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HIV Incidence in Sub-Saharan Africa: A Review of Available Data with Implications for Surveillance and Prevention Planning

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Abstract

Background: ***HIV incidence estimation is increasingly being incorporated into HIV/AIDS surveillance activities in both resource-rich and developing countries. We conducted a systematic review to assess the availability of HIV incidence data from sub-Saharan Africa.***

Methods: ***We examined peer-reviewed articles, conference proceedings and technical reports published from 1987-2008. Incidence estimates were classified by country, year, population group, and estimation method (prospective study or the serologic testing algorithm for recent HIV seroconversion; STARHS).***

Results: ***Our search yielded HIV incidence estimates for 15 of 44 sub-Saharan African countries, with 57 studies generating 264 unique estimates. Of these, 239 (91%) were obtained via prospective studies, and 25 (9%) via the STARHS method (24 using the BED-CEIA assay). Only five countries reported population-based estimates, and less than two-thirds of studies reported risk factor information. STARHS use increased over time, comprising 20% of estimates since 2006. However, studies that compared STARHS estimates with prospectively observed or modeled estimates often found substantial levels of disagreement, with STARHS often overestimating HIV incidence.***

Conclusions: ***Population-based HIV incidence estimates and risk factor information in sub-Saharan Africa remain scant but increasingly available. Regional STARHS data suggest a need for further validation prior to widespread use and incorporation into routine surveillance activities. In the meantime, prevalence and behavioral risk factor data remain important for HIV prevention planning.*** **(AIDS Rev. 2009;11:140-56)**

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Key words

Africa. HIV incidence. Surveillance. Prevention. Risk factors. Serologic testing algorithm for recent HIV seroconversion (STARHS). BED-CEIA. Avidity index. Seroincidence.

Introduction

Sub-Saharan Africa has more new HIV infections than any other region in the world. An estimated 1.9 million new infections occurred in sub-Saharan Africa in 2007, representing more than two-thirds of new infections occurring globally that year[1]. While HIV care and treatment scale-up has increased coverage of antiretroviral treatment (ART) in the region from 5% to 30% of those in need during 2004-2007[2], an estimated 2-3 new infections occur for every one person placed on ART[1], highlighting the critical role of prevention. The national HIV seroprevalence estimates in 2007 for the 44 countries in this region ranged widely, from < 0.1% in Comoros to 26.1% in Swaziland[1].

HIV incidence data have been cited as a critical component of HIV prevention planning and evaluation. National surveillance programs, however, have historically been focused on measuring behaviors alongside HIV prevalence. From a primary prevention standpoint, this approach is less than ideal because HIV prevalence does not distinguish between long-term infections

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and new infections in the population[3]. Additionally, the current scale-up of antiretroviral treatment programs in sub-Saharan Africa will most likely result in increases in HIV prevalence because of improved survival[4,5], which will add challenges to using data on prevalence to guide prevention programming and evaluation.

Key public health agencies are therefore recommending country-level monitoring of HIV incidence. For example, HIV incidence surveillance is a major strategy being employed to combat the epidemic in resource-rich settings[6-8]. Incidence surveillance has proven to be valuable, for example, demonstrating significantly higher incidence estimates in the USA than those previously appreciated via statistical modeling and back-calculation, and identifying key risk groups[6]. Moreover, several recent reports[7-10], including one by the World Health Organization[11], emphasize the importance of tailoring prevention and service delivery approaches to the epidemic context, central to which is access to good data on HIV incidence.

Incidence can be estimated by a variety of methods, including prospective studies, the serologic testing algorithm for recent HIV seroconversion (STARHS), laboratory tests to identify acute HIV infections, and mathematical models. Each approach has strengths and limitations. While prospective cohort studies are considered the "gold standard" approach[3], they are not always feasible or practical. The identification of an appropriate study population is often complex, and prospective studies often require long and costly follow-up[12,13]. Prospective data are also subject to biases such as the Hawthorne effect[14,15]. STARHS is an assay-based approach that allows estimation of HIV incidence in cross-sectional designs[16-18]. The BED-CEIA[19] and Avidity Index[20] STARHS assays measure antibody response to HIV infection. Other assays such as the anti-p31, p24, or RNA assays measure elements of the HIV virus itself and target the short period before HIV seroconversion. Conversely, antibody-based assays are designed to identify new HIV infections in a longer post-seroconversion period and are thus theoretically better suited for population-level incidence estimation. Currently, STARHS is used for national HIV incidence surveillance in the USA[6,21], and increasingly in Europe[22]. The use of STARHS is still evolving, especially in populations with HIV non-B subtypes, for which the current generation of assays have not been fully optimized[23,24]. The availability of cross-sectional approaches such as STARHS signals an important shift in HIV incidence surveillance, with the possibility of collecting more timely data. Mathematical modeling or statistical approaches to estimating HIV incidence include: using prevalence, for example from young pregnant women, as a surrogate for incidence rates[25-27]; software programs, such as the Epidemic Projection Package and Spectrum, to derive incidence rates from prevalence data[26-29]; or back-calculation methods to reconstruct past trends in HIV incidence from AIDS cases and other data[6,29-31]. While these approaches can be useful, statistical assumptions can be problematic, and the data they require may be unavailable or of questionable quality[32-36].

To gain a better understanding of the available information on HIV incidence for the region, we reviewed data on HIV incidence rates by country, demographic, temporal, and epidemiologic factors. The review has two primary aims: (i) to highlight progress, gaps in knowledge, and opportunities for further work in the area of HIV incidence in sub-Saharan Africa; and (ii) to examine the relative utility of data on HIV incidence and prevalence for epidemic monitoring and prevention planning by comparing data from two example countries.

