, Mills EJ. Aging with HIV in Africa: the challenges of living longer. AIDS. 2012;26 Suppl 1:S1-5.
3. Nyirenda M, Chatterji S, Falkingham J, Mutevedzi P, Hosegood V, Evandrou M, et al. An investigation of factors associated with the health and well-being of HIV-infected or HIV-affected older people in rural South Africa. BMC Public Health. 2012;12:259.
4. Gomez-Olive FX, Angotti N, Houle B, Klipstein-Grobusch K, Kabudula C, Menken J, et al. Prevalence of HIV among those 15 and older in rural South Africa. AIDS Care. 2013;25(9):1122-8.
5. Wallrauch C, Barnighausen T, Newell ML. HIV prevalence and incidence in people 50 years and older in rural South Africa. S Afr Med J. 2010;100(12):812-4.
6. Rosenberg MS, Gomez-Olive FX, Rohr JK, Houle BC, Kabudula CW, Wagner RG, et al. Sexual Behaviors and HIV Status: A Population-Based Study Among Older Adults in Rural South Africa. J Acquir Immune Defic Syndr. 2017;74(1):e9-e17.
7. UNAIDS. The Gap Report: The beginning of the end of the AIDS epidemic. Joint United Nations Programme on HIV/AIDS:
UNAIDS / JC2656; ISBN 978-92-9253-062-4. 2014.
8. Barnighausen T, Tanser F, Newell ML. Lack of a decline in HIV incidence in a rural community with high HIV prevalence in South Africa, 2003-2007. AIDS research and human retroviruses. 2009;25(4):405-9.

9. Rehle TM, Hallett TB, Shisana O, Pillay-van Wyk V, Zuma K, Carrara H, et al. A decline in new HIV infections in South Africa: estimating HIV incidence from three national HIV surveys in 2002, 2005 and 2008. PLoS One. 2010;5(6):e11094.
10. Barnighausen T, McWalter TA, Rosner Z, Newell ML, Welte A. HIV incidence estimation using the BED capture enzyme immunoassay: systematic review and sensitivity analysis. Epidemiology. 2010;21(5):685-97.
11. Kahn K, Collinson MA, Gomez-Olive FX, Mokoena O, Twine R, Mee P, et al. Profile: Agincourt health and socio-demographic surveillance system. Int J Epidemiol. 2012;41(4):988-1001.
12. Gomez-Olive FX, Montana L, Wagner RG, Kabudula CW, Rohr JK, Kahn K, et al. Cohort Profile: Health and Ageing in Africa: a Longitudinal Study of an INDEPTH Community in South Africa (HAALSI). Int J Epidemiol. 2018.
13. Gonzalez R, Augusto OJ, Munguambe K, Pierrat C, Pedro EN, Sacoor C, et al. HIV Incidence and Spatial Clustering in a Rural Area of Southern Mozambique. PLoS One. 2015;10(7):e0132053.
14. Dube K, Zango A, van de Wijgert J, Meque I, Ferro JJ, Cumbe F, et al. HIV incidence in a cohort of women at higher risk in Beira, Mozambique: prospective study 2009-2012. PLoS One. 2014;9(1):e84979.
15. Hallett TB, Stover J, Mishra V, Ghys PD, Gregson S, Boerma T. Estimates of HIV incidence from household-based prevalence surveys. Aids. 2010;24(1):147-52.
16. Barnighausen T, Tanser F, Gqwede Z, Mbizana C, Herbst K, Newell ML. High HIV incidence in a community with high HIV prevalence in rural South Africa: findings from a prospective population-based study. AIDS. 2008;22(1):139-44.
17. Corbett EL, Makamure B, Cheung YB, Dauya E, Matambo R, Bandason T, et al. HIV incidence during a cluster-randomized trial of two strategies providing voluntary counselling and testing at the workplace, Zimbabwe. Aids. 2007;21(4):483-9.
18. Matovu JK, Gray RH, Makumbi F, Wawer MJ, Serwadda D, Kigozi G, et al. Voluntary HIV counseling and testing acceptance, sexual risk behavior and HIV incidence in Rakai, Uganda. Aids. 2005;19(5):503-11.
19. Baryarama F, Bunnell R, McFarland W, Hudes ES, Neilands TB, Ransom RL, et al. Estimating HIV incidence in voluntary counseling and testing clients in Uganda (1992-2003). J Acquir Immune Defic Syndr. 2007;44(1):99-105.
20. Kassanjee R, McWalter TA, Barnighausen T, Welte A. A new general biomarker-based incidence estimator. Epidemiology. 2012;23(5):721-8.
21. Mossong J, Grapsa E, Tanser F, Barnighausen T, Newell ML. Modelling HIV incidence and survival from age-specific seroprevalence after antiretroviral treatment scale-up in rural South Africa. AIDS. 2013;27(15):2471-9.
22. Barnighausen T, Hosegood V, Timaeus IM, Newell ML. The socioeconomic determinants of HIV incidence: evidence from a longitudinal, population-based study in rural South Africa. AIDS. 2007;21 Suppl 7:S29-38.

