AIDS-defining and non-AIDS-defining cancers in the post-HAART era:

A study on the capacity of low-, middle- and high-income regions to document, screen, diagnose and treat HIV-related malignancies

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Glossary of tables and figures

Abbreviations

ADC	AIDS-defining cancers
AIDS	Acquired Immunodeficiency Syndrome
ART	Antiretroviral treatment
AFP	Alpha-fetoprotein
CDC	Center for Disease Control and Prevention
CT	Computerized tomography
EBV	Epstein-Barr virus
FNA	Fine needle aspirate
FOBT	Fecal occult blood in the stool
HAART	Highly active antiretroviral therapy
HHV-8	Human herpesvirus 8
HIV	Human Immunodeficiency virus
HPV	Human papillomavirus
ICAP	International Center for AIDS care and treatment programs
IeDEA	International epidemiologic Databases to evaluate AIDS
KS	Kaposi sarcoma
KSHV	Kaposi-associated herpesvirus
NADC	Non-AIDS-defining cancers
NHL	Non Hodgkin lymphoma
PSA	Prostate-specific antigen
SIR	Standardized incidence ratio
UNAIDS	Joint United Nations Program on HIV/AIDS
U/S	Ultrasound
VIA	Visual inspection with acetic acid
WHO	World Health Organization

Abstract:

Josephine Tsai, MD, Denis Nash, PhD, MPH, 2010. AIDS-defining cancer and non-AIDS-defining cancers in the post-HAART era. Key words: AIDS-defining cancer, non-AIDS-defining cancer, capacity, screening, diagnosis, treatment. International epidemiologic Databases to evaluate AIDS (IeDEA), International Center for AIDS care and Treatment Programs (ICAP) at Columbia University Mailman School of Public Health, New York City, USA

Introduction: Since the introduction of antiretroviral treatment (ART) in 1996, the incidence of AIDS-defining cancers (ADCs), such as Kaposi sarcoma (KS) and non-Hodgkin lymphoma (NHL), has decreased in high-income countries. However, non-AIDS-defining cancers (NADCs), such as anal cancer and Hodgkin lymphoma, are on the rise.

In resource-limited settings where access to ART is limited, the incidence of KS and NHL remains high, particularly in sub-Saharan Africa. There is some increasing, albeit scanty, epidemiological evidence of NADCs in low- and middle-income countries.

However, there is a dire lack of information in resource-limited settings on the present capabilities for the documentation, screening, diagnosis and treatment of ADCs and NADCs.

Objective: This study aims to increase knowledge of cancer care capacities in six regions of the world as well as to identify differences between resource-rich and resource-limited settings in order to make recommendations regarding cancer care in a period of HAART scale up.

Methods: 95 IeDEA-participating HIV/AIDS health care facilities in 6 regions of the world responded to a standardized, multi-question survey on cancer care in HIV-infected patients. These data were merged and analyzed to produce preliminary statistics.

Findings: Even though ART access and scale up has occurred almost a decade later in Africa compared to middle- and high-income countries, a large proportion of sites from Africa (45%, (95% CI: 76-98%) - 62% (95% CI:80-94)) have reported NADCs among their HIV-infected cancer patients

Recommendations: National HIV surveillance and cancer registries should be established in order to improve the validity of epidemiologic studies in low- and middle-income countries, particularly regarding emerging NADCs. Cost-effective ways to increase capacity for the prevention and care of HIV-related malignancies should be implemented.

Declaration:

Where other people's work has been used (either from a printed source, internet or any other source) this has been carefully acknowledged and referenced in accordance with departmental requirements.

The thesis. 'AIDS-defining and non-AIDS-defining cancers in the post-HAART era', is my own work.

Josephine Yi-Fin Tsai

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Introduction:

According to the latest AIDS epidemic update in December 2009 by the Joint United Nations Programme on HIV/AIDS (UNAIDS) and the World Health Organization (WHO), an estimated 33.4 million people are living with HIV/AIDS, an estimate which is 20% higher than in 2000 (UNAIDS/WHO. AIDS epidemic update: November 2009). This increase in overall HIV prevalence is due to a combination of new HIV infections as well as to an increase in access to antiretroviral drugs which in turn leads to greater longevity for HIV- positive persons (UNAIDS/WHO. AIDS epidemic update: November 2009).

An estimated 2.7 million new HIV infections occurred in 2008, with sub-Saharan Africa as the region most heavily affected, representing 71% of all incident HIV cases (UNAIDS/WHO. AIDS epidemic update: November 2009).

Over 5 million HIV-positive people in low- and middle- income countries had access to antiretroviral treatment (ART) at the end of 2009, marking a 12-fold increase in access since 2003, with East and southern Africa achieving a high treatment coverage of 48% (UNAIDS/WHO. AIDS epidemic update: November 2009). As a consequence, the 2 million AIDS-related deaths in 2008 represented a 10% reduction since 2004 (UNAIDS/WHO. AIDS epidemic update: November 2009).

