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COHORT PROFILE

Cohort Profile: The TASO-CAN Cohort Collaboration

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What is TASO-CAN and how did it come about?

Sub-Saharan Africa has scaled-up access to combination anti-retroviral therapy (cART) at unprecedented rates, yet data on patient-related outcomes remain sparse. Representative databases that facilitate high-quality collection, harmonization and analysis of HIV-related information from clinical and research-related sites are needed. The large sample sizes that nationally representative databases permit facilitate identification of rare outcomes and emerging problems and the elucidation of more complex relationships involving the use of cART. These efforts also allow meaningful comparisons between regional treatment programmes that differ in their operational procedures and serve diverse communities in different settings. Unique features of individual sites exist, such as language used and cultural norms, research and care capacity, infrastructure development, personnel training and experience, and collection of data elements that differ in type, number, definition or method of laboratory. Furthermore, the use of innovative databases and informatics approaches can provide a principled approach to pool national data, and improve uniformity and consistency in data management in such heterogeneous settings.

We have initiated a large multi-centre national cohort study in Uganda to address these issues. This is a Ugandan–Canadian collaboration. The principal organization is The AIDS Support Organization (TASO), the oldest and largest community-based provider of cART in Africa. We call this study TASO-CAN (TASO-Canadian).

Who is involved in TASO-CAN?

This cohort study is a collaboration between researchers at the University of Ottawa and University of British Columbia in Canada and TASO in Uganda. The Canadian investigators have a long-term relationship with TASO, involving teaching, mentoring and research.

Founded in 1987, TASO provides psycho-social support, clinical care and cART to individuals infected with HIV. TASO began providing widespread cART in 2004 and now provides cART to more than 24 000 patients. Since its inception, TASO has expanded the scope of its work to include nutritional support, vocational training, HIV education and capacity building of health-care workers. TASO's mission is to restore hope and improve the quality of life of individuals, families and communities affected by HIV and related diseases. TASO provides support to over 100 000 HIV-infected patients and supports family members through education, counselling and educational stipends. TASO provides services through 11 regional TASO centres, 35 mini-TASO centres in rural districts.

TASO receives its core cART funding through the United States President's Emergency Plan for AIDS Relief (PEPFAR) as well as funding from Irish AID and Swedish SIDA. The Ugandan Ministry of Health refers newly diagnosed HIV-infected children and adults to TASO clinical sites for care. Many of the populations serviced by TASO represent marginalized and neglected groups, including infants and children, orphans, conflict-affected populations, internally displaced people, widows, prisoners and family members of HIV-infected patients that may require urgent

support. TASO programmes emphasize adherence and retention and include innovative approaches to maintaining patient interest, including drama and social groups, diary-writing and involvement of patients in clinical duties to become 'expert patients'.

TASO provides a range of services including HIV testing, clinical care, provision of cART and psychosocial support. Laboratory services are limited, but include CD4 analysis, complete blood analysis, tuberculosis and malaria diagnosis and urine assessments. Criteria used for initiation of cART at TASO includes a World Health Organization (WHO) Stage III or IV or a CD4 cell count <250 cells/mm^3. Criteria for children's clinical admittance into the TASO cART programme are based on Ugandan Ministry of Health Guidelines. Children are eligible for cART if they have WHO paediatric Stage III, advanced Stage II or Stage I with CD4 cell percentage $<15\%$ for those <18 months of age and $<20\%$ for those >18 months of age.[1] The Uganda Ministry of Health National Anti-retroviral Treatment and Care Guidelines for Adults and Children have not yet been updated to reflect the WHO's newest recommendations for clinical staging and immunological classification.[2]

When a patient attends a TASO clinic, clinicians will complete standardized patient forms detailing patient demographics, as well as clinical, psycho-social and drug utilization data. These data are then hand-entered, in duplicate, into the TASO clinical administrative data collection. Patients are provided with a unique confidential identifying number. Patients requiring cART typically receive an initiation regimen, which is non-nucleoside reverse transcriptase inhibitor based with first-line treatment comprising nevirapine, lamivudine and stavudine and boosted lopinavir, didanosine and zidovudine as second line.[3] Patients requiring treatment for tuberculosis (TB) co-infection will receive their combination care at a TASO clinic.