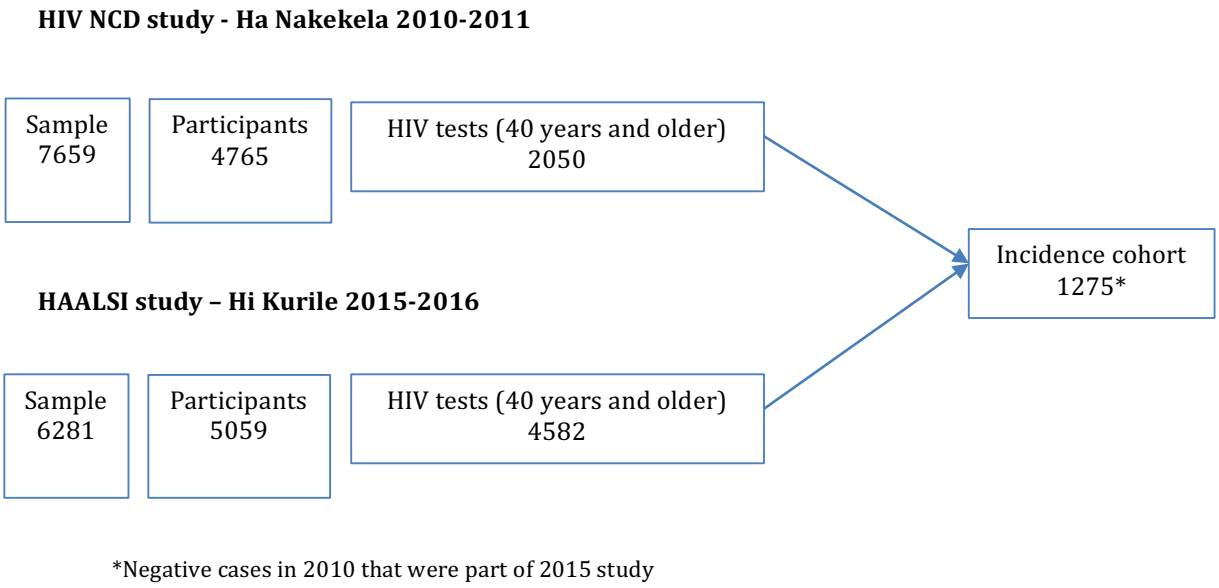

Figure 1. Creation of the HIV negative cohort from the Ha Nakekela (2010) study and the HAALSI (2015) study in the Agincourt HDSS, rural South Africa

Table 1. Crude HIV incidence rate and incidence rate ratios across key sociodemographic covariates per 100 person-years for a cohort of older adults age 40 years or older over 5 years of follow up (2010-2015).

	Cases	PYRS	IR (95% CI)	IRR (95% CI)	
Overall incidence	33	5295	0.6 (0.4 - 0.9)	-	
Sociodemographic variables					
Sex					P value
Male	7	1880	0.4 (0.2 - 0.8)	1	
Female	26	3415	0.8 (0.5 - 1.1)	2.1 (0.9 – 5.0)	0.073
Age group					
40 - 49	18	1347	1.3 (0.8 – 2.1)	1	
50 - 59	11	1072	1.0 (0.6 – 1.9)	0.8 (0.4 – 1.7.)	0.564
60 - 69	2	1223	0.2 (0.04 – 0.6)	0.2 (0.1 – 0.7)	0.009
70 - 79	2	1043	0.2 (0.1 – 0.8)	0.2 (0.04 – 0.6)	0.018
80+	0	696	0 (0 – 0)	0 (0 – 0)	-
Men, Age group					
40 - 49	4	411	1.0 (0.4 - 2.6)	-	
50 - 59	1	315	0.3 (0.04 - 2.3)	-	
60 - 69	1	472	0.2 (0.03 - 1.5)	-	
70 - 79	1	438	0.2 (0.03 - 1.6)	-	
80+	0	243	0 (0 – 0)	-	
Women, Age group					
40 - 49	14	932	1.5 (0.9 - 2.5)	-	
50 - 59	10	733	1.4 (0.7 - 2.5)	-	
60 - 69	1	822	0.1 (0.02 - 0.9)	-	
70 - 79	1	551	0.2 (0.03 - 1.3)	-	
80+	0	378	0 (0 – 0)	-	
Country of origin					
South African	24	3881	0.6 (0.4 – 0.9)	1	
Non-South African	9	1599	0.6 (0.3 - 1.1)	0.7 (0.3 – 1.6)	0.416
Marital status					
Not in a union	12	2393	0.5 (0.3 – 0.9)	1	
Currently in a union	21	3088	0.7 (0.4 – 1.4)	1.2 (0.6 – 2.5)	0.606
Employment status					
Employed	8	1330	0.6 (0.3 - 1.2)	1	
Not employed	24	4032	0.6 (0.4 - 0.9)	1.1 (0.5 – 2.4)	0.867
Education status					
No Formal Education / Some primary	25	4255	0.6 (0.4 - 0.9)	1	
Some secondary or more	8	1092	0.7 (0.4 - 1.5)	1.3 (0.6 – 2.9)	0.529
Household structure					
One/Two-person household	1	596	0.2 (0.02 – 1.2)	1	
Three or more-person household	32	4884	0.7 (0.5 – 0.9)	3.2 (0.4 – 23.2)	0.251

*p-value represents the join test of significance of the individual regressions.