Within sub-Saharan Africa, southern Africa remains the region which is most heavily affected by the HIV epidemic, comprising the nine countries with the highest prevalence in the world (UNAIDS/WHO. AIDS epidemic update: November 2009). With the largest antiretroviral therapy program in the world, South Africa has reaped substantial public health benefits with increased access to ART. In the Western Cape Province of South Africa, six-month mortality among patients at an HIV treatment decreased from 12.7% to 6.6% between 2001 when the antiretroviral therapy program began to 2005. An estimated 79% of adults enrolled in an antiretroviral treatment program in Botswana were alive 5 years later (UNAIDS/WHO. AIDS epidemic update: November 2009).

Evidence suggests that HIV prevalence in East Africa may be stabilizing, although increases in particular settings are concerning. In Kenya, HIV prevalence has increased since 2003 which may reflect a decrease in HIV-related mortality due to a scale-up of ART as well as an increase in risky sexual behavior in rural areas, where HIV prevalence has increased among adults compared to adults living in urban areas (UNAIDS/WHO. AIDS epidemic update: November 2009).

Although HIV prevalence is lower overall in West and Central Africa compared to southern Africa, these regions still harbor country-specific HIV epidemics. For example, while HIV prevalence is below 1% in Cape Verde, Niger and Senegal in West Africa, nearly 4% and 2% of the population in Cote d'Ivoire and Ghana, respectively, are living with HIV (UNAIDS 2008).

In addition, antiretroviral therapy coverage is generally higher in East and southern Africa (48%) than in West and Central Africa (30%) (UNAIDS/WHO: 2009 AIDS epidemic).

With 4.7 million people living with HIV in 2008, including 350,000 incident cases, Asia is second only to sub-Saharan Africa in terms of numbers of people living with HIV. India accounts for about half of Asia's overall prevalence. Although every country in Asia, except Thailand, has an HIV prevalence below 1%, because Asia comprises up to 60% of the world's population, this prevalence translates into a heavy HIV burden (UNAIDS/WHO. AIDS epidemic update: November 2009).

As of December 2008, antiretroviral coverage in Asia was 37%, below the global average of 42% for low- and middle-income countries but representing a sevenfold increase in treatment over 5 years (UNAIDS/WHO. AIDS epidemic update: November 2009).

Although the Caribbean accounts for a small proportion of the global HIV burden (0.7% of people living with HIV and 0.8% of incident cases in 2008), the Caribbean has the second highest regional adult HIV prevalence with 1.0% of their population infected with HIV. Efforts have been made to scale up access to ART, resulting in treatment coverage of 51% in December 2008, higher than the global average of 42% for low-and middle-income countries (UNAIDS/WHO. AIDS epidemic update: November 2009).

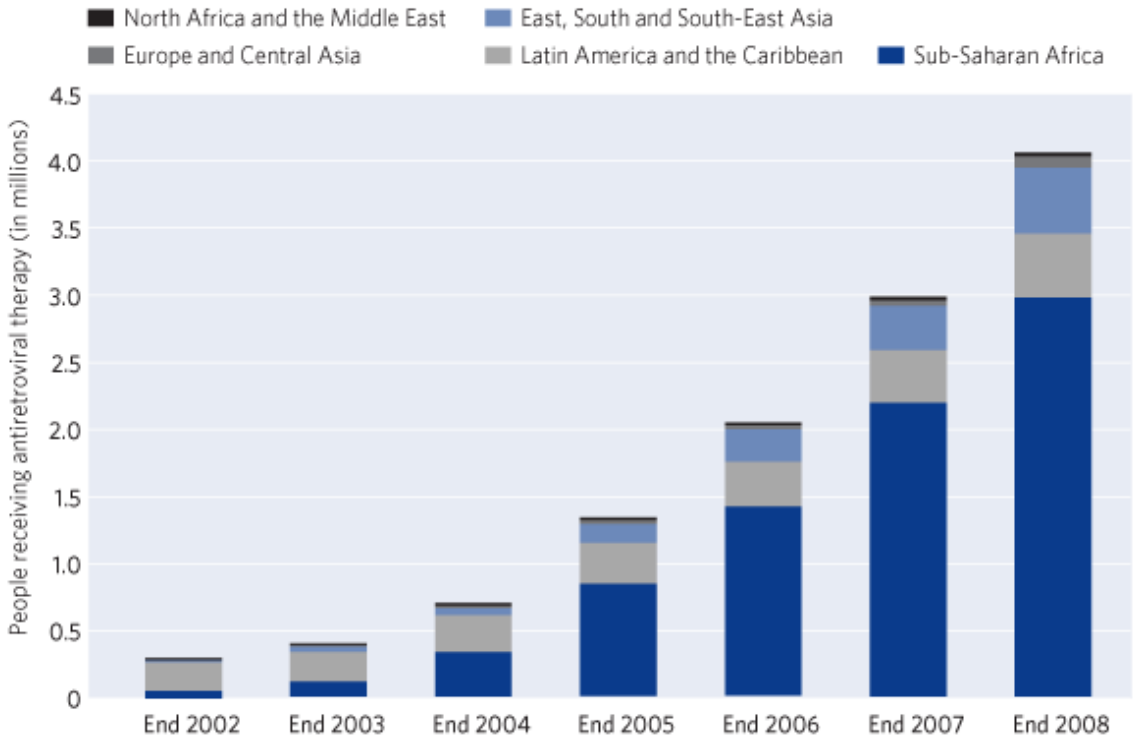
Epidemiological evidence suggests that the HIV epidemic in Latin America remains stable with a regional prevalence of 0.6%, comprising mainly low-level and concentrated epidemics (UNAIDS/WHO. AIDS epidemic update: November 2009).

