Cango Lyec (Healing the Elephant): HIV incidence in post-conflict Northern Uganda

Achilles Katamba[a], Martin D. Ogwang[b], David S. Zamar[c], Herbert Muyinda[d], Alex Oneka[e], Stella Atim[e], Kate Jongbloed[c], Samuel S. Malamba[f], Tonny Odongping[e], Anton J. Friedman[c], Patricia M. Spittal[c,g,*], Nelson K. Sewankambo[a], Martin T. Schechter[c]

[a] Makerere University College of Health Sciences, School of Medicine, Uganda
[b] St Mary's Hospital - Lacor, Northern Uganda Program on Health Sciences
[c] University of British Columbia, School of Population & Public Health, Canada
[d] Makerere University, Child Health Development Center, Uganda
[e] Cango Lyec Project, Makerere University, Child Health Development Center, Uganda
[f] Uganda Virus Research Institute (UVRI) - HIV Reference Laboratory Program, Uganda
[g] BC Children's Hospital Research Institute, Canada

ABSTRACT

Background: Civil war in Northern Uganda resulted in widespread atrocities, human rights violations, and death, and caused millions to flee to internally displaced persons camps. War-related traumas combined with difficulties accessing HIV prevention and health services has led to extreme HIV-related vulnerability among conflict-affected people who survived the war. Objectives were to (1) determine HIV incidence among conflict-affected people in Northern Uganda and (2) identify vulnerabilities associated with HIV infection.

Methods: The Cango Lyec (Healing the Elephant) Project is a prospective cohort involving conflict-affected populations in three districts in Northern Uganda. In 2011, eight randomly selected communities were mapped, and a census was conducted. Consenting participants aged 13−49 years were followed over three rounds of follow-up. Longitudinal data collected included war-related experiences, sexual vulnerabilities, and sociodemographics. Blood samples were tested for HIV-1 at baseline and each 12-month follow-up. Multivariable Cox proportional hazard models determined factors associated with HIV incidence.

Findings: Overall, 1920 baseline HIV-negative participants with at least one follow-up contributed 3877 person-years (py) for analysis. Thirty-nine (23 female, 16 male) participants contracted HIV during follow-up. Age- and gender-standardised HIV incidence rate was 10•2 per 1000py (95%CI: 7•2-14•0). Stratified by sex, the age-adjusted HIV incidence was 11•0 per 1000py (95%CI: 6•9-16•6) among women and 9•4 per 1000py (95%CI: 5•3-15•3) among men. Adjusting for confounders, factors associated with risk of HIV included: having been abducted (HR: 3•70; 95%CI: 1•87-7•34), experiencing ≥12 war-related traumatic events (HR: 2•91 95%CI: 1•28-6•60), suicide ideation (HR: 2•83; 95%CI: 1•00-8•03), having ≥2 sexual partners (HR: 4•68; 95%CI: 1•36-16•05), inconsistent condom use (HR: 6•75; 95%CI: 2•49-18•29), and self-reported genital ulcers (HR: 4•39; 95%CI: 2•04-9•45).

Interpretation: Conflict-affected participants who had experienced abduction and multiple traumas during the war were at greater risk of HIV infection. Trauma-informed HIV prevention and treatment services, and culturally-safe mental health initiatives, are urgent for Northern Uganda.

1. Introduction

Two decades of war in Northern Uganda (1986-2006) involving widespread atrocities, human rights violations, and displacement continue to impact the health and wellbeing of conflict-affected people in Acholiland. Over 1•8 million people (90% of the population) in the region were displaced from homes and communities [1, 2]. In

* Corresponding author: Patricia M. Spittal, BC Children's Hospital Research Institute, V3-323 Clinical Support Building, 950 W 28th Ave Vancouver, BC V5Z4H4, Canada, +1-604-875-2345, ext. 5944.
E-mail address: spittal@sm.hivnet.ubc.ca (P.M. Spittal).

Research in context

Evidence before the study

The impact of the conflict and post-conflict context on HIV in Northern Uganda is not well captured in currently available data, including antenatal surveillance and the Uganda AIDS Indicator survey. Studies during the immediate aftermath of the civil war demonstrated elevated HIV prevalence in the region compared to national estimates. However, no existing evidence has assessed HIV incidence among conflict-affected Acholi people in Northern Uganda.

Added value of this study

This study presents previously unavailable population-level estimates of HIV incidence in a random sample of conflict-affected communities in Northern Uganda. Further, it examines linkages between war-related experiences and HIV risk to help identify trauma-informed and healing-centred HIV risk reduction strategies in this unique setting.

Implications of all the available evidence

High HIV incidence observed in post-conflict Northern Uganda (2•5 times higher than national estimates) is cause for alarm. Evidence presented in this study highlights the urgency of HIV prevention strategies that address the ongoing impacts of war-related traumas and disruption of traditional ways of life on HIV risk among Acholi people in Northern Uganda.

13 years since the cessation of hostilities agreement was signed, people displaced during the war have left internally displaced persons (IDP) camps to return to their ancestral homes. As those who experienced war-related traumas navigate new environments outside of conflict zones and IDP camps, concerns remain regarding significant HIV-related vulnerabilities exacerbated by disruption of community and family life, breakdown of services, IDP camp living, and exposure to sexual violence [3-5].

