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Jarvis, JN; Meintjes, G; Wood, R; Harrison, TS; (2010) Testing but not treating: missed opportunities and lost lives in the South African antiretroviral therapy programme. *AIDS* (London, England), 24 (8). pp. 1233-5. ISSN 0269-9370 DOI: <https://doi.org/10.1097/QAD.0b013e3283383aeb>

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Published in final edited form as:

*AIDS*. 2010 May 15; 24(8): 1233–1235. doi:10.1097/QAD.0b013e3283383aeb.

## Testing but not treating: missed opportunities and lost lives in the South African ART programme

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Recently published WHO guidance recommends starting ART in HIV-infected adults with CD4 counts of  $\geq 350$  cells/ $\mu$ l [1]. There is mounting evidence that such a policy will lead to lower mortality among HIV-infected individuals [2]. Also modeling data suggests that expanded testing and earlier treatment will reduce HIV transmission [3]. In South Africa ART coverage is not meeting current needs, even using the CD4 count criteria of  $<200$  cells/ $\mu$ l, and mortality early in ART programmes is high due to advanced immunosuppression at initiation [4]. Fortunately, following limited government leadership around HIV in the past, South African President Jacob Zuma has encouraged widespread HIV testing, and announced that he will undertake an HIV test [5].

However, expanded testing will only reduce mortality if patients testing HIV-positive are effectively and quickly channeled into treatment programmes. Our experience in Cape Town suggests that even at current levels of testing this is not the case. For the past two years, as part of ongoing clinical trials of cryptococcal meningitis (CM) treatment, we have prospectively identified all patients presenting with CM at a secondary level hospital serving a population of 1.3 million, with free access to HIV-testing and treatment services. As an opportunistic infection affecting primarily those with CD4 counts of  $<100$  cells/ $\mu$ l, rates of CM would be expected to decline rapidly in the face of effective ART programmes, as has been seen in the developed world [6].

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Author's contributions

JNJ conceptualized the piece, collected the data and wrote the initial draft. GM and TSH critically reviewed the draft and contributed to the writing of the final manuscript.

Conflict of Interests

None to declare.

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In our setting, despite ART roll-out, annual numbers of CM cases have remained fairly constant, as the number of patients developing stage 4 disease exceeds the numbers starting ART [7]. Most patients with CM are ART-naïve [8]; however in contrast to our expectations the majority (73%, 134 /183) were already known to be HIV-positive. Patients had tested positive a median of 4 months (IQR 2-12) prior to presentation with CM, and of those with documented CD4 counts at initial HIV diagnosis, 91% (64/70) were  $< 200$  cells/ $\mu$ l. Many patients are being tested, but not treated.

Our findings fit with data showing high mortality and loss to follow-up rates in ART programmes prior to ART initiation. In a cohort with extremely good retention in Cape Town, despite a median time from enrollment to ART initiation of only 34 days, almost half of all deaths in the programme occurred in this pre-treatment period [4]. The situation in much of the South African public sector is even more concerning. In a large cohort from the Free State province over 50% of eligible patients never received ART (3774 of 6899). Fifty-three percent of the cohort died, and 87% of these had not received ART [9].

Establishing why patients are testing but not initiating treatment is difficult. In South Africa mixed messages regarding safety and efficacy of ART may contribute to poor patient uptake of existing services [10]. Under-funding of HIV-services, heavy patient loads and long waiting times are likely to also contribute. Additionally, current guidelines [11, 12] specifying that patients should return for 3 separate outpatient visits prior to ART initiation, when transport costs have been identified as a barrier to accessing care in many areas [13], and encouraging disclosure of a stigmatizing diagnosis to treatment supporters, may discourage many from accessing care.

While the rationale behind such guidance arose from an urgent need to create effective, implementable and reproducible ART services, subsequent experience in regions where the majority of patients present with advanced immunosuppression suggests efforts are now needed to “fast-track” ART initiation. Initial concerns about adherence in African patients have been dispelled, with recorded adherence in African cohorts matching or surpassing the developed world [14]. Evidence for the efficacy of adherence interventions such as repeated counseling sessions prior to ART, which in practice are often weeks apart, is limited [15]. Nonetheless, in many ART programmes, this seems to outweigh the compelling evidence demonstrating that even minor delays in ART initiation in patients with advanced HIV leads to unacceptably high levels of mortality [4, 9].

In settings such as ours, where 22% of patients still present with CD4 counts below 50 cells/ $\mu$ l [16], current focus on the “workup” prior to ART initiation needs to be shifted to efforts aimed at quickly establishing vulnerable patients on treatment, coupled with ongoing adherence support. Linkage from testing to care must be improved, and while there may be a minority who will not adhere with “fast-track” initiation, the adherent majority will no longer be exposed to extreme risk of opportunistic infections such as cryptococcal meningitis, and the associated mortality, while waiting for ART.