Antiretroviral coverage is generally higher in South America than Central America with an overall coverage proportion in Latin America of 54% in 2008. In Brazil, the largest Latin American country with the highest number of AIDS cases in Latin America (Sampaio et al, 2007), ART has been available since 1996. As a consequence, average survival after an AIDS diagnosis in Sao Paulo state increased from 4 months in 1992-1995 to 50 months in 1998-2001 (UNAIDS/WHO. AIDS epidemic update: November 2009).

Data from high-income countries, where ART has been universally available since 1996, continue to reveal the incredible public health benefits of antiretroviral treatment. In the USA, the number of AIDS-related deaths in 2007 (CDC, 2009) was 69% lower than in 1994 (CDC, 1996). The multicountry CASCADE study in Europe, Australia and Canada reports that mortality rates for HIV-infected people during the first 5 years after diagnosis approach that of the HIV-uninfected population, although excess mortality in HIV-infected people is being seen with longer durations of infection (UNAIDS/WHO. AIDS epidemic update: November 2009).

Graph 1. summarizes the increase in ART access from 2002-2008, particularly in sub-Saharan Africa.

Graph 1. Antiretroviral therapy coverage by region, 2002-2008



UNAIDS/WHO:AIDS epidemic update, 2009.
http://data.unaids.org/pub/Report/2009/JC1700_Epi_Update_2009_en.pdf

Background:

Most of the epidemiological evidence regarding the impact of antiretroviral treatment for HIV- infected people has come from developed countries in North America, Western Europe and Australia where highly active antiretroviral therapy (HAART) was introduced in 1996 and where HIV surveillance systems were well-established. Since then, HIV-related mortality rates have significantly decreased in these high-income regions and the lifespan of HIV- infected individuals has increased, resulting in a large number of older individuals living with HIV/AIDS (Silverberg, 2007).

For older individuals living with HIV/AIDS, cancer has become a growing concern with up to 30% of all deaths in HIV-infected people related to cancer (Silverberg, 2007). The impact of HAART, however, on the incidence of cancer in HIV-infected people is not so clear. Some have argued that an aging population naturally has an increased cancer risk (International Collaboration, 2000) while others have theorized that certain risk factors, such as alcohol, cigarette smoking and viral co-infections, which are more prevalent in

HIV-infected people than HIV-uninfected people, may explain differences seen in cancer risk by HIV status (Silverberg, 2007). In addition, with more people on HAART living longer with partial immune suppression, the effects of these chronic changes in immunity and persistent co-infections with viral oncogenes are unknown (Simard, 2010).

Since the first case reports of Kaposi sarcoma in 1981 among HIV-positive men in the USA, it has been recognized that HIV-infected people have a higher risk of cancer (Simard, 2010, Silverberg, 2007). Three cancers have been designated by WHO as AIDS-defining cancers (ADCs) : Kaposi sarcoma (KS), non-Hodgkin lymphoma (NHL) and invasive cervical cancer (ICC). These three cancers are associated with oncogenic viruses, namely human herpesvirus 8 (HHV-8) or KS-associated herpesvirus (KSHV) for KS; Epstein-Barr virus (EBV) for the AIDS-defining NHL subtypes and human papillomavirus (HPV) for cervical cancer.

A 2000 report from the International Collaboration on HIV and Cancer, which included data from 23 prospective studies with nearly 48,000 HIV-infected people in North America, Europe and Australia, revealed a substantial and significant reduction in the incidence of KS and NHL from 1997-1999 compared with the pre-HAART era of 1992-1996 (International Collaboration on HIV and Cancer, 2000). In addition, the incidence of 22 NADCs, including Hodgkin disease and anal cancer, were examined. No significant changes in the incidence of NADCs were seen and the authors concluded that the 'widespread use of HAART…do not, at this stage, support the view that cancer incidence rates might increase as HIV-infected people survive longer' (International Collaboration on HIV and Cancer, 2000).