Currently, approximately 1•3 million people are living with HIV in Uganda; estimates suggest that over 6% of people aged 15 and over are HIV-positive [6, 7]. Recent national data compiled by UNAIDS identified new infections are occurring at a rate of 1•37 per 1000 population [6]. However, HIV rates in post-conflict Northern Uganda are less understood. Antenatal surveillance from 2005 reported that HIV prevalence in Northern Uganda was 8•2% [8]. A 2010 cross-sectional study involving 384 young (15-29 years of age) transit camp residents in Gulu District estimated an HIV prevalence of 12•8% [3]. The 2011 Uganda AIDS Indicator Survey reported HIV prevalence across the mid-Northern region was 8•3% [9]. The Cango Lyec (Healing the Elephant) cohort study, involving over 2000 Acholi people in three districts in Northern Uganda, has provided additional evidence related to the lasting impacts of conflict on HIV prevalence and vulnerabilities in the region [10, 11]. Baseline data collected in 2011/12 observed an overall HIV prevalence of 12•2%, with women significantly more likely to be living with HIV [10]. To our knowledge, no studies have assessed HIV incidence in this post-conflict context of Northern Uganda.

HIV infection in post-conflict Northern Uganda must be understood in the context of war-related traumas. A recent review of 33 studies globally highlighted that consequences of conflict on mental health and wellbeing contribute to increased risk of HIV infection and disease progression [12]. Atrocities including massacres, abductions, and sexual violence during the Northern Ugandan conflict are now being linked to HIV risk post-conflict [3, 10]. Among young transit camp residents surveyed in 2010, the strongest predictor of HIV infection was non-consensual sexual debut [3]. Among *Cango Lyec* participants, reporting 12 or more war-related traumas, post-traumatic stress disorder, major depressive disorder, or thinking about suicide were all associated with increased odds of living with HIV at baseline [10]. Relationships between HIV and war-related sexual violence were especially pronounced among women in *Cango Lyec* [11]. HIV vulnerability may be exacerbated post-conflict through increased sexual violence, negative social determinants of health stemming from disruption of livelihoods and social structures, breakdown of health and HIV services infrastructure, and stigma and discrimination related to war-time experiences [13, 14].

The Cango Lyec (Healing the Elephant) Project cohort involving conflict-affected Acholi people was initiated by Ugandan and Canadian collaborators in response to concerns of a simmering HIV epidemic in Northern Uganda. Objectives of this study were to (1) determine population-wide HIV incidence among conflict-affected people in Northern Uganda and (2) identify vulnerabilities associated with HIV infection, to inform development of prevention programs and support healing.

2. Methods

2.1. Study design and population

Cango Lyec is an open cohort involving conflict-affected people in Gulu, Nwoya and Amuru districts in mid-northern Uganda. The rationale and organization of the Cango Lyec cohort have been described in detail elsewhere [10, 11]. Between November 2011-July 2012, eight study communities, randomly selected out of 32, were mapped and a house-to-house census was conducted to enumerate the entire population. The study period included three rounds of data collection between November 2011 and March 2015 (baseline, follow-up 1, and follow-up 2). A total of 3143 (2539 at baseline and 604 in follow-up 2) consenting participants aged 13−49 years were enrolled, and interviewer-administered questionnaires collected data on trauma, mental health, and socio-demographic-behavioural characteristics. Data collection took place in settings of participants' choosing. Given that some questions may elicit memories of trauma and victimization, participants who requested care were referred to a nearby health unit with a psychiatric nurse and/or civil society organization with a trauma focus, based on participant choice. Participants were followed up every 12 months, to March 2015. Venous blood was taken for HIV at baseline and each follow-up visit. Complete serodata was available for 3077 (97.9%) participants. The range of missing values among independent variables varied between 0 and 1.8%. No imputation was conducted for missing data. The reporting of this study conforms to the STROBE statement [15].

2.2. Ethical approvals

We received approvals from University of British Columbia-Providence Healthcare Research Ethics Board (Canada), Makerere College of Health Sciences-School of Public Health (Uganda), and Uganda National Council of Science and Technology (Uganda). The Office of the President of Uganda issued a letter of approval, which was then signed by the Resident District Commissioner in each district.

2.3. Data collection and measures

Participants were eligible if they were aged 13−49 years; were resident in their household for over one month; permission was given by the head of household; and they provided informed consent. Unemancipated minors, as defined by Uganda National Council of Science and Technology, were asked to provide individual informed assent if written consent was provided by parent/guardian. Minors who did not want to participate were not enrolled.

The primary outcome was HIV-1 infection, determined by blood specimen collection at baseline and each study round. Two ELISA tests, Vironostika HIV Uni-Form II plus O (Biomerieux SA, Marcy l'Etoile, France) and Murex HIV-1.2.O (Diasorin S.P.A, Dartford, United Kingdom) were used in parallel to test for HIV infection at the Uganda Virus Research Institute IAVI-laboratory. Western Blot (Genetic Systems, Bio-Rad Laboratories) served as tiebreaker if ELISA results were discordant; any indeterminate Western Blot results were resolved using a qualitative Roche Cobas AmpliPrep/Cobas TaqMan HIV-1 Polymerase Chain Reaction (PCR) test (RT). Trained HIV counsellors provided pre-test/post-test counselling and participants were encouraged, but not required, to receive test results. HIV-positive individuals were referred to clinical services providing ART at the health facility of their choice. Active syphilis was determined using rapid plasma regain (RPR) test and confirmatory treponema pallidum haemagglutination test (TPHA) in event of a positive screen. Active syphilis was treated with a single-dose of azithromycin.

Questionnaires assessing socio-demographic characteristics, conflict-related experiences and sexual behaviours were administered at baseline and follow-up visits. All instruments were translated into Luo through a process of forward-backward translation by an experienced team of health professionals working independently. Where there was disparity, translations were discussed and revised to achieve intended meaning. The term 'recent' is used to indicate time-varying factors collected at each follow up visit; all others are time-invariant factors collected at baseline.

Socio-demographics included age (years), ethnicity (Acholi/other), district of residence (Amuru/Gulu/Nwoya), marital status (married/not married), educational attainment (≤primary/≥secondary), religion (Roman Catholic/Protestant/Moslem/Other), recently experiencing ill health without access to medical care, and living in a female-headed household.