Methods

Publications with HIV incidence estimates included in this review were identified through searches of: (i) the MEDLINE/PubMed and POPLINE electronic databases for peer-reviewed, published papers; (ii) public-access databases of papers presented at scientific conferences; (iii) scientific and technical reports published on the internet; and (iv) additional pertinent references recommended by experts in the field. Electronic databases were searched using the keywords: "HIV incidence", "seroincidence and HIV", "HIV/AIDS and sub-Saharan Africa", "HIV incidence estimation", "recent HIV infection", "antibody-based assays", "STARHS", "BED-CEIA", "Avidity Index", and "incidence and prevalence comparison". We included peer-reviewed publications (in English only) published from the late-1980s to early 2008, and conference abstracts and scientific reports from 1999 onwards. The review excludes modeling studies and studies using incidence assays other than the BED-CEIA and Avidity Index.

HIV incidence estimates were classified by country, population(s) (e.g. female sex workers, pregnant women, urban/rural) and measurement methods (prospective seroconversion study, intervention study, or STARHS). Publications were reviewed if they reported estimates of HIV incidence as a primary endpoint, identified the study population(s), and reported the time period during which seroconversions occurred. Most publications presented the incidence rate as "number of HIV infections

per 100 person-years" (PY); if a different unit was used it was converted into 100 person-years. The majority of the publications reported 95% confidence intervals (CI) around the incidence estimate. For publications that did not report CI but reported the necessary data, 95% CI were calculated using the normal distribution approximation formula for Poisson rates[37]. Data from multicenter intervention trials were disaggregated by site or country as appropriate and when possible, and only incidence rates for control groups were reported to avoid reporting rates that may have been altered by the intervention. Finally, when multiple incidence estimates were reported for the same study population, the most recent publication was used, unless incidence estimates were calculated for different time periods or by different methods (e.g. STARHS and prospective study[38,39]).

A subset of the publications reported predictors of incident HIV infection, and these data were summarized by country, population, time period, and study method. For prospective studies, risk factors were considered positive or negative predictors of infection if they were statistically significant (generally at the $p < 0.05$ level) in multivariate analysis. Non-significant and unexamined risk factors were summarized in the text. In STARHS studies, we examined statistically significant correlates of incident (or "recent") HIV infection as determined by antibody-based assays.

To explore the added utility of incidence data over prevalence data, We conducted a qualitative comparison analysis of risk factors for incident and prevalent HIV infection for two countries (Uganda and Zimbabwe) that had population-based data for both prevalent and incident HIV infection collected within two years of one another.

Results

HIV incidence rates in sub-Saharan Africa

Our review yielded a total of 57 studies, reporting 264 HIV incidence estimates for 15 of the 44 countries in sub-Saharan Africa (Fig. 1). While these 15 countries represent only 33% of countries in the region, they represent 83% of people living with HIV/AIDS according to UNAIDS estimates. Four of the nine countries with HIV prevalence > 10% according to UNAIDS (Lesotho, Mozambique, Namibia, and Swaziland) had no information on HIV incidence. Of the six countries with UNAIDS prevalence rates between 5-10%, three countries (Gabon, Cameroon and the Central African Republic) had no data on incidence.

Incidence estimates ranged from 0.6 infections per 100 PY (95% CI: 0.52-0.68) in a prospective study among adults in rural Uganda[15], to 17 infections per 100 PY (no CI) in a STARHS study among pregnant women in rural South Africa[40] (Table 1). Forty-nine (86%) studies were prospective studies, 18 of which were control arms of intervention trials evaluating the effect of female-controlled HIV prevention methods (vaginal microbicides, diaphragm), treatment of sexually transmitted infections (STI), or male circumcision, on HIV incidence; and eight (14%) studies estimated incidence using STARHS (primarily the BED-CEIA assay). The number of published incidence estimates for sub-Saharan Africa increased between 1987 and 2008, with prospective studies producing the most estimates (91%, observational and intervention combined), and STARHS producing fewer estimates (9%) (Fig. 2).

Despite their broad range, about two-thirds of HIV incidence estimates fell between one and six infections per 100 PY. The sparseness and heterogeneity of the data precluded a summary analysis of rates by sub-region; the majority of incidence data comes from Southern and Eastern Africa, as compared to Western and Central Africa.

There were different degrees of within-country variability in reported incidence estimates. In some countries, estimates fell within narrow ranges (3.1-7.6 for Côte d'Ivoire, 4.2-4.9 for Malawi, and 2.7-6.9 for Rwanda). In other countries the data were considerably more heterogeneous. For example, estimates in South Africa, the country with the most studies estimating HIV incidence, ranged from 1.8 to 17 infections per 100 PY. This particularly wide range can be explained by marked heterogeneity in study populations (urban, rural, sex workers, general population); methods (both methods represented); and time periods (1996-2007).

The majority (53%) of HIV incidence studies were conducted exclusively among women; only six (10%) of the 57 studies exclusively enrolled men, and 21 (37%) were mixed. Studies among women only had the widest range of incidence estimates (1.2-17 infections per 100 PY for women only, 1.3-6.6 for men only, and 0.6-9 for mixed populations. Several incidence estimates for female sex workers and pregnant women were substantially higher than the highest estimates for the general population.

Risk factors for incident HIV infection in sub-Saharan Africa

Thirty-six (63%) of the 57 studies reported 28 different risk factors for incident HIV infection (Table 2; risk factors presented in descending frequency of reporting