However, subsequent studies in developed countries, particularly large studies which have linked population-based HIV and cancer registries, have shown a statistically significant increase in the standardized incidence ratio (SIR) and relative risks of many NADCs, including anal, Hodgkin disease, head and neck, liver, lung, skin, conjunctiva and leukemia. In developed countries, overall, NADCs account for more morbidity and mortality than ADCs in the post-HAART era (Silverberg, 2007, Pantanowitz, 2006).

Data from the HIV/AIDS Cancer Match study in the United States, a representative cohort of over 250,000 HIV-infected people diagnosed in 1980-2004 matched to population-based cancer registries, were analyzed to capture incident cancers during the years 3-5 and 6-10 after AIDS onset, thus representing the longest cancer risk follow-up study of persons with AIDS (Simard, 2010). Standardized incidence ratios (SIR) were used to assess cancer risk relative to the general population and relative risks were calculated to compare cancer risk before and after 1996, the pre- and post- HAART periods, respectively.

Incidence of KS declined dramatically by 80% from before 1996 to after 1996 and NHL incidence decreased by 70% during the same time period (Simard, 2010). Cervical cancer incidence did not change significantly between the pre- and post-HAART periods

(Simard, 2010). During the HAART era, persons with AIDS had significantly higher risk for ADCs compared to the general population (Simard, 2010).

In addition, risk was elevated for persons with AIDS compared to the general population for all NADCs combined as well as for the following specific NADCs: Hodgkin lymphoma, head and neck, anal, liver, lung and penis. Among NADCs, anal cancer and Hodgkin lymphoma incidences increased significantly in the post-HAART era (Simard, 2010). A commentary of the article noted that "the NADCs are here to stay."

The majority of information from low- and middle-income countries regarding HIV and cancer has come from sub-Saharan Africa, albeit relatively few studies from this region have examined the relationship of HIV infection and cancer. KS has been more frequent in sub-Saharan Africa compared to Western countries, even before the HIV epidemic (Sasco, 2010). The incidence of KS has increased in sub-Saharan Africa with the AIDS epidemic with a 20-fold increase in Uganda and Zimbabwe during the last 15 years, making KS the most common malignancy among men and the second most common malignancy in women following cervical cancer (Sasco, 2010, Orem, 2004).

The first study in sub-Saharan Africa linking a large HIV cohort with a population-based cancer registry was conducted in Uganda and included over 12,000 HIV-infected people diagnosed from 1988 to 2002. Standardized incidence ratios (SIRs) of cancers were calculated in the early-incident (4-27 months after registration) and late-incident (28-60 months) periods (Mbulaiteye, 2006).

Results showed that the ADCs comprised most of the early-incident cancers with significantly elevated SIRs of 6.4 (95% CI 4.8-8.4) for KS, 6.7 (95% CI 1.8-17) for NHL and 2.4 (95% CI: 1.1-4.4) for cervical cancer. KS and cervical cancer were also increased in the late-incident period. In the combined periods, the risks of all three ADCs were significantly increased compared to the general population (Mbulaiteye, 2006).

The persistence of a high incidence of KS in Africa in contrast to a dramatic decreased incidence in developed countries is certainly due in large part to lack of access to ART in low-income countries since successful KS treatment is highly dependent on the restoration of immunity (Sasco, 2010).

In addition, human herpesvirus 8 (HHV-8), a necessary cause of KS, is highly prevalent among adult Africans with estimated prevalences ranging from 20-80% (Mbulaiteye, 2006). High HHV-8 prevalences in sub-Saharan Africa combined with limited access to ART are largely responsible for persistently high incidences of KS in this region.

NHL incidence has also increased in sub-Saharan Africa compared to a decline in high-income countries even though the association between HIV and NHL is weaker in Africa, perhaps due to underreporting of NHL because of its costly and difficult histological

diagnosis as well as earlier deaths from AIDS-associated causes before NHL can be manifested (Del Maso, 2001).

In addition, the association of cervical cancer and HIV infection is weaker in sub-Saharan Africa compared to developed countries, perhaps due to a high underlying prevalence of cervical cancer which could have masked the affect of HIV infection on the incidence of cervical cancer (Del Maso, 2001) . In general, although invasive cervical cancer has been designated as an ADC since 1993, the association between HIV and cervical cancer remains unclear (Del Maso, 2001).

However, cervical cancer is the most common malignancy among women in many African countries independently of HIV risk, and this is important to understand for HIV-infected women given that effective and low cost screening methods such as visual inspection with acetic acid (VIA) are available (Sasco, 2010).