War-related experiences included abduction and community displacement status (displaced/transient/permanent). Displaced settlements were those created to accommodate IDP during the war; transient settlements were those created to accommodate IDP returning to war-impacted communities that required rebuilding; and permanent settlements were those that existed prior to the war and residents were never displaced. Sexual assault within the context of war included rape outside of abduction but related to war, for example gang rape in IDP camps. Exposure to trauma and mental health concerns were assessed using Luo versions of the Harvard Trauma Questionnaire (HTQ) and Hopkins Symptom Check List-25 (HSCL-25), developed and validated for use in Gulu district [16]. Exposure to traumatic war-related experiences were collected using HTQ Part I, consisting of 16 questions regarding prior traumatic life events with four possible answers: "Experienced," "Witnessed", "Heard about it," or "No". Scores were dichotomized (<12 vs. ≥12 severe traumatic events) based on previous research indicating this threshold to be a predictor of post-traumatic stress disorder (PTSD) and depression in Northern Uganda [16]. HTQ Part IV includes 16 questions addressing trauma symptoms measured using a four-point severity scale for a one-week recall period to identify symptoms indicative of probable PTSD [17]. Sums of all answered items in Part IV were divided by the number of answered items; scores ≥2•0 were classified as meeting criteria for screening positive for PTSD [18]. The HSCL-25 identified recent suicidal ideation and symptoms indicative of recent probable depression. Mean scores of ≥1•75 on HSCL-25 Part II were classified as meeting criteria for screening positive for recent probable depression [18]. Both scales have been found to be reliable and valid in war-affected African countries [16, 19-23]. Cronbach's alpha coefficient was calculated for the HTQ Part IV ($\alpha = 0.87$) and the HSCL-25 Part II ($\alpha = 0.85$), with both indicating high internal consistency in this study. Participants with summed responses of ≥25 (HSCL-25) or ≥28 (HTQ), as well as those who reported feeling hopeless about the future, thoughts about ending their life, and feelings of worthlessness, were referred immediately to mental healthcare.

Sexual vulnerabilities included: age at sexual debut (dichotomized at 16 years), coerced sexual debut, age difference of first sex partner (dichotomized at 10 years), condom use at sexual debut, number of sexual partners (recent, 0/1/2+), consistency of condom use with last three partners (not always/always), circumcised (males only), most recent male partner circumcised (females only), self-reported sex with genital ulcers (past year), and sex for exchange (defined as receiving money, shelter, food, gifts, or alcohol for sex).

3. Analysis

Questionnaires and HIV test results were entered in duplicate using Microsoft Access software. Analyses were carried out using R statistical computing language [24]. Participants who were HIV-positive at baseline were excluded. We compared baseline characteristics of males and females using Fisher's exact test for categorical variables, and Mann-Whitney U test for continuous variables. HIV incidence density was calculated for participants who were HIV-negative at baseline and completed at least 2 surveys, by dividing number of events of HIV seroconversion by number of person-years (py) of follow-up. Follow-up time was calculated as time between first negative test and most recent negative test or incident infection. Seroconversions were assumed to have taken place at the midpoint between last HIV-negative test and first HIV-positive test. As the intervals between last negative and first positive test was long (approximately 1 year by design), we conducted a sensitivity analysis to investigate the robustness of our results to uncertainty in the event-times.

Cox proportional hazards regression models with time-dependent variables determined factors associated with HIV seroconversion. Factors found significant in univariate analysis were included in a stepwise multivariate Cox model adjusted for age, gender, marital status, religion, education, and district, with entry criteria $p \leq 0•10$. Backward and forward stepwise variable selection determined a final model. Unadjusted and adjusted odds ratios with standard errors and 95% confidence intervals are provided. A p-value of 0•05 was considered statistically significant. Poisson 95% confidence intervals (CIs) were calculated for overall incidence density. HIV incidence estimates were age-and gender-standardised using the census population.

Loss to follow-up was 28.5%. To account for the potential bias in results due to attrition, the analysis was further weighted using inverse probability weighting (IPW) based on socio-demographic characteristics age, gender, displacement status, and marital status.

4. Role of Funding Source

The funders of the study had no role in study design; in the collection, analysis, and interpretation of data; in the writing of the report; nor in the decision to submit the paper for publication.