What is the primary objective of TASO-CAN?

The overall objective of the TASO-CAN collaboration is to support the collation of data from all TASO clinic sites across Uganda to develop a nationally representative observational cohort database of HIV-infected patients on cART. The development of the TASO-CAN cohort allows for monitoring clinical care and programmatic outcomes across a nationally representative large cohort of HIV-infected patients in Uganda.

Who is in the sample?

The analyses were based on a cohort of 22 315 individuals $\geqslant 14$ years of age who initiated cART at TASO clinics in Uganda between 2000 and 2009. Patients were followed for a median of 31 months [interquartile range (IQR) 19–45]. Table 1 shows the demographical and clinical characteristics of patients. The median age among patients was 37 years (IQR: 31–43 years) and the majority (69.4%) of patients were female. The median CD4 cell count at cART initiation was 142 cells/mm^3 (IQR: 70–206 cells/mm^3) (72.5% initiated cART with a CD4 cell count <200 cells/mm^3). A higher percentage of patients (58.1%) started cART with a WHO disease Stage of either II or III. 1498 patients died during follow-up (6.7%) and 1433 (6.4%) of patients were lost to follow-up.

What are the recruitment and attrition rates?

Since the TASO-CAN cohort is based on de-identified electronic clinical administrative records, patients are not individually recruited into this study. Currently, there are more than 24 000 patients who have

Table 1 Selected baseline characteristics of the TASO-CAN cohort

Variable	*n* (%)
Age	
14–19	333 (1.5)
20–24	866 (3.9)
25–29	2620 (11.7)
30–34	4801 (21.5)
35–39	4973 (22.3)
40–44	3944 (17.7)
45–49	2348 (10.5)
50–54	1271 (5.7)
$\geqslant 55$	1159 (5.2)
Gender	
Female	15 492 (69.4)
Male	6823 (30.6)
CD4 cell count (cells/mm^3) (missing 3817)	
<50	3452 (18.7)
50–99	2942 (15.9)
100–149	3410 (18.4)
150–199	3597 (19.4)
200–249	2143 (11.6)
250–299	874 (4.7)
$\geqslant 300$	2080 (11.2)
WHO clinical disease stage	
Stage I	465 (2.1)
Stage II	7985 (35.8)
Stage III	4982 (22.3)
Stage IV	1220 (5.5)
Missing	7663 (34.3)

initiated cART at TASO. All the patients are included in the TASO-CAN cohort. Patients are only lost to follow-up in the TASO-CAN cohort if they are lost to follow-up at one of the TASO sites.

TASO uses field adherence monitoring teams equipped with motorcycles who are responsible for active patient retention and follow-up. Patients who fail to show up for any appointment or patients who have requested home-based care are visited by the field adherence monitoring team. As a result of this active retention strategy, TASO has a nationwide, loss-to-follow-up rate of only 7%. This stands in contrast to an average of 40% loss-to-follow-up when passive retention strategies are used.[4,5] The team consists of medical attendants capable of conducting HIV testing, adherence counselling, clinical observation and cART distribution.

How are the data collected and managed?

At each TASO site in Uganda, data on all patients receiving clinical care is input into a standardized clinical administrative database. This database contains information on demographics, therapeutics, laboratory, clinical, adherence and other important descriptors. Each TASO site has a data management officer and data entry clerks. The records clerks manage patients' files. TASO data staff make modifications and improvements to the database regularly, and the Canadian collaborators have played an active role in improving the number of variables captured. Data from each site are sent to TASO headquarters in Kampala, Uganda, on a monthly basis. Data are stored in a secure manner. The server runs an automated backup on daily basis. Each data management officer is expected to have a folder structure that includes archived data. The computer system is protected by a firewall prohibiting unauthorized entry. Any data transmitted to offsite locations are encrypted. All TASO sites are secured on a nightly basis and protected with armed guards.