There have been few studies in Africa examining the association of HIV and NADCs. The 2006 Kampala linkage study reported 8 of 37 NADCs as fulfilling the criteria for possible association with HIV infection (SIR increased in 1 of 2 incident periods or in the combined periods): conjunctival cancer, Hodgkin lymphoma and to a lesser extent, kidney, thyroid, uterus, breast, nasopharynx and lung (Mbulaiteye, 2006). Unfortunately, there is a paucity of cancer registries in Africa, making it difficult to assess associations between HIV and NADCs.

Even fewer epidemiological data regarding HIV-related cancers are available from Asia and Latin America. The first study from India, the country with the highest number of people living with HIV/AIDS in Asia, included 251 HIV-positive cancer patients diagnosed and treated at a tertiary hospital (Dhir, 2007). There were no reported cases of KS and an increase in NHL and cervical cancers was found in HIV-infected individuals compared to an expected number in a similar population from the hospital-based cancer registry (Dhir, 2007). NADCs with a higher proportional incidence ratio included anal cancer, Hodgkin disease, colon cancer, testicular and head and neck cancers (Dhir, 2007).

Brazil has the highest number of AIDS cases in Latin America (Sampaio, 2007). Even though HAART has been available through government mandate since 1996, there is also extreme poverty in both urban and rural areas (Sampaio, 2007). There are a limited number of studies on HIV-related malignancies in Brazil.

However, one noted distinction, according to a study from Brazil, is the association of AIDS-defining lymphomas with oncogenic viruses, particularly with EBV (Sampaio, 2007). Another unique aspect is the high incidence of dual infection with HIV and human T cell leukemia virus type 1 (HTLV-1) (Sampaio, 2007). Efforts in Latin America have been aimed primarily on improving HIV surveillance rather than studying the effects of HAART on the incidence of ADCs and NADCs.

With the scale-up of HAART, chronic conditions such as HIV-related cancers will represent a growing burden of HIV-associated morbidity as low- and middle-income countries are not only reporting high incidences of ADCs, but also have reported some evidence of an association between HIV and NADCs (Sasco, 2010). In many high-income countries, NADCs account for more morbidity than ADCs with one long-term population-based study showing an overall 20% increase in the incidence of NADCs between the pre- and post-HAART periods (Simard, 2010, Silverberg, 2007).

Linkage studies of population-based HIV and cancer registries, as have been conducted in high-income countries, have shown an increase in the SIR and relative risk of many NADCs (Pantanowitz, 2006). However, the role that immunosuppression plays in the development of NADCs is unclear since the increased risk of NADCs has not been shown to be associated with low CD4 cell counts as has been shown for KS and to a lesser extent NHL (Silverberg, 2007, International Collaboration on HIV and Cancer, 2000).

Given the increased risk of NADCs in HIV-infected populations, there is a need for cancer prevention and care strategies for people living with HIV/AIDS as HIV-infected patients are expected to live longer with the scale-up of antiretroviral treatment.

Primary prevention should include efforts to reduce smoking and risky sexual behavior. Secondary prevention includes regular examinations and screening for cervical cancer (cervical PAP, VIA, HPV vaccine), anal cancer (anal PAP), colon cancer (occult blood in the stool) and hepatocellular cancer (ultrasound, alpha-fetoprotein, Hepatitis B vaccine).

Tertiary prevention efforts should be aimed at improving cancer treatments, particularly refining and modifying cancer treatments in low- and middle-income countries which cannot deliver complicated treatment regimens and which cannot support treatment-related complications. Improvements in palliative care are needed, also particularly in low-resource settings where patients often present with late-stage disease.

In addition, based on increased evidence of improved survival and decreased HIV-related illnesses with earlier initiation of ART, WHO updated their recommendations in 2009 stating that ART should be started for HIV-infected individuals with CD4 counts less than or equal to 350 cells/mm^3 (WHO, Rapid advice: antiretroviral therapy for HIV infection in adults and adolescents, 2009). Earlier initiation of ART could certainly impact the incidence of ADCs, particularly KS and perhaps NHL, in sub-Saharan Africa.

In addition to scale up of ART, prevention and care strategies for HIV-related malignancies should also be improved. However, in resource-limited settings, the hallmarks of cancer prevention and treatment are shortages of trained cancer specialists and a scarcity of screening, diagnostic and treatment resources. There is a critical need to increase capacity, but in order to effectively understand the gaps and efficiently increase

capacity, we must have a better understanding about the resources which are presently available.

However, there is a dire lack of information in resource-limited settings on the present capabilities for the documentation, screening, diagnosis and treatment of ADCs and NADCs. This present study thus aims to increase knowledge of these resources in HIV/AIDS care facilities around the world in order to make recommendations regarding the care and treatment of HIV-infected people with cancer as well as to identify differences between resource-rich and resource-limited settings which may, in part, account for the regional differences in the observed epidemiology of these cancers.