5. Results

Overall, 1920 participants who were HIV-negative at baseline with at least one follow-up contributed 3877 person-years for analysis (Figure 1). More than half (n=1023; 53•2%) were women and the majority were Acholi (n=1732; 90•2%) (Table 1). Compared to men, women were older, and more likely to be married, have lower educational attainment, live in a female-headed household, experience ill health without access to medical care, and report inconsistent condom use. Women were more likely than men to experience probable depression, probable PTSD, and suicide ideation. Women also were more likely to report sexual assault in the context of war, coerced sexual debut, and a first sexual partner ≥10 years older. Men were more likely to have been abducted, report experiencing ≥12 war-related traumatic events, and have ≥2 sexual partners in the past year.
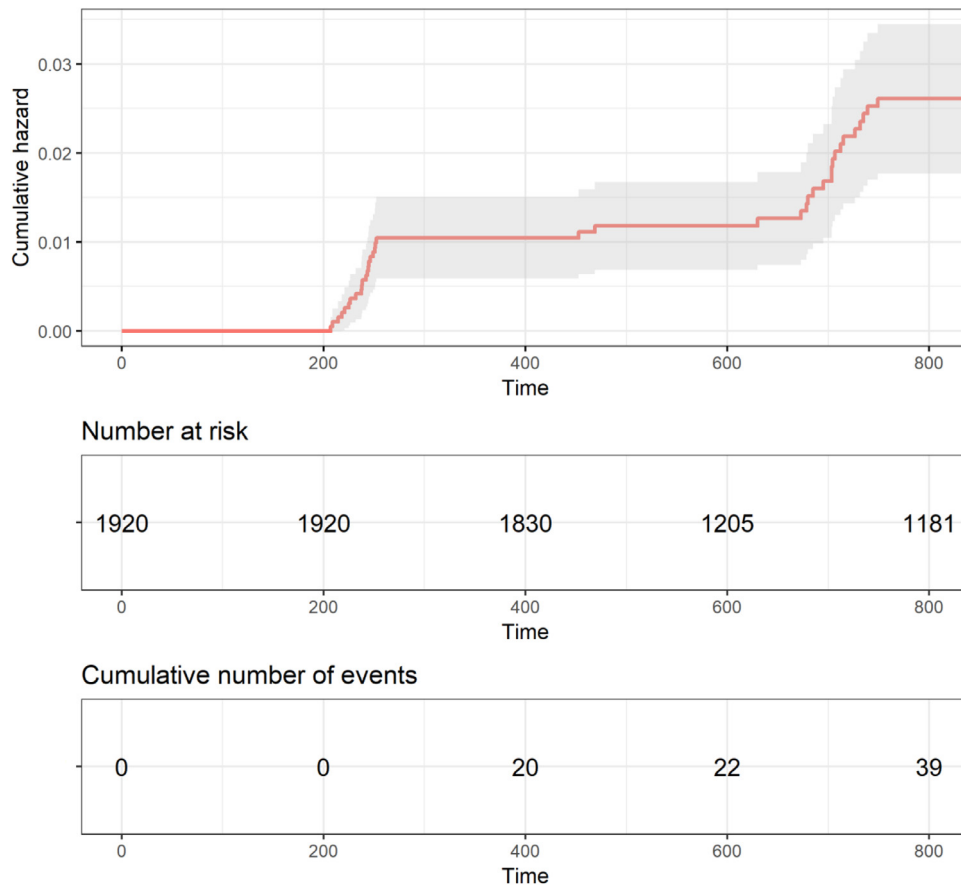
Figure 1. Cumulative hazard function for HIV infection describing the rate at which hazards are accumulated over time. In this study, the probability of contracting HIV by 800 days or fewer is approximately 2•6% (95%CI: 1•8 − 3•4).

Thirty-nine participants (23 female, 16 male) contracted HIV during follow-up. Crude HIV incidence rate was 10•1 (95%CI: 7•2-13•8) per 1000py (Table 2). Stratified by sex, crude HIV incidence rate was 11•1 (95%CI: 7•0-16•7) per 1000py among women and 8•9 (95%CI: 5•1-14•4) per 1000py among men. Age standardized incidence rate was 10•2 (95%CI: 7•2-14•0) per 1000py overall, and slightly higher among women (11•0; 95%CI: 6•9-16•6) than men (9•4; 95%CI: 5•3-15•3).

Correlates of HIV incidence adjusted for age, sex, marital status, district, displacement status, and religion are presented in Table 3. War-related traumas and mental health factors significantly associated with increased risk of HIV infection included: having been abducted (HR: 3•70; 95%CI: 1•87-7•34), experiencing ≥12 war-related traumatic events (HR: 2•91; 95%CI: 1•28-6•60), and suicide ideation (HR: 2•83; 95%CI: 1•00-8•03). Sexual vulnerabilities significantly associated with HIV incidence included: having ≥2 sexual partners (HR: 4•68; 95%CI: 1•36-16•05), inconsistent condom use (HR: 6•75; 95%CI: 2•49-18•29), and self-reported genital ulcers (HR: 4•39; 95%CI: 2•04-9•45).

In a final multivariate model (Table 4), living in a transient community (HR: 0•47; 95%CI: 0•22-0•99) and being married (HR: 0•35; 95%CI: 0•15-0•79) were associated with reduced risk of HIV infection. Having been abducted (HR: 3•21; 95%CI: 1•61-6•38), inconsistent condom use (HR: 4•61; 95%CI: 1•66-12•79), and having sex with genital ulcers (HR: 3•33; 95%CI: 1•53-7•24) were associated with increased risk.

In a sub-analysis of cohabiting couples, risk of seroconversion among discordant couples was significantly greater (OR: 4•62, 95%CI: 1•25-17•34). Empirically observed conditional probabilities of HIV infection among discordant and HIV-negative concordant couples in the study were 8•33% and 1•93%, respectively.

Notably, among all HIV-positive cohort participants (n=218), including new infections and those who were positive at baseline, 179 (82•1%) reported being on antiretrovirals (ART). More women (128/147; 87•1%) reported being on ART, compared to men (51/71; 71•8%).

To investigate the robustness of our results to uncertainty in the event-times, Monte Carlo simulations were performed by first uniformly drawing event times from the intervals from which they were known to have occurred and then fitting the Cox proportional hazard regression model assuming the event times were known exactly. Results obtained were similar with pooled Monte Carlo coefficient estimates differing on average by only 1 percent to those obtained using the midpoint. As such, interval-censorship was assumed to be random or non-informative.

An analysis of attrition of those variables included in the final model showed that, at least for some variables (gender, age, and displacement status), there were significant differences between participants who remained in the sample and those who did not. However, HIV-related vulnerabilities included in the final model, such as condom use, abduction, and genital ulcers were found not to be associated with attrition. Furthermore, results were found not to be significantly impacted, with an average relative difference in effect measure of 2 percent between IPW weighted and unweighted final models.