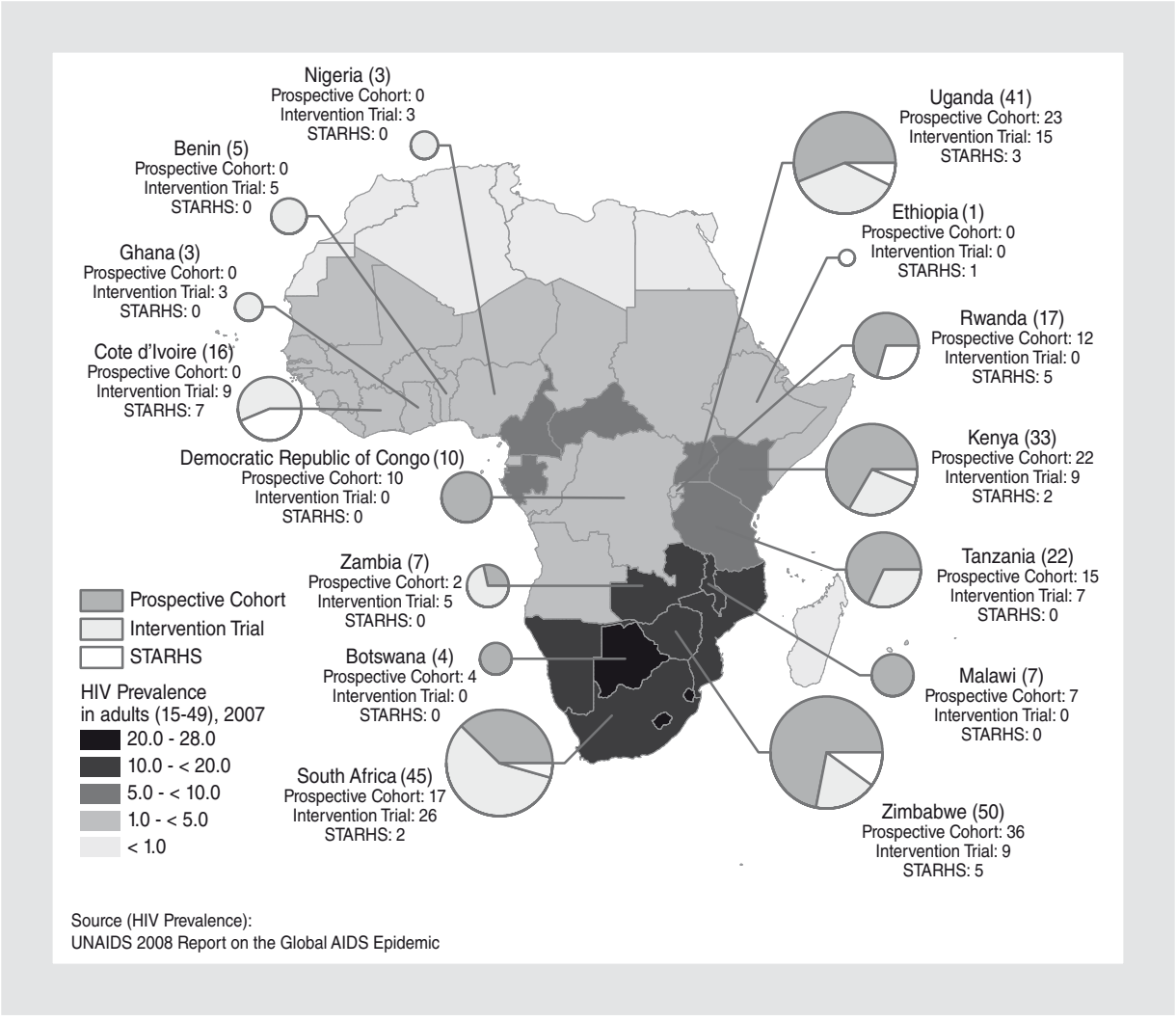

Figure 1. *Number of HIV incidence estimates by country and method, 1987-2008. (note: UNAIDS' 2008 report on the Global Epidemic lists 44 countries in sub-Saharan Africa).*

from left to right). The three community-level intervention trials[41-43] did not report risk factors.

The risk factors examined can be broadly categorized as demographic (e.g. age, education level, place of residence), sexual risk (e.g. partnership status, STI diagnosis, condom use) or other risk factors (e.g. alcohol use, history of injections). Seventeen of the 27 studies that examined age found that younger persons (generally < 25 years) were at higher risk for HIV infection than older persons; seven studies found no association. Eighteen of the 22 studies examining current or recent STI found that those with current/recent STI were at increased HIV risk; the remaining four found no association. Results were inconsistent with regard to concurrency or multiple sex partners, single marital status, condom use, male circumcision, and HIV risk. For example, while eight studies found that single/divorced marital status or being widowed increased HIV risk, four showed no association, and one study found that being married was a positive risk factor. Nine of 16 studies found that having concurrent or multiple partners increased the risk for HIV, but the remaining seven found no association. Further, eight of 12 studies found no independent association between condom use and incident HIV, while four reported a protective relationship. Finally, five observational studies reported an increased HIV risk among uncircumcised men while four others found no association.

The remaining risk factors in table 2 were examined in seven or fewer studies, and many were only examined in one or two studies. Some of these less-frequently reported risk factors (e.g. recent sexual debut, transactional sex, coital frequency) did show consistent albeit weak evidence of a relationship with incident HIV infection.