The TASO-CAN cohort is based on this clinical administrative database. An electronic data extraction of a pre-defined set of variables is performed annually from the clinical administrative database. This data extraction is performed at TASO Headquarters. All data are stripped of names and other personal identifiers and a unique study identification number is assigned to each participant. TASO-CAN currently includes only those who have initiated cART. Table 2 lists the variables currently captured in the TASO-CAN database.

The secondary use of TASO clinical administrative data for the purposes of developing the TASO-CAN cohort has received ethical approval from the institutional review boards of the University of Ottawa and the University of British Columbia in Canada, and the institutional review board at TASO in Uganda.

What are the main strengths and weaknesses?

With a nationally representative sample of more than 24 000 participants, TASO-CAN is the largest cohort of individuals who have initiated cART in sub-Saharan Africa. The TASO-CAN cohort represents cART patients nationwide, thus capturing a wide range of differing patient experiences and allowing for regional comparisons. Furthermore, the diverse population included in the TASO-CAN cohort is likely comparable with those in other areas of sub-Saharan Africa, including adolescents and elderly patients, those suffering from conflict and food insecurity and those who have switched treatments since initiation.

There are a number of inherent limitations, however, that must be recognized. Most notably, patients are not randomly assigned to cART or sampled. Additionally, TASO does not have the capacity to routinely collect information on HIV viral load or HIV resistance, which are important indicators of HIV disease progression and, as such, these variables are not currently included in the TASO-CAN database. While loss to follow-up is a major concern in any cohort study, TASO is a remarkable organization to address

Table 2 Summary of variables collected in the TASO-CAN database

Category of variable	Variables
Demographics	Age, sex, height, weight, place of residence, family and marital status, occupation
Therapeutic	Year of entry into care, clinic visit dates, CD4 cell count
Concurrent treatments	TB, pregnancy, STI
Laboratory (HIV related)	CD4, CD8, CD4%
Laboratory (non-HIV related)	Platelets, haemoglobin
Clinical	WHO Stages I, II, III, IV
Adherence	Determined by pharmacy refill records, 3-day self-report and drug possession ratio
Other	Death date and AIDS or non-disease death

this major concern. As mentioned, TASO utilizes active retention through field officers on motorcycles, thereby reducing overall loss-to-follow-up to only 7%, a rate unrivalled in Uganda. Our data suffer from some missing variables; for example, those listed in Table 1. We address this using Monte Carlo Markov Chain (MCMC) multiple imputations. Furthermore, the TASO-CAN dataset will be enhanced annually at each subsequent data cut by inclusion of more cohort members and a wider selection of variables.

What has been found?

The development of the TASO-CAN cohort collaboration was the obvious next step following an extensive partnership between the Canadian and Ugandan investigators involved. Together, many database evaluations, cohort studies, policy analysis and qualitative studies have been conducted. Several of these studies are described in detail further.

Investigators assessed outcomes among children receiving cART in a conflict setting in northern Uganda. Results of this study indicated that there were no differences between orphans and non-orphans in terms of CD4 cell counts, weight, presence of tuberculosis or WHO staging at initiation of cART. Furthermore, it was found that adherence to cART was >95% in the vast majority of both orphans and non-orphans. These findings were presented at the International AIDS Society Conference in Mexico (2008) and at the UN General Assembly Special Session on HIV/AIDS (2008) and later published in the journal *AIDS*.[6]

This first study was followed-up with a nationwide assessment of clinical outcomes for children receiving cART at all TASO sites. Results indicated positive clinical outcomes in older children, but younger children were largely absent. This study was published in *AIDS*.[7] As a result of these findings, TASO has implemented a programme to directly target infants and young children.

Investigators also examined the outcomes of patients on cART in a conflict-affected setting in northern Uganda. Findings indicated that patients receiving cART in conflict-affected northern Uganda had a mortality rate comparable with that of patients in peaceful, low-income settings and better adherence than patients in higher income settings. These findings highlighted the need to expand access to cART in populations affected by armed conflict, and have influenced international policies on cART provision in conflict settings. These data were also presented at the International AIDS Society Conference in Mexico (2008) and at the UN General Assembly Special Session on HIV/AIDS (2008) and later published in the journal *BMJ*.[3]