6. Discussion

We observed a high HIV incidence rate of 10•2 per 1000py among people who have survived the war in Northern Uganda. This is 2•5 times higher than 2014 Ugandan national estimates, which reported incidence of 4•2 per 1000 population [25]. Stratified by

Table 1
Baseline Characteristics for Males and Females in Post Conflict Northern Uganda

Variable	Female (n=1023, 53•2%)		Male (n=897, 46•8%)		P^1
	n/N	%	n/N	%	
Sociodemographic Characteristics					
Median age (IQR)	25 (19, 33)		23 (17, 32)		<0•001
Ethnicity					0•701
Acholi	920/1023	89•9	812/897	90•5	
Other Tribes	103/1023	10•1	85/897	9•5	
District of residence					0•095
Amuru	315/1023	30•8	280/897	31•2	
Gulu	494/1023	48•3	396/897	44•1	
Nwoya	214/1023	20•9	221/897	24•6	
Marital status					<0•001
Not married	375/1006	37•3	432/891	48•5	
Married	631/1006	62•7	459/891	51•5	
Highest education attained					<0•001
Primary or less	808/1013	79•8	491/886	55•4	
Secondary or more	205/1013	20•2	395/886	44•6	
Religion					<0•001
Roman Catholic	752/1023	73•5	672/896	75•0	
Protestant	148/1023	14•5	156/896	17•4	
Moslem	7/1023	0•7	21/896	2•3	
Other	116/1023	11•3	47/896	5•2	
Female headed household	272/1007	27•0	135/884	15•3	<0.001
War-related trauma and mental health					
Community displacement status					0•091
Displaced	177/1023	17•3	162/897	18•1	
Transient	395/1023	38•6	383/897	42•7	
Permanent	451/1023	44•1	352/897	39•2	
Ever abducted	231/1022	22•6	244/894	27•3	0•017
Sexual assault in context of war	110/1017	10•8	13/894	1•5	<0•001
≥12 traumatic events	77/1023	7•5	93/897	10•4	0•030
Probable depression	164/1023	16•0	70/896	7•8	<0•001
Probable PTSD	121/1023	11•8	75/897	8•4	0•013
Suicide ideation	134/1022	13•1	59/896	6•6	<0•001
Sexual Vulnerabilities					
Age at sexual debut					0•560
≥16 years old	469/829	56•6	353/642	55•0	
<16 years old	360/829	43•4	289/642	45•0	
Coerced sexual debut	161/836	19•3	16/678	2•4	<0•001
First sex partner ≥ 10 yrs older	89/760	11•7	0/628	0•0	<0•001
No condom use at sexual debut	565/830	68•1	446/676	66•0	0•408
Sexual partners (past yr)					<0•001
0	270/1015	26•6	270/888	30•4	
1	722/1015	71•1	363/888	40•9	
≥2	23/1015	2•3	255/888	28•7	
Condom use with last 3 partners (past yr)					<0•001
Not always	700/1022	68•5	508/894	56•8	
Always	44/1022	4•3	107/894	12•0	
No sex	278/1022	27•2	279/894	31•2	
Most recent partner is circumcised	96/830	11•6			
Circumcised			87/894	9•7	
Sex for exchange (past yr)					0•063
No	732/1007	72•7	604/883	68•4	
Yes	6/1007	0•6	11/883	1•2	
No sex	269/1007	26•7	268/883	30•4	
HIV and STIs					
Sexually contracted genital ulcers (past yr)					0•103
No	660/1007	65•5	558/881	63•3	
Yes	77/1007	7•7	53/881	6•0	
No sex	270/1007	26•8	270/881	30•7	
Active syphilis	39/1020	3•8	34/892	3•8	1•000
Ill health without medical care	356/1019	34•9	227/895	25•4	<0•001

[1] Fisher exact test was used for categorical variables and Mann-Whitney U test for continuous variables

Table 2
HIV Incidence Rate

	Combined	Sex	
		Male	Female
Number of Incident HIV cases	39	16	23
Person-years of follow-up	3877	1805	2072
Crude Incidence Rate[1] (95% CI)	10•1 (7•2, 13•8)	8•9 (5•1, 14•4)	11•1 (7•0, 16•7)
Standardized Incidence Rate[2]	10•2 (7•2, 14•0)	9•4 (5•3, 15•3)	11•0 (6•9, 16•6)