## Acknowledgments

JNJ and GM are supported by the Wellcome Trust, London, UK (WT081794 and WT081667).

## References

1. World Health Organization. accessed 8th December 2009 Rapid advice: antiretroviral therapy for HIV infection in adults and adolescents. WHO press. 2009 November 2009. [www.who.int/entity/hiv/pub/arv/rapid\\_advice\\_art.pdf](http://www.who.int/entity/hiv/pub/arv/rapid_advice_art.pdf)

2. NIH News Release. accessed 8th December 2009 Starting Antiretroviral Therapy Earlier Yields Better Clinical Outcomes. Interim analysis of CIPRA HT 001. 2009 Monday 8th June. [http://www3.niaid.nih.gov/news/newsreleases/2009/CIPRA\\_HT\\_01.htm](http://www3.niaid.nih.gov/news/newsreleases/2009/CIPRA_HT_01.htm)
3. Granich RM, Gilks CF, Dye C, De Cock KM, Williams BG. Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: a mathematical model. *Lancet*. 2009; 373:48–57. [PubMed: 19038438]
4. Lawn SD, Myer L, Harling G, Orrell C, Bekker LG, Wood R. Determinants of mortality and nondeath losses from an antiretroviral treatment service in South Africa: implications for program evaluation. *Clin Infect Dis*. 2006; 43:770–776. [PubMed: 16912954]
5. BBC News. accessed 1st December 2009 South Africa vows to treat all babies with HIV. 2009 <http://news.bbc.co.uk/2/hi/africa/8388178.stm>
6. Mirza SA, Phelan M, Rimland D, Graviss E, Hamill R, Brandt ME, et al. The changing epidemiology of cryptococcosis: an update from population-based active surveillance in 2 large metropolitan areas, 1992–2000. *Clin Infect Dis*. 2003; 36:789–794. [PubMed: 12627365]
7. Jarvis JN, Boulle A, Loyse A, Bicanic T, Rebe K, Williams A, et al. High ongoing burden of cryptococcal disease in Africa despite antiretroviral roll out. *Aids*. 2009; 23:1181–1185. [PubMed: 19451795]
8. Bicanic T, Meintjes G, Wood R, Hayes M, Rebe K, Bekker LG, Harrison T. Fungal burden, early fungicidal activity, and outcome in cryptococcal meningitis in antiretroviral-naïve or antiretroviral-experienced patients treated with amphotericin B or fluconazole. *Clin Infect Dis*. 2007; 45:76–80. [PubMed: 17554704]
9. Fairall LR, Bachmann MO, Louwagie GM, van Vuuren C, Chikobvu P, Steyn D, et al. Effectiveness of antiretroviral treatment in a South African program: a cohort study. *Arch Intern Med*. 2008; 168:86–93. [PubMed: 18195200]
10. Ojikutu B, Jack C, Ramjee G. Provision of antiretroviral therapy in South Africa: unique challenges and remaining obstacles. *J Infect Dis*. 2007; 196(Suppl 3):S523–527. [PubMed: 18181705]
11. Guidelines: Antiretroviral Therapy in Adults. *Southern African Journal of HIV Medicine*. 2008 Summer; 18–31. 2008. ([www.hst.org.za/uploads/files/clinicalguide\\_adults.pdf](http://www.hst.org.za/uploads/files/clinicalguide_adults.pdf)):18–31.
12. National Antiretroviral Treatment Guidelines. National Department of Health South Africa. 2004
13. Amuron B, Namara G, Birungi J, Nabiryo C, Levin J, Grosskurth H, et al. Mortality and loss-to-follow-up during the pre-treatment period in an antiretroviral therapy programme under normal health service conditions in Uganda. *BMC Public Health*. 2009; 9:290. [PubMed: 19671185]
14. Mills EJ, Nachega JB, Buchan I, Orbinski J, Attaran A, Singh S, et al. Adherence to antiretroviral therapy in sub-Saharan Africa and North America: a meta-analysis. *Jama*. 2006; 296:679–690. [PubMed: 16896111]
15. Amico KR, Harman JJ, Johnson BT. Efficacy of antiretroviral therapy adherence interventions: a research synthesis of trials, 1996 to 2004. *J Acquir Immune Defic Syndr*. 2006; 41:285–297. [PubMed: 16540929]
16. Boulle A, Bock P, Osler M, Cohen K, Channing L, Hilderbrand K, et al. Antiretroviral therapy and early mortality in South Africa. *Bull World Health Organ*. 2008; 86:678–687. [PubMed: 18797643]