Study Objectives:

The UNAIDS/WHO AIDS epidemic update of 2009 states that 'the substantial diversity of national (HIV) epidemics underscores not only the need to tailor prevention strategies to local needs but also the importance of decentralizing AIDS responses' (UNAIDS/WHO: AIDS epidemic update, November, 2009).

This study aims to address the diversity of regional capacity to prevent, care for and treat HIV-related cancers through a unique research consortium, the International epidemiologic Databases to Evaluate AIDS (IeDEA), that relies on data collected through 134 HIV/AIDS health care facilities in 7 regions of the world.

The primary objective of this study is to compare by region the capacities of 134 IeDEA-participating HIV/AIDS health care facilities to:

- document data on ADCs and NADCs
- screen for ADCs and NADCs
- diagnose ADCs and NADCs
- treat and offer palliative care for ADCs and NADCs

Documentation capacity will be inferred by evaluating the availability of data on various factors associated with cancer care and the proportion of patients with documentation of these same cancer care variables.

Screening, diagnostic and treatment capacity will be inferred by the availability of various cancer screening, diagnostic and treatment methods as well as the availability of palliative and comfort care.

Anticipated results include, for example, that cancer screening, diagnostic and treatment methods will be more available in high-income settings (North America region) compared to low-income settings (East Africa region) and that documentation capacity will be more available in middle-income settings (Latin America region) compared to low-income settings (Central Africa region).

Methods:

The International epidemiologic Databases to Evaluate AIDS (IeDEA) is a United States National Institute of Health (NIH)-funded global consortium which was established in 2006 to develop seven regional centers for the collection of data in order to address research questions in HIV/AIDS care and treatment which could not be answered with single cohorts (IeDEA, http://www.iedea-hiv.org/about/).

The U.S. National Institute of Allergy and Infectious Diseases (NIAID) provides funding for the seven regional data centers and their affiliated clinical sites. The U.S. National Institute of Child Health and Development (NICHD) supports pediatric research and the U.S. National Cancer Institute (NCI) initiates cancer-related research in Africa through the IeDEA regional centers and its sites.

By pooling the data collected through the seven regional centers and its affiliated clinical sites, large datasets can be created in a cost-effective manner and the quality of the data can be maintained at a high level by using pre-determined, standardized data elements (IeDEA, http://www.iedea-hiv.org/about/). Each regional center is responsible for establishing mechanisms for receiving and combining data from their affiliated sites, standardizing the variables, verifying the quality of the data as well as training personnel in data collection, processing and cleaning.

The IeDEA Site Assessment Tool was created and finalized in June, 2009 as a collaborative effort between IeDEA and the International Center for AIDS Care and Treatment Programs (ICAP) at Columbia University Mailman School of Public Health in New York City, USA. The Site Assessment Tool was created in order to document the resources available at the site- and regional- level to care for and treat HIV/AIDS patients, understanding that there are wide disparities in available resources between low-income and high-income settings.

Documentation of HIV/AIDS care and treatment resources may not only initiate action to improve the means by which patients are cared for in low-resource settings, but also may comment upon the epidemiology of HIV-related cancers in different regions of the world.

The site assessment survey is composed of three main sections: Site and program characteristics, care and treatment of tuberculosis in HIV-infected patients and adult and pediatric cancer care in HIV-infected patients. This study focuses on the responses from the adult cancer section of the site assessment tool.

Table 1. shows the estimated number of individuals covered in each region of the IeDEA consortium. Nearly 525,000 HIV infected persons in 43 countries are represented in the IeDEA initiative (2009-2010 update).

Table 1 Estimated number of HIV-infected individuals in IeDEA-participating sites and regions

Region	Countries	No. Adults	No. Children	Total
North America	USA, Canada	115,615	None	115,615
Caribbean and Central and South America	Argentina, Brazil, Chile, Haiti, Honduras, Mexico, Peru	18,000	300	18,300
Asia and Australia	Australia, Cambodia, China, Indonesia, Japan, Malaysia, Papua New Guinea, Philippines, Singapore, South Korea, Taiwan, Thailand, Vietnam	8,256	2,599	10,855
West Africa	Benin, Burkina Faso, Côte d'Ivoire, Gambia, Ghana, Mali, Nigeria, and Senegal	33,378	2,473	35,851
Central Africa	Cameroon, Democratic Republic of Congo, Burundi, Rwanda	28,000	1,284	29,284
East Africa	Kenya, Uganda, Tanzania	89,965	16,344	106,309
Southern Africa	South Africa, Botswana, Zimbabwe, Zambia, Malawi, Mozambique	185,318	22,154	207,472
Total		**478,532**	**45,154**	**523,686**

Source: IeDEA website: http://www.iedea-hiv.org/about/

Site eligibility:

One hundred and thirty-four IeDEA-participating HIV/AIDS health care facilities were approached and asked to complete the IeDEA Site Assessment Tool (Appendix 1). These 134 sites were organized into seven regions: Asia and Australia (n=30), Caribbean and Central and South America (n=7), North America (n=9), Central Africa (n=16), East Africa (n=32), southern Africa (n=19) and West Africa (n=20). Key variables were obtained from the adult cancer section of the IeDEA Site Assessment tool.