Table 1. HIV Incidence rates in sub-Saharan Africa

Country/population (reference)	Period	Method*	Incidence rate (per 100 person-years, with 95% confidence interval)
			1.0 5.0 10.0 15.0 20.0
Benin			
Urban female sex workers (*van Damme*[68])	1996-2000	Intervention	8.3†
Botswana			
Urban high-risk men & women (*Djomand*[69])	2003-2006	Prospective	2.3
Cote d'Ivoire			
Urban & rural pregnant women (*Kim*[23])	1998-2004	STARHS	3.1
Urban female sex workers (*van Damme*[68])	1996-2000	Intervention	7.4†
Urban female sex workers (*Ghys*[70])	1994-1997	Intervention	7.6†
Democratic Republic of Congo			
Urban female sex workers (*Behets*[71])	1988-1989	Prospective	7.7†
Male and female urban workers (*Ryder*[72])	1987-1990	Prospective	0.9‡
Urban discordant couples (*Ryder*[73])	1987-1990	Prospective	5.2†
Ethiopia			
Urban pregnant women (*Wolday*[54])	2003§	STARHS	2.0
Ghana			
Urban adult women (*Peterson*[74])	2004-2006	Intervention	1.2†
Kenya			
Urban female sex workers (*Bosire*[50])	2006-2007	Prospective	2.9
Rural & semi-urban adults (*Karita*[75])	2004	STARHS	3.5
Urban & rural general adult pop. (*Kim*[23])	2003	STARHS	2.3
Urban adult men (*Bailey*[76])	2002-2005	Intervention	4.1
Urban female sex workers (*McClelland*[77])	1993-2003	Prospective	7.7†
Urban female sex workers (*Kaul*[78])	1998-2002	Intervention	3.2†
Urban male truck drivers (*Rakwar*[79])	1993-1997	Prospective	3.1†
Urban female sex workers (*Martin*[80])	1993-1994	Prospective	16.4
Urban male truck drivers (*Martin*[80])	1993-1994	Prospective	6.6
Malawi			
Urban women (*Kumwenda*[81])	1999-2001	Prospective	4.9
Urban postpartum women (*Taha*[82])	1990-1993	Prospective	4.2
Nigeria			
Urban adult women (*Feldblum*[83])	2004-2006	Intervention	1.4†
Rwanda			
Urban & rural women (*Bulterys*[38])	1991-1993	Prospective	2.7
Urban young women (*Bulterys*[39])	1989-1993	STARHS	5.7
Urban women (*Leroy*[84])	1988-1993	Prospective	3.5
Urban discordant couples (*Allen*[85])	1988-1990	Prospective	6.9†
South Africa			
Urban high-risk women (*van Damme*[51])	2005-2007	Intervention	3.3¶
Rural high-risk women (Van *Loggerenberg*[86])	2004-2007	Prospective	7.2
Urban & semi-urban women (*Skoler-Karpoff*[52])	2004-2007	Intervention	3.8
National adult population (*Rehle*[87])	2005	STARHS	2.4
Urban adult women-Durban (*Padian*[88])	2003-2005	Intervention	7.0†
Urban adult women-Jo'burg (*Padian*[88])	2003-2005	Intervention	3.3†
Rural women-KZN (*Bärnighausen*[63])	2003-2005	Prospective	7.9
Rural men-KZN (*Bärnighausen*[63])	2003-2005	Prospective	5.1
Urban 35+ women-Cape Town (*Myer*[89])	2001-2005	Prospective	1.8†
Urban adult women-Durban (*Ramjee*[90])	2003-2004	Prospective	5.0
Rural women-Hlabisa (*Ramjee*[90])	2003-2004	Prospective	6.0
Semi-urban men-Orange Farm (*Auvert*[91])	2002-2004	Intervention	2.1
Semi-urban women-Or. Farm (*Kleinschmidt*[92])	1999-2001	Intervention	4.4†
Urban sex workers-Durban (*van Damme*[68])	1996-2000	Intervention	16.5†
Rural pregnant women-Hlabisa (*Gouws*[40])	1999	STARHS	17.0‡

(continue)

Table 1. HIV Incidence rates in sub-Saharan Africa *(continued)*

Country/population (reference)	Period	Method*	Incidence rate (per 100 person-years, with 95% confidence interval)
Tanzania			
Semi-urban bar girls (*Watson-Jones*[53])	2004-2006	Intervention	4.1
Urban bar girls (*Kapiga*[93])	2002-2005	Prospective	4.6
Urban bar girls & general pop. (*Ramjee*[90])	2003-2004	Prospective	1.3
Rural adults (*Boerma*[94])	1994-1997	Prospective	0.8
Rural discordant couples (*Hugonnet*[95])	1991-1995	Prospective	7.5†
Rural/semi-urban adults (*Grosskurth*[96])	1991-1994	Intervention	1.9†
Uganda			
Rural/semi-urban adult men (*Gray*[46])	2002-2006	Intervention	1.3†
National adult population (*Mermin*[49])	2004-2005	STARHS	1.8
Rural adults (*Karita*[75])	2004	STARHS	6.1
Urban adult women (*Morrison*[45])	1999-2004	Prospective	1.6
Rural adults (*Kamali*[41])	1994-2000	Intervention	0.7†
Rural adults (*Mbulaiteye*[15])	1990-1999	Prospective	0.6
Rural adults (*Wawer*[43])	1994-1996	Intervention	1.5†
Male military recruits (*Hom*[97])	1993-1995	Prospective	3.5
Rural discordant couples (*Serwadda*[98])	1990-1991	Prospective	9.0†
Rural adults (*Wawer*[99])	1989-1990	Prospective	2.1
Zambia			
Urban general & high-risk women (*Celum*[100])	2003-2007	Intervention	3.1¶
Urban adult women (*Ramjee*[90])	2003-2004	Prospective	2.6
Zimbabwe			
Urban adult women (*Padian*[88])	2003-2005	Intervention	2.5†
Urban adult women (*Morrison*[45])	1999-2004	Prospective	4.1
Rural/semi-urban women (*Lopman*[44])	1998-2003	Prospective	1.6
Rural/semi-urban men (*Lopman*[44])	1998-2003	Prospective	2.0
Rural/semi-urban adults (*Gregson*[42])	1998-2003	Intervention	1.5†
Pregnant urban women (*Mbizvo*[101])	2001**	Prospective	4.8
Urban women (*Kumwenda*[81])	1999-2001	Prospective	4.9
Urban postpartum women (*Humphrey*[102])	1997-2001	Prospective	3.4
Urban postpartum women (*Hargrove*[62])	1997-2001	STARHS	3.5
Rural adult women (*Kjetland*[103])	1998-2000	Prospective	3.1†
Blood donors (*McFarland*[104])	1993-1995	Prospective	2.1†
Urban male factory workers (*Mbizvo*[105])	1993-1995	Prospective	2.9

*STARHS: Serologic Testing Algorithm for Recent HIV Seroconversion; Prospective: prospective observational study; Intervention: clinical intervention trial. Studies in bold were used for the incidence/prevalence comparative analysis, Tables 3(a, b) and 3(c).
†Confidence interval (CI) not reported in publication, but calculated one based on data provided.
‡No CI reported in publication, unable to calculate one based on data provided.
§Annual incidence rate for final year of study period.
¶Incidence rate is for African sites combined; disaggregated data were not reported.
**Indicates year paper was published; data collection period unclear.

Comparison of predictors for incident and prevalent HIV infection

Tables 3(a, b) and 3(c) present the results of two types of incidence versus prevalence comparisons for Uganda and Zimbabwe: "internal comparison" of incidence and prevalence risk factor data from the same sample (Zimbabwe only[44]); and "independent-sample comparison" of risk factor data from a population-based incidence study in each country[45,46] with Demographic and Health Survey (DHS) prevalence data from the same time period.