An evaluation of ageing and survival was recently undertaken among patients on cART at TASO. Results indicated that elderly patients (aged $\geqslant 50$ years) had worse survival rate when compared with non-elderly counterparts. These results suggest that elderly patients may require focused clinical care that extends beyond HIV treatment. TASO is currently translating these findings within the organization and community to determine the necessary actions that need to be taken. This study was presented at the International AIDS Society Conference in Vienna (2010) and later published in the journal *AIDS*.[8]

More recently, investigators have examined life expectancy of patients on cART at TASO and found that widespread anti-retroviral therapy in Uganda has resulted in a substantial increase in life expectancy. Results indicate that Ugandan patients receiving cART can expect an almost-normal life expectancy. These results have been presented at the International AIDS Society Conference in Vienna (2010) and are currently under review for publication. Further studies include qualitative and case series examinations.[9,10]

What is the plan for knowledge translation and exchange?

TASO-CAN investigators and their institutions are involved with policy-making and programme development initiatives. For example, investigators have been working with various ministries in Uganda and will ensure that research findings are translated and disseminated directly to these authorities. Additionally, investigators will ensure that local and international non-governmental partners working in Uganda will receive and understand study implications. Furthermore, investigators will provide the research results to the patients and families at TASO sites, and will create open discussions and community forums to actively engage these individuals.

Investigators will also utilize traditional systems of knowledge transfer, including open-access academic publications and dissemination of findings at national and international conferences. In addition to providing information of immediate value to the clinical and public health community, we expect the outcomes of this project will serve as the groundwork for further research in the topics addressed. Investigators will also seek funding from other agencies to conduct interventional research aimed at improving knowledge of treatment and services.

How can I collaborate?

A list of publications and additional information can be obtained by contacting the principal investigator, Dr Edward Mills, at edward.mills@uottawa.ca. Collaboration with national and international studies is welcome and can be proposed to Dr Mills at the email address above.

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Conflict of interest: None declared.

References

[1] Uganda Ministry of Health. *National Antiretroviral Treatment and Care Guidelines for Adults and Children*, 2003. *http://wwwaidsugandaorg/pdf/ARV_Clinical_Guidelines_Final_draftpdf* (15 February 2010, date last accessed).

[2] World Health Organization. *WHO Case Definitions of HIV for Surveillance and Revised Clinical Staging and Immunological Classification of HIV-related Disease in Adults and Children*. Geneva 2008.

[3] Kiboneka A, Nyatia RJ, Nabiryo C *et al*. Combination antiretroviral therapy in population affected by conflict: outcomes from large cohort in northern Uganda. *BMJ* 2009; **338:**a2662.

[4] Rosen S, Fox MP, Gill CJ. Patient retention in antiretroviral therapy programs in sub-Saharan Africa: a systematic review. *PLoS Med* 2007;**4:**e298.

[5] Braitstein P, Brinkhof MW, Dabis F *et al*. Mortality of HIV-1-infected patients in the first year of antiretroviral therapy: comparison between low-income and high-income countries. *Lancet* 2006;**367:**817–24.

[6] Kiboneka A, Nyatia RJ, Nabiryo C *et al*. Pediatric HIV therapy in armed conflict. *AIDS* 2008;**22:**1097–98.

[7] Kiboneka A, Wangisi J, Nabiryo C *et al*. Clinical and immunological outcomes of a national paediatric cohort receiving combination antiretroviral therapy in Uganda. *AIDS* 2008;**22:**2493–99.

[8] Bakanda C, Birungi J, Mwesigwa R *et al*. Association of aging and survival in a large HIV-infected cohort on antiretroviral therapy in Uganda. *AIDS* 2010. [Epub ahead of print].

[9] Cooper CL, Mills E, Wabwire BO, Ford N, Olupot-Olupot P. Chronic viral hepatitis may diminish the gains of HIV antiretroviral therapy in sub-Saharan Africa. *Int J Infect Dis* 2008;**13:**302–06.

[10] Olupot-Olupot P, Katawera A, Cooper C, Small W, Anema A, Mills E. Adherence to antiretroviral therapy among a conflict-affected population in Northeastern Uganda: a qualitative study. *AIDS* 2008;**22:**1882–84.