All 19 sites from the southern Africa region were unable to complete the adult cancer section, resulting in a total sample of 6 regions. In total, including the 19 sites from the southern Africa region, 39 sites were unable to complete the adult cancer section of the Site Assessment tool, resulting in a total sample size of 95 sites. Appendix 2. shows the 95 sites and corresponding regions which were able to contribute data about cancer care

and treatment in their HIV/AIDS health care facilities. Appendix 3. shows the sites and corresponding regions which were unable to complete the adult cancer section of the survey.

Key variables:

Key data were obtained from site-level responses to the IeDEA Site Assessment Tool, focusing on responses to the adult cancer section of the survey.

Key variables were divided into five variable categories: facility characteristics, documentation capacity, cancer screening capacity, diagnostic capacity and treatment capacity.

Facility characteristics were operationalized into two variables: Type of site and type of cancers seen at the facility. Types of site included individual clinic, a clinic within a group, a multi-center site or academic hospital. Types of cancers seen at the site were further operationalized into ADCs and NADCs as well as organ-specific cancers.

Documentation capacity was defined in two ways: availability of data on and proportion of patients with documentation of various aspects of cancer care and treatment.

Cancer screening capacity was defined in two ways: availability of various methods of cancer screening and whether these methods were used for diagnosis only or for diagnosis and screening.

Cancer diagnostic and treatment capacity were defined as to whether the individual sites used various methods of diagnosis and screening.

Appendix 4. summarizes the key variables and their corresponding survey questions, variable categories and units of measure.

Statistics:

After responses to the IeDEA Site Assessment tool were collected from individual sites, the data were merged at Vanderbilt University in Nashville, Tennessee, USA. The data were coded, cleaned and analyzed at the International Center for AIDS Care and Treatment Programs (ICAP) at Columbia University Mailman School of Public Health.

Descriptive statistics were used to compare summary measures (proportions, means) across the 6 IeDEA regions for each key variable noted in Appendix 4.

SAS statistical software was used for descriptive statistics.

Results:

Facility characteristics:

Fifty-nine percent of the IeDEA sites stated that they were academic hospitals. The next most common types of facility reported were individual clinic (15%), multi-center study site (7%) and 3% of sites self-reported as a group of medical clinics (data not shown).

A large majority of the IeDEA sites reported seeing cancer patients at their facilities, ranging from 70% of sites (Central Africa) to 100% of sites (West Africa and Caribbean/Latin America. The North American sites did not respond to this survey question). Data were missing from 11 sites.