Published HIV incidence rates for Zimbabwe ranged from 1.5 to 4.9 infections per 100 PY, with a median of three infections per 100 PY. The 2005-2006 DHS in Zimbabwe found an overall adult prevalence of 18%, with 17.6% prevalence in rural areas and 18.9% in urban areas[47]. Table 3(a, b) presents the comparison of risk factors for incident and prevalent HIV infection in Zimbabwe. In the internal comparison by Lopman, et al., several risk factors were found to be similarly (positively) associated with both incident and prevalent infections, including age, current/recent STI, concurrent/multiple partners, and being divorced or separated.

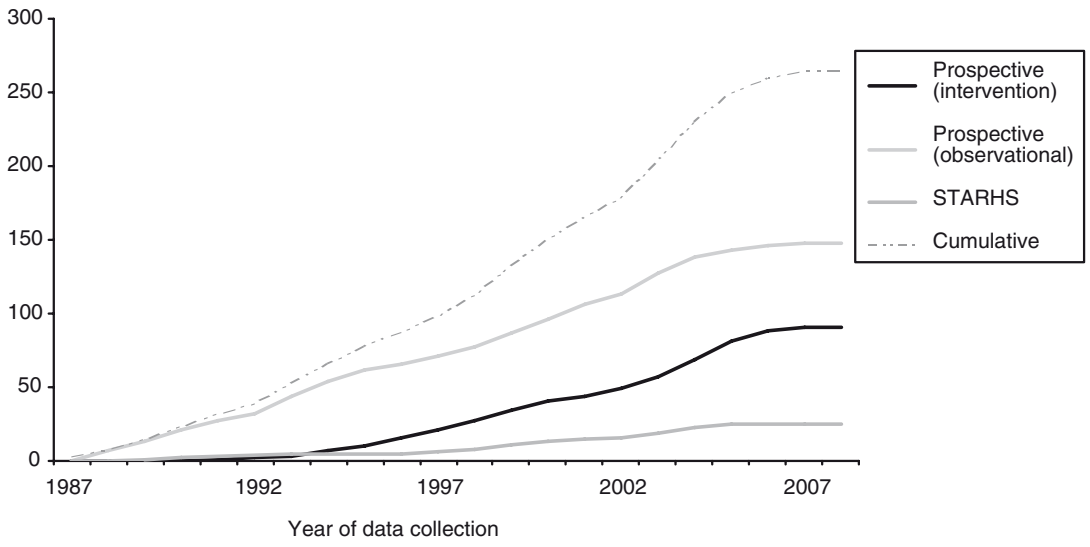

Figure 2. *Number of HIV incidence estimates by year and method of data collection, cumulative 1987-2008 (note: it is likely that the numbers for recent years (e.g. 2006-2008) are affected by delays in publishing study results since completion of data collection).*

Incidence analyses also indicated, however, that high education and traditional religion were risk factors specifically for incident HIV infection, and not prevalent infection, in this population. In our independent-sample comparison of data from Morrison, et al. and DHS, the only additional information provided by incidence data over prevalence data was that young age was associated with incident infection, while older age was associated with prevalent infection.

Published HIV incidence rates for Uganda ranged from 0.6 to 9.0 infections per 100 PY, with a median of 1.7 infections per 100 PY. The 2004-2005 DHS found an overall adult HIV prevalence of 6.3%, with 5.7% prevalence in rural areas and 10.1% in urban areas[48]. Table 3(c) presents the comparison of risk factors for incident and prevalent HIV infection in Uganda. In the independent-sample comparison of data from Gray, et al. and DHS, incidence data did not provide additional information over prevalence data in identifying risk factors. An additional study in Uganda by Mermin, et al.[49] (not shown in Table 3(c)) compared the characteristics of individuals with incident HIV infection directly to those with prevalent infection in a national sample. Geographic region was the only statistically significant risk factor for incident HIV infection.

Discussion

Our review found 57 published studies producing incidence data for 15 of 44 countries in sub-Saharan Africa, with population-based incidence estimates for only five countries. While these 15 countries cover 83% of the burden of HIV in the region and the five countries cover 52%, the amount of HIV incidence data available more recently for prevention planning is troublingly sparse. Multiple factors likely underlie the relative paucity of incidence data, including limited resources, logistical and methodological challenges in estimating incidence, and competing public health priorities. Available data are concentrated in certain countries such as Zimbabwe (48 of 245 estimates), South Africa (45), and Uganda (41), which may be due in part to these countries participating in international research networks, as well as being focus countries for major funding initiatives such as the US President's Emergency Plan for AIDS Relief (PEPFAR). Indeed, the amount of available data and ongoing collective effort to gather additional data on HIV incidence in countries such as these likely exceeds that in many countries in other regions with concentrated epidemics. Nonetheless, sub-Saharan Africa remains the global epicenter of the HIV epidemic and in great need of data for

Table 2. Risk factors for incident HIV infection in sub-Saharan Africa, by country

Country	Time period (Reference)	Method	Risk factor*												
			Young age (27)	Current or recent STI (22)	Concurrent or multiple sex partners (16)	Condom use (12)	Being unmarried, single or widowed (12)	Being uncircum-cised (men) (9)	High education (7)	Urban residence (5)	Use of hormonal contraception (5)	Alcohol use (5)	Not living with partner (5)	Sexually high-risk partner (5)	Being married (5)
Cote d'Ivoire	1998-2004 (Kim)	STARHS	+												
	1994-1997 (Ghys)	Intervention		+											
Ethiopia	2003 (Wolday)	STARHS	–												
Kenya	2006-2007 (Bosire)	Prospective		+								+			
	2003 (Kim)	STARHS	–												
	2002-2005 (Bailey)	Intervention		+				+							
	1993-2003 (McClelland)	Prospective													
	1998-2002 (Kaul)	Intervention		+											
	1993-1997 (Rakwar)	Prospective						+						+	
Malawi	1999-2001 (Kumwenda)	Prospective	+	+	↔	↔	+		+				+		
	1990-1993 (Taha)	Prospective	+												
Nigeria	2004-2006 (Feldblum)	Intervention	+												
Rwanda	1991-1993 (Bulterys)	Prospective	+	+	+		+			↔	↔				
	1989-1993 (Bulterys)	STARHS	↔	↔	↔		↔								
	1988-1990 (Allen)	Prospective		↔		–		↔			↔	+		+	–
South Africa	2005 (Rehle)	STARHS	↔		+	–	+			+					
	2003-2005 (Bärnighausen)	Prospective					+			+					
	2001-2005 (Myer)	Prospective	+	↔			+							↔	
	2003-2004 (Ramjee)	Prospective	+	+											
	2002-2004 (Auvert)	Intervention						+							
	1999-2001 (Kleinschmidt)	Intervention	↔	+	↔	↔					↔				
	1999 (Gouws)	STARHS	+												