[1] Expressed in units of incident HIV cases per 1000 person-years

Table 3
Proportional hazards model of predictors of HIV seroconversion

Parameter	N	HIV+ n	Unadjusted HR (95% CI)	p	Adjusted[1] HR (95% CI)	p
Sociodemographic Characteristics						
Highest education attained						
Primary or less	2067	30	Ref		Ref	
Secondary or more	923	8	0•60 (0•28, 1•31)	0•201	0•59 (0•26, 1•36)	0•219
Missing	29					
Female headed household						
No	2344	29	Ref		Ref	
Yes	634	9	1•15 (0•54, 2•43)	0•717	1•13 (0•48, 2•63)	0•780
Missing	41					
War-Related Trauma & Mental Health						
Ever been abducted						
No	2252	20	Ref		Ref	
Yes	762	19	2•81 (1•50, 5•27)	0•001	3•70 (1•87, 7•34)	<0•001
Missing	5					
Sexual assault in context of war						
No	2807	35	Ref		Ref	
Yes	197	4	1•60 (0•57, 4•49)	0•375	1•46 (0•49, 4•31)	0•495
Missing	15					
≥12 traumatic events						
No	2746	31	Ref		Ref	
Yes	273	8	2•58 (1•19, 5•62)	0•017	2•91 (1•28, 6•60)	0•011
Probable depression (HCL ≥1•75) (recent)						
No	2864	35	Ref		Ref	
Yes	152	4	2•30 (0•81, 6•51)	0•116	2•41 (0•83, 7•00)	0•105
Missing	3					
Suicide ideation (recent)						
Not at all	2890	35	Ref		Ref	
A little/quite a bit/extremely	125	4	2•77 (0•98, 7•79)	0•054	2•83 (1•00, 8•03)	0•051
Missing	4					
Sexual Vulnerabilities						
Age at sexual debut						
≥16 years old	1310	20	Ref		Ref	
<16 years old	1050	14	0•87 (0•44, 1•72)	0•691	0•80 (0•40, 1•60)	0•524
Missing	659					
First sex partner ≥ 10 yrs older						
No	2080	27	Ref		Ref	
Yes	140	4	2•22 (0•78, 6•35)	0•136	1•88 (0•62, 5•67)	0•265
Missing	799					
Coerced sexual debut						
No	2136	30	Ref		Ref	
Yes	289	4	0•98 (0•34, 2•77)	0•963	0•96 (0•32, 2•85)	0•943
Missing	594					
Condom use at sexual debut						
No	1652	19	Ref		Ref	
Yes	761	16	1•84 (0•94, 3•57)	0•074	1•68 (0•78, 3•61)	0•183
Missing	606					
Number of sex partners in past year (recent)						
0	682	6	Ref		Ref	
1	1881	23	1•38 (0•56, 3•39)	0•484	1•55 (0•56, 4•29)	0•395
≥2	447	10	2•53 (0•92, 6•96)	0•072	4•68 (1•36, 16•05)	0•014
Missing	9					
Inconsistent condom use in past year at baseline						
No	1088	7	Ref		Ref	
Yes	1927	32	2•64 (1•17, 5•98)	0•020	6•75 (2•49, 18•29)	<0•001
Missing	4					
Health and Medical Care						
Sex with genital ulcers in past year at baseline						
No	2765	29	Ref		Ref	
Yes	205	9	4•35 (2•06, 9•20)	<0•001	4•39 (2•04, 9•45)	<0•001
Active syphilis						
No	2879	36	Ref		Ref	
Yes	125	3	1•96 (0•60, 6•38)	0•262	2•00 (0•60, 6•65)	0•257
Missing	15					
Ill health without medical treatment (recent)						
No	2327	29	Ref		Ref	
Yes	689	10	1•18 (0•58, 2•43)	0•648	1•18 (0•57, 2•44)	0•655
Missing	3					

'Recent' refers to time-dependent variables measured at each follow-up
[1] Adjusted for age, sex, marital status, district of residence, displacement status, and religion.

gender, incidence rates in this study were 9.4 and 11.0 per 1000py for men and women, respectively. Although underpowered to identify gender differences, these disparities corroborate recent findings that new HIV infections continue to disproportionately affect women in sub-Saharan Africa, accounting for 59% of new adult HIV infections in 2017 [6]. Gendered structural and interpersonal violence continue to

Table 4
Final model resulting from backward and forward stepwise regression of variables significant at p<0.10 in bivariate analysis

Risk factors	HR (95% CI)	p
Gender		
Male	Ref	
Female	1•08 (0•56, 2•07)	0•826
District of residence		
Amuru	Ref	
Gulu	1•15 (0•53, 2•51)	0•723
Nwoya	0•93 (0•38, 2•27)	0•872
Religion		
Roman Catholic	Ref	
Protestant	0•60 (0•20, 1•83)	0•367
Other	1•21 (0•49, 3•02)	0•675
Age (yrs)	0•98 (0•94, 1•02)	0•261
Community Displacement Status		
Permanent	Ref	
Displaced	0•62 (0•25, 1•51)	0•293
Transient	0•47 (0•21, 1•03)	0•058
Marital Status		
Not Married	Ref	
Married	0•35 (0•13, 0•92)	0•034
Ever been abducted		
No	Ref	
Yes	3•23 (1•64, 6•34)	<0•001
Inconsistent condom use in past 12 months		
No	Ref	
Yes	4•76 (1•53, 14•87)	0•007
Sex with genital ulcers in past 12 months		
No	Ref	
Yes	3•12 (1•33, 7•30)	0•009

place women and girls in harm's way, underpinned by lack of power, coerced first sex, early marriage, limited health services, extreme poverty, and sexual violence [26-28]. High incidence observed in this study, combined with Uganda's increasing HIV rates among adolescents (especially women), indicate an urgent need to understand HIV risk and experiences of young women and girls in this setting [29]. Results demonstrate that although hostilities have ended, war continues to impact the health and wellbeing of Acholi people, despite tremendous resilience. Findings contribute to mounting evidence that investment in trauma-informed and healing-centred approaches to addressing war-related traumas is essential to post-conflict HIV response.

Those who experienced abduction were over three times more likely to become HIV infected; experiencing multiple war-related traumatic events and thinking about suicide were also associated with increased risk. Conflict analysts suggest that the relationship between HIV/AIDS and conflict is complex as it may decrease risk through reduced population mobility and access to services in IDP camp settings, or conversely may increase risk through disrupted livelihoods, infrastructure, and services, as well as exposure to sexual violence [13, 14, 30, 31]. Our results affirm that intersections between war-related trauma, mental health, and HIV continue to unfold after war has come to an end. Research demonstrates that sexual violence in the context of war can directly result in both HIV infection and mental health sequelae including depression, PTSD, and anxiety [12]. Further, mental health impacts of war-related traumas may contribute to sexual vulnerabilities such as condom-less sex, sex for exchange, and sexually transmitted infections [12]. Finally, psychological, physiological, and social impacts of becoming HIV-positive may intensify mental health concerns [12]. Interrupting these cycles requires an understanding of HIV prevention that extends beyond condoms, circumcision, and HIV treatment to include individual and community healing. As a result, wholistic care integrating HIV prevention with trauma-informed approaches is urgently required.