(Continue)

Table 2. Risk factors for incident HIV infection in sub-Saharan Africa, by country *(continued)*

Country	Time period (Reference)	Method	Risk factor*												
			Young age (27)	Current or recent STI (22)	Concurrent or multiple sex partners (16)	Condom use (12)	Being unmarried, single or widowed (12)	Being uncircum-cised (men) (9)	High education (7)	Urban residence (5)	Use of hormonal contraception (5)	Alcohol use (5)	Not living with partner (5)	Sexually high-risk partner (5)	Being married (5)
Tanzania	2004-2006 (Watson-Jones)	Intervention	+									+			
	2002-2005 (Kapiga)	Prospective	↔	+	↔	↔	↔		↔			↔			↔
	2003-2004 (Ramjee)	Prospective	–	+											
	1994-1997 (Boerma)	Prospective								+					
	1991-1994 (Grosskurth)	Intervention	↔												
Uganda	2002-2006 (Gray)	Intervention		+				+							
	2004-2005 (Mermin)	STARHS	↔	+	+	–	+	+	↔	↔		↔			
	1999-2004 (Morrison)	Prospective	+	+	+	↔		↔			↔		+	+	
	1994-1996 (Wawer)	Intervention			+										
	1993-1995 (Hom)	Prospective		↔	↔		↔		↔						
	1989-1990 (Wawer)	Prospective	+		+										
Zambia	2003-2004 (Ramjee)	Prospective	+	+											
Zimbabwe	1999-2004 (Morrison)	Prospective	+	+	+	↔		↔			↔		+	+	
	1998-2003 (Lopman)	Prospective	↔	+	+	↔	↔	↔	+						↔
	2001 (Mbizvo)	Prospective	+			–									+
	1999-2001 (Kumwenda)	Prospective	+	+	↔	↔	+		+				+		
	1997-2001 (Humphrey)	Prospective	+			↔	+		↔						
	1993-1995 (McFarland)	Prospective	+		↔										–
	1993-1995 (Mbizvo)	Prospective		+	+								+		

(Continue)

Table 2. Risk factors for incident HIV infection in sub-Saharan Africa, by country *(continued)*

Country	Time period (Reference)	Method	Religious affiliation (4)	Employ-ment (4)	History of injections/ transfusion (3)	High coital frequency (3)	Intra-vaginal practices (3)	Recent sexual debut (3)	Recent transaction-al sex (3)	Partner with low education (2)	Current pregnancy (2)	Proximity to health clinic/ road (2)	Unwell partner (2)	Recent partner change or acquisition (2)	Age at first sex (2)	Parity (1)	Illiteracy (1)
Cote d'Ivoire	1998-2004 (Kim)	STARHS															
	1994-1997 (Ghys)	Intervention															
Ethiopia	2003 (Wolday)	STARHS															
Kenya	2006-2007 (Bosire)	Prospective															
	2003 (Kim)	STARHS															
	2002-2005 (Bailey)	Intervention															
	1993-2003 (McClelland)	Prospective					+										
	1998-2002 (Kaul)	Intervention				+											
	1993-1997 (Rakwar)	Prospective	+	+				+									
Malawi	1999-2001 (Kumwenda)	Prospective															
	1990-1993 (Taha)	Prospective															
Nigeria	2004-2006 (Feldblum)	Intervention															
Rwanda	1991-1993 (Bulterys)	Prospective			↔			+									
	1989-1993 (Bulterys)	STARHS						+									
	1988-1990 (Allen)	Prospective											↔				+
South Africa	2005 (Rehle)	STARHS									+	+					
	2003-2005 (Bärnighausen)	Prospective										+					
	2001-2005 (Myer)	Prospective					↔							↔			
	2003-2004 (Ramjee)	Prospective															
	2002-2004 (Auvert)	Intervention															
	1999-2001 (Kleinschmidt)	Intervention															
	1999 (Gouws)	STARHS															

(Continue)

Table 2. Risk factors for incident HIV infection in sub-Saharan Africa, by country *(continued)*

Country	Time period (Reference)	Method	Religious affiliation (4)	Employ-ment (4)	History of injections/ transfusion (3)	High coital frequency (3)	Intra-vaginal practices (3)	Recent sexual debut (3)	Recent transaction-al sex (3)	Partner with low education (2)	Current pregnancy (2)	Proximity to health clinic/ road (2)	Unwell partner (2)	Recent partner change or acquisition (2)	Age at first sex (2)	Parity (1)	Illiteracy (1)
Tanzania	2004-2006 (Watson-Jones)	Intervention															
	2002-2005 (Kapiga)	Prospective								↔							
	2003-2004 (Ramjee)	Prospective															
	1994-1997 (Boerma)	Prospective															
	1991-1994 (Grosskurth)	Intervention															
Uganda	2002-2006 (Gray)	Intervention															
	2004-2005 (Mermin)	STARHS	↔	↔	↔						↔				↔		
	1999-2004 (Morrison)	Prospective				+			+								
	1994-1996 (Wawer)	Intervention															
	1993-1995 (Hom)	Prospective													↔		
	1989-1990 (Wawer)	Prospective			↔												
Zambia	2003-2004 (Ramjee)	Prospective															
Zimbabwe	1999-2004 (Morrison)	Prospective				+			+								
	1998-2003 (Lopman)	Prospective	+	↔			↔						+				
	2001 (Mbizvo)	Prospective								+							
	1999-2001 (Kumwenda)	Prospective															
	1997-2001 (Humphrey)	Prospective	↔	+										↔		+	
	1993-1995 (McFarland)	Prospective							↔								
	1993-1995 (Mbizvo)	Prospective															

*Factors that increase risk for HIV infection are indicated by "+"; negative or protective risk factors by "-"; and risk factors with no association to incident HIV infection on multivariate analysis by "↔". Publications that did not analyze or report risk factors are not listed in table 2.

Table 3 A. Risk factors for HIV incidence and prevalence in ZIMBABWE

	Internal comparison (Lopman, et al.)	
Risk Factor*	**Incident HIV vs. HIV negative**	**Prevalent HIV† vs. HIV negative**
Concordant		
Age (older)	+	+
Current or recent STI/symptoms	+	+
Concurrent or multiple partners	+	+
Being divorced or separated	+	+
Divergent‡		
Differential detection‡		
Condom use	↔	+ (women)
Age difference with partner	↔	+
Being employed	↔	+
Being widowed	↔	–
Spouse has other partners	↔	+ (women)
High education	↔ **(men), + (women)**	– (men), ↔ (women)
History of HIV test(s)	↔	+ (women)
Traditional religion	**+ (women)**	↔ (women)
Unclear, full data not available		
Having an unwell partner	+	
Intravaginal practices (incl. dry sex)	↔	
Being uncircumcised (men)	↔	
Sex outside marriage	↔	

*Factors that increase risk are indicated by "+"; negative or protective risk factors by "-"; and risk factors with no association on multivariate analysis by "↔". A blank indicates the risk factor was either not explored in the analysis or was not reported in the publication.
†NB: includes cases labeled as incident HIV.
‡"Divergent" refers to risk factors found to be significantly associated with both incident and prevalent infection, but in different directions. "Differential detection" refers to risk factors that were detected as significant by one method but not the other; bolded risk factors are those detected by incidence but not prevalence analyses.

targeting, monitoring, and evaluating prevention strategies. Incidence data are non-existent for 29 countries in sub-Saharan Africa, and are considerably outdated for countries such as Benin, the Democratic Republic of Congo, and Rwanda. It should be noted that HIV incidence studies are currently ongoing in some of these understudied countries, such as Rwanda and Mozambique, and perhaps others.

Few incidence studies are population-based or nationally representative; much of the available data was derived from individual studies or surveys, with too much heterogeneity in study populations and methods to allow meaningful summarization or time-trend analysis. In general, however, HIV incidence rates are high for the region. Several of the most recent studies suggest substantial ongoing HIV transmission in certain populations, for example among Kenyan sex workers[50], urban South African women[51,52], and Tanzanian "bar girls"[53]. However, the tendency for incidence studies to be preferentially conducted among high-risk (often non-pregnant) women may lead to underrepresentation of HIV incidence in other population groups, such as men and lower-risk women.

Young people, individuals in concurrent or multiple sexual partnerships, and individuals with a current or recent STI were most consistently identified as being at risk for HIV infection. Interestingly, two of the three studies reporting a negative association between young age and incident HIV infection were STARHS studies[23,54]. These counterintuitive findings could reflect the tendency of STARHS assays to misclassify longer-term infections that are more prevalent in older age groups as incident infections, thereby skewing the relationship between age and incident infection. HSV-2 seropositivity was predictably the strongest cofactor among the different STI evaluated (most commonly HSV-2, gonorrhea, chlamydia, and bacterial vaginosis), and has been reported by many others as strongly linked with HIV acquisition[55,56]. The relationship between marital status and HIV acquisition varied across and within countries, and marital status may be defined differently across studies (legal versus cultural definitions). Finally, the association between condom use and incident infection was equivocal in the studies examined in this review. These results could be biased by measurement error since condom use was generally

Table 3 B. Risk factors for HIV incidence and prevalence in ZIMBABWE

	Independent-sample comparison	
Risk Factor*	**Incident HIV vs. HIV negative (Morrison, et al.)**	**Prevalent HIV vs. HIV† negative (DHS)**
Concordant		
Current or recent STI/symptoms	+	+
Concurrent or multiple partners	+	+ (women)
Divergent‡		
Age	**+ (young age)**	+ (older age)
Differential detection‡		
Condom use	↔	+ (ever use)
Unclear, full data not available		
Current pregnancy (women)		–
Age at sexual debut		↔
History of HIV testing		↔
High education		– (men)
Being employed		+
High socioeconomic status		+ (women)
Religious affiliation		–
Being divorced, separated or widowed		+
Being married		–
Polygamy		+
Sex outside marriage/co-habitation		+ (women)
Number of sex partners (lifetime)		+
Spending time away from home		+
Sexually high-risk partner	+	
Not living with partner	+	
Being uncircumcised (men)	↔	
High coital frequency	+	
Recent sex work	+	
Hormonal contraception use (women)	↔	

*Factors that increase risk are indicated by "+"; negative or protective risk factors by "-"; and risk factors with no association on multivariate analysis by "↔". A blank indicates the risk factor was either not explored in the analysis or was not reported in the publication.
†NB: includes cases labeled as incident HIV.
‡"Divergent" refers to risk factors found to be significantly associated with both incident and prevalent infection, but in different directions. "Differential detection" refers to risk factors that were detected as significant by one method but not the other; bolded risk factors are those detected by incidence but not prevalence analyses.

ascertained by self-report, and was likely measured by different constructs (e.g. condom use at last sex versus always). Moreover, individuals who report condom use may not use them consistently or correctly[57].