Participants with more sexual partners were over four times more likely to become HIV infected. This is consistent with existing evidence; however, in Northern Uganda it must be understood in relation to unresolved complex war-related trauma. Previous research has demonstrated links between stressful or traumatic life events, and sexual vulnerabilities contributing to HIV risk [32, 33]. During the war, both men and women faced abduction by the Lord's Resistance Army, including 25% of Cango Lyec participants. Community reintegration following cessation of hostilities has been a challenge as war experiences and mental health consequences are not well understood or accepted. Trauma sequelae may contribute to difficulty sustaining intimate long-term relationships, moving from partner to partner, and subsequently seeking out relationships with other former abductees. Narrowly focusing on sexual risk behaviours in absence of a response to the syndemic of trauma in Northern Uganda's post-conflict context may fail to address root causes underpinning HIV vulnerability.

Living in a transient settlement was associated with reduced risk of HIV infection compared to permanent settlements. This may be related to population mobility and dynamics of town life post-conflict. Following the war, the majority of displaced people left camps and returned home. However, lingering impacts on traditional livelihoods and social structures, as well as limited resources such as health care, employment, and education in ancestral villages, contributed to an influx of displaced people to towns, especially Gulu town [34]. As ancestral homes are redeveloped, young people who are sent to town without parental supervision may be vulnerable to predation. Those remaining in town are younger and poorer, and may face considerable vulnerabilities, such as lack of skills, resources, and family or social connections, that contribute to HIV risk [34].

We observed increased HIV risk associated with inconsistent condom use, ulcerative sexually transmitted infections, and HIV-discordant relationships. These are well-known contributors to the HIV epidemic and suggest that significant barriers to HIV prevention remain. Notably, we did not observe significant associations between HIV incidence and active syphilis. Ensuring access to ART for those living with HIV – especially those whose partners are HIV-negative – is also critical to reducing high infection rates observed in this study. While national estimates indicate that 72% of all Ugandans living with HIV are on ART, concerns remain that young people are marginalized from care [6, 7]. Additional research is urgently required to understand engagement with ART and HIV prevention in post-conflict Northern Uganda, especially among adolescent women and girls.

This study has some potential limitations. Use of self-reported data may result in misclassification of exposure. Responses to historical questions may be influenced by ability to recall event(s). Social desirability and stigma may lead to underestimation of some risk behaviours. Low prevalence of some factors (e.g. syphilis) may limit the power to detect associations. Though it would have been preferable to conduct sex stratified analyses, the relatively small number of incidence cases (16 among men and 23 among women) prevented sex-stratification to explore gendered risk factors, and the mechanisms underpinning associations between war-related traumas and HIV risk. While it is not possible to rule out selection bias, recruitment methods and rigorous eligibility criteria increases confidence that Cango Lyec's sample is representative of people residing in study communities. While the HTQ and HSCL-25 have been demonstrated to be reliable and valid in this setting, they are screening tools and not diagnostic, which may lead to conflation in levels of probable PTSD and depression. Loss-to-follow-up was high (28.5%), though not associated with HIV status. Like all longitudinal data collection projects, and in particular those conducted in conflict affected populations in rural Sub-Saharan Africa, the Cango Lyec Project faced problems of sample attrition – that is, not all individuals surveyed in earlier rounds could be found or re-interviewed during later rounds. The strong association between attrition and displacement status in

the Cango Lyec Project reveals that attrition was mainly due to domestic migration. This has been well documented in other studies [35].

High HIV incidence observed in post-conflict Northern Uganda (2•5 times higher than national estimates) is cause for alarm. Our findings underscore that although the conflict in Northern Uganda has come to an end, the legacy of war-related traumas on mental health remain unaddressed, and are linked with HIV infection in this setting. Evidence presented in this study highlights the urgency of HIV prevention strategies that address the ongoing impacts of war-related traumas and disruption of traditional ways of life on HIV risk among Acholi people in Northern Uganda.

Declaration of Competing Interest

The authors have no conflict of interests to disclose.

Acknowledgements

Statement of Authorship

AK contributed to study conception, data collection, research design, and led manuscript development. HM, MDO and PMS co-conceived the study and study design, helped draft and edit the manuscript, and interpret results. DSZ, SSM, AK, KJ, and AJF were responsible for statistical analysis, and drafting and editing the manuscript. SA, TO, and AO contributed to data collection, management of field activities, manuscript editing, and interpretation of results. NKS and MTS supervised the study and protocol implementation, contributed to manuscript development and interpretation of results. All authors read and approved the final submitted version of the manuscript.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.eclinm.2020.100408.

References

[1] Republic of Uganda Ministry of Health, World Health Organization. Health and mortality survey among internally displaced persons in Gulu, Kitgum and Pader districts, northern Uganda. Geneva: World Health Organization; 2005.

[2] World Health Organization. In: Health action in crisis: Taking stock of WHO's work in crises in Uganda; 2007.

[3] Patel S, Schechter MT, Sewankambo NK, Atim S, Kiwanuka N, Spittal PM. Lost in transition: HIV prevalence and correlates of infection among young people living in post-emergency phase transit camps in Gulu District, Northern Uganda. PloS One 2014;9(2):e89786.

[4] Carballo M, Clérisme C, Harris B, Kayembe P, Serdarevic F, Small A. Post-conflict transition and HIV. Forced Migration Review 2010;20.

[5] Hanson BW, Wodak A, Fiamma A, Coates TJ. Refocusing and prioritizing HIV programmes in conflict and post-conflict settings: funding recommendations. AIDS 2008;22(Suppl 2):S95.

[6] UNAIDS. UNAIDS Data 2018. 2018.

[7] Uganda Ministry of Health, ICAP. Uganda Population-Based HIV Impact Assessment: Summary Sheet Preliminary Findings. 2017.