There were no risk factor data for Benin, Botswana, Ghana, or the Democratic Republic of Congo. Several risk factors for incident HIV were only examined in a few studies, including alcohol/substance use, urban residence, transactional sex, and partner sexual risk. Other factors such as non-alcohol substance use, knowledge and attitudes, HIV testing history, sexual orientation, and stigma experience, were not examined by any study. Furthermore, few HIV incidence data are available to support existing prevention policies such as promotion of mutual monogamy, fidelity, and delayed sexual debut. Not examining potentially important risk factors, or factors perceived to be important for prevention, could lead to missed opportunities for intervention or to incomplete prevention messages. Moreover, risk factors for incident HIV infection should be measured as a component of monitoring and evaluation of interventions, with the goal of describing differential changes among risk behaviors in the context of interventions. An important example is monitoring of factors related to secondary transmission among patients attending antiretroviral treatment programs.

Our review highlights that application of STARHS in sub-Saharan Africa is increasing, with 20% of incidence estimates published since 2006 from STARHS studies (data not shown). Availability of STARHS could facilitate

Table 3 C. Risk factors for HIV incidence and prevalence in UGANDA

	Independent-sample comparison	
Risk Factor*	**Incident HIV vs. HIV negative (Gray, et al.)**	**Prevalent HIV† vs. HIV negative (DHS)**
Concordant		
Recent STI/symptoms	+	+
Being uncircumcised (men)	+	+
Number sex partners	↔	↔
Condom use	↔	↔
Education	↔	↔
Divergent‡		
Differential detection‡		
Age	↔	+ (older age)
Marital status	↔	widowed/divorced/never married: + (women), – (men)
Non-marital sex/relationships	↔	+ (women)
Unclear, full data not available		
Alcohol use	↔	
Urban residence		+
Employment		+
Young age at first sex		+ (women)
High-risk partner		+ (women)
History of HIV test(s)		+
Current pregnancy (women)		↔
Religious affiliation		↔

*Factors that increase risk are indicated by "+"; negative or protective risk factors by "-"; and risk factors with no association on multivariate analysis by "↔". A blank indicates the risk factor was either not explored in the analysis or was not reported in the publication.
†NB: includes cases labeled as incident HIV.
‡"Divergent" refers to risk factors found to be significantly associated with both incident and prevalent infection, but in different directions. "Differential detection" refers to risk factors that were detected as significant by one method but not the other.

more timely collection and dissemination of incidence data, especially in resource-limited settings. There is, however, ongoing debate about the validity of STARHS assays, especially the BED-CEIA[58-60]. Important efforts to evaluate the performance of current assays across diverse settings, and to refine these assays and develop new ones, are ongoing. In the interim, several approaches may help improve the validity of STARHS incidence estimates. For example, researchers can adjust estimates with average "false recent" rates, or ideally internal, population-specific rates when available[61-63]; confirm assay classifications against patient-level clinical or epidemiologic data such as CD4 count or HIV testing history; or employ a sequential testing algorithm in which the results of two assays (e.g. BED and Avidity Index) are used to classify an infection[61]. Moreover, there is much to be learned about the epidemiologic utility (its combined validity in estimating incidence and ability to distinguish predictors of HIV incidence from prevalence) and cost-benefit of the STARHS approach in different settings, and especially in sub-Saharan Africa.

In any country experiencing an HIV/AIDS epidemic, the relationship between prevalence and incidence, and the behavioral and demographic profiles of already-infected versus at-risk individuals, changes over time as the epidemic becomes more established in the population[14]. In the comparative analyses we presented, incidence data from Zimbabwe identified only a few new predictors that were not identified by prevalence data, and incidence data from Uganda identified no new predictors. This may reflect the reality of few differences between incident and prevalent infections in these settings and/or populations. Alternatively, the correct risk factors may not have been examined by the studies we included. Indeed, results of the independent-sample comparison should be interpreted with caution, given the important design differences in the source studies. Furthermore, that analysis was not able to evaluate the utility of incidence data for examining trends over time,

or for assessing the impact of prevention programs. Nonetheless, a few important factors appear to distinguish incident from prevalent HIV infections in these settings, including higher education level, geographic region, and young age. Future incidence studies should consider further examination of these factors.

Countries with contemporaneous incidence and prevalence data should perform analyses to evaluate whether prevalence data can be the primary source of information on the epidemic, or if collection of incidence data is necessary. The DHS and other population-based surveys provide a rich data source for such analyses. For countries currently lacking HIV incidence data, dedicating resources to measure incidence in the population would enable jurisdictions to assess the value of the new data compared with existing prevalence data for surveillance and prevention planning. Incidence estimation methods such as antibody-based assays may make the assessment more feasible, particularly with improved validity. When incidence data are being collected, rates and risk factors for infection should be measured concurrently and as comprehensively as possible, and when feasible, trends in HIV incidence should be monitored carefully.

This review has several potential limitations. Our findings could have been affected by publication[64] or measurement biases. Data on risk factors related to sexual activity often suffer from social desirability bias[65], which may be particularly strong for sensitive or criminalized behaviors such as anal sex or sex between men. Low statistical power (especially in lower-risk study populations) could have inhibited more detailed risk factor analyses. As stated above, the independent-sample prevalence/incidence comparison should be interpreted cautiously. Notably, risk factors for prevalent HIV came from DHS surveys and were not controlled for confounding. In addition, DHS surveys are nationwide cross-sectional surveys, whereas incidence data came from multiple studies with heterogeneous data collection, study populations, and analysis methods. Finally, this review did not consider incidence of perinatal HIV infection, another important and highly preventable source of new infections in the region.

Conclusion

Sub-Saharan Africa remains the epicenter of the global HIV/AIDS pandemic, with significant numbers of individuals already infected and in need of treatment, and scores of others at risk of becoming infected[66,67]. There is a great need to enhance the global response by better characterizing the diverse and dynamic sub-epidemics within this region, a key part of which may be scale-up of systems to monitor HIV incidence. The added value of incidence data will vary by country and possibly other factors, and the feasibility of its collection will depend on the methods and resources available. Despite current limitations, however, methods that allow cross-sectional incidence estimation are an exciting development, and will hopefully be accompanied by ongoing improvements in epidemiologic utility in the next few years as more experience is gained, and as the assays and methods are further refined. In the meantime, prevalence and behavioral risk factor data remain an important mainstay for HIV prevention planning.

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