[8] Fabiani M, Nattabi B, Pierotti C, Ciantia F, Opio AA, Musinguzi J, et al. HIV-1 prevalence and factors associated with infection in the conflict-affected region of North Uganda. Conflict and health 2007;1(1):1.

[9] Republic of Uganda Ministry of Health. In: Uganda AIDS Indicator Survey 2011; 2011.

[10] Malamba S, Muyinda H, Spittal P, Ekwaru P, Kiwanuka N, Ogwang M, et al. Cango Lyec - Healing the Elephant: HIV related vulnerabilities of post-conflict affected populations aged 13−49 years living in three Mid-Northern Uganda districts. BMC Infectious Diseases 2016;16:690.

[11] Spittal P, Malamba S, Ogwang D, Musisi S, Ekwaru J, Sewankambo N, et al. Cango Lyec - Healing the Elephant: Gender differences in HIV infection in post-conflict Northern Uganda. Journal of Acquired Immune Deficiency Syndromes 2018;78 (3):257−68.

[12] Koegler E, Kennedy CE. A scoping review of the associations between mental health and factors related to HIV acquisition and disease progression in conflict-affected populations. Conflict and health 2018;12(1):20.

[13] Spiegel PB. HIV/AIDS among conflict−affected and displaced populations: Dispelling myths and taking action. Disasters 2004;28(3):322−39.

[14] Mock NB, Duale S, Brown LF, Mathys E, O'Maonaigh HC, Abul-Husn NK, et al. Conflict and HIV: A framework for risk assessment to prevent HIV in conflict-affected settings in Africa. Emerging themes in epidemiology 2004;1(1):1.

[15] Von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Journal of clinical epidemiology 2008;61(4):344−9.

[16] Roberts B, Ocaka KF, Browne J, Oyok T, Sondorp E. Factors associated with post-traumatic stress disorder and depression amongst internally displaced persons in northern Uganda. BMC Psychiatry 2008;8(1):38.

[17] Shoeb M, Weinstein H, Mollica R. The Harvard trauma questionnaire: adapting a cross-cultural instrument for measuring torture, trauma and posttraumatic stress disorder in Iraqi refugees. International Journal of Social Psychiatry 2007;53 (5):447−63.

[18] Mollica RF. Measuring trauma, measuring torture: instructions and guidance on the utilization of the Harvard Program in Refugee Trauma's Harvard Versions of the Hopkins Symptom Checklist-25 (HSCL-25) & The Harvard Trauma Questionnaire (HTQ). Cambridge: Harvard University; 2004.

[19] Fox SH, Tang SS. The Sierra Leonean refugee experience: Traumatic events and psychiatric sequelae. Journal of nervous and mental disease 2000;188 (8):490−5.

[20] Pham PN, Weinstein HM, Longman T. Trauma and PTSD symptoms in Rwanda: implications for attitudes toward justice and reconciliation. JAMA 2004;292 (5):602−12.

[21] Yeomans PD, Herbert JD, Forman EM. Symptom comparison across multiple solicitation methods among Burundians with traumatic event histories. Journal of Traumatic Stress 2008;21(2):231−4.

[22] Roberts B, Damundu EY, Lomoro O, Sondorp E. Post-conflict mental health needs: a cross-sectional survey of trauma, depression and associated factors in Juba. Southern Sudan. BMC Psychiatry 2009;9(1):1.

[23] Ovuga E, Oyok TO, Moro E. Post traumatic stress disorder among former child soldiers attending a rehabilitative service and primary school education in northern Uganda. African Health Sciences 2008;8(3):136−41.

[24] R Development Core Team. In: R: A language and environment for statistical computing; 2019.

[25] UNAIDS. AIDSinfo Uganda: HIV incidence per 1000 population (15-49). 2018 UE; 2018. editor.

[26] Amaro H. Love, sex, and power: Considering women's realities in HIV prevention. American Psychologist 1995;50(6):437.

[27] Westerhaus M. Linking anthropological analysis and epidemiological evidence: formulating a narrative of HIV transmission in Acholiland of northern Uganda. SAHARA-J: Journal of Social Aspects of HIV/AIDS 2007;4(2):590−605.

[28] Patel S, Schechter MT, Sewankambo NK, Atim S, Lakor S, Kiwanuka N, et al. War and HIV: Sex and gender differences in risk behaviour among young men and women in post-conflict Gulu District. Northern Uganda. Global public health 2014;9(3):325−41.

[29] Uganda AIDS Commission, Uganda HIV/AIDS Partnership. Uganda HIV/AIDS Country Progress Report July 2016 - June 2017. 2017.

[30] Mills EJ, Singh S, Nelson BD, Nachega JB. The impact of conflict on HIV/AIDS in sub-Saharan Africa. International Journal of STD & AIDS 2006;17(11): 713−7.

[31] Hankins CA, Friedman SR, Zafar T, Strathdee SA. Transmission and prevention of HIV and sexually transmitted infections in war settings: implications for current and future armed conflicts. AIDS 2002;16(17):2245−52.

[32] LeGrand S, Reif S, Sullivan K, Murray K, Barlow ML, Whetten K. A Review of Recent Literature on Trauma Among Individuals Living with HIV. Current HIV/AIDS Reports 2015;12(4):397−405.

[33] Sales JM, Swartzendruber A, Phillips AL. Trauma-informed HIV prevention and treatment. Current HIV/AIDS Reports 2016;13(6):374−82.

[34] Branch A. Gulu in war… and peace? The town as camp in northern Uganda. Urban Studies 2013;50(15):3152−67.

[35] Gerritzen B. Women's empowerment and HIV prevention in rural Malawi. Feminist Economics 2016;22(3):1−25.