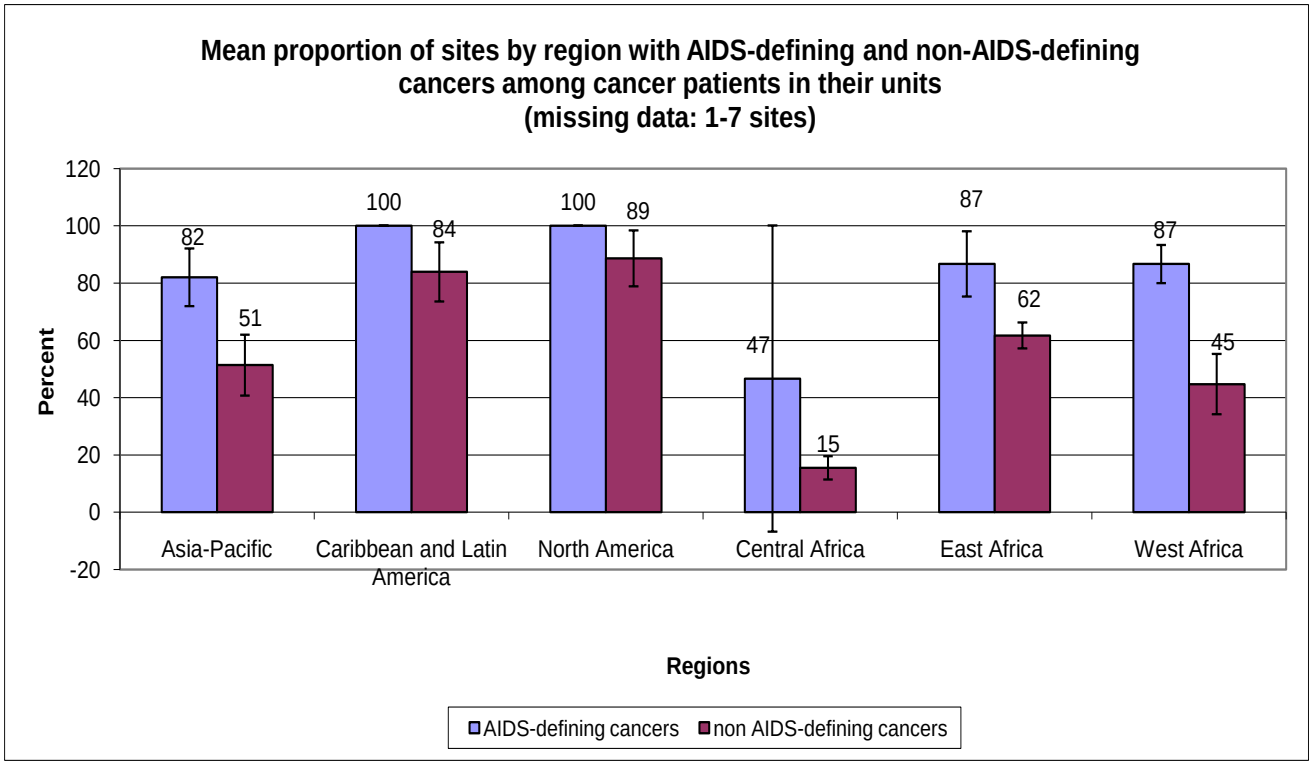
Sites were also asked to estimate the percentage that each of the following cancer types was found among the cancer patients in their units: KS, NHL, cervix, anal, breast, colorectal, head and neck, Hodgkin disease, leukemia, liver, lung, penis, prostate and stomach.

The five available graded responses were 0%, 1-5%, 6-20%, 20-75% and >75%. Sites which answered 0% were categorized as those for which that particular cancer type was not seen among their unit's cancer patients. Sites which answered the other four responses were categorized as those for which that particular cancer type was seen among their unit's cancer patients.

The average of the proportions of sites which found KS, NHL or cervical cancer among the cancer patients in their units was defined as the mean proportion of sites which reported ADCs among their cancer patients. The average of the proportions of sites which found anal, breast, colorectal, head and neck, Hodgkin disease, leukemia, liver, lung, penis, prostate or stomach among the cancer patients in their units was defined as the mean proportion of sites which reported NADCs among their cancer patients.

Graph 2 represents the mean proportion of sites per region which reported ADCs and NADCs seen among the cancer patients in their unit.

Graph 2.



*Black bars represent 95% confidence intervals

As seen in graph 2, all six regions report a higher proportion of sites with ADCs compared to NADCs. In addition, a higher proportion of sites in the North American and Caribbean/Latin American regions report seeing NADCs compared to sites in the Asia/Pacific and African regions. However, nearly 50% and over of the sites in the Asia-Pacific, East Africa and West Africa regions report seeing NADCs among their cancer patients. Central Africa is an exception with a low proportion of sites reporting NADCs among their cancer patients.

In the Caribbean/Latin American and North American regions, there were no statistical differences between the mean proportion of sites which reported ADCs and the mean proportion of sites which reported NADCs. However, the regions of Asia/Pacific, East and West Africa do show significant differences between the mean proportions of sites which report ADCs and the mean proportion of sites which report NADCs.

As mentioned, sites were categorized as to whether or not they found specific cancer types among the cancer patients in their units.

A summary of the proportion of sites per region with specific cancer types is seen in Table 2.

Table 2. Proportion of sites per region which reported presence of cancer type among cancer patients in their units

Cancer type	Asia-Pacific (%)	Caribbean and Latin America (%)	North America (%)	Central Africa (%)	East Africa (%)	West Africa (%)
Kaposi sarcoma	79	100	100	100	96	91
non-Hodgkin	92	100	100	10	76	80
Cervix	75	100	100	30	88	89
Anal	61	100	100	10	50	33
Breast	30	60	100	20	76	44
Colon	52	100	100	0	52	55
Lung	61	83	100	20	64	44
Head/Neck	62	100	86	10	58	33
Hodgkin	67	100	100	20	72	56
Leukemia	62	100	86	20	60	67
Liver	78	80	100	20	62	75
Penis	23	60	67	10	60	12
Prostate	30	80	86	20	60	40
Stomach	39	60	50	20	65	33

Except for the Asia-Pacific region, among the other 5 regions, the highest proportions of sites which reported specific cancer types were those which reported KS. The second and third highest proportions of sites were those which reported cervical cancer and NHL, respectively. Among the Asia-Pacific sites, the highest proportion of sites reported NHL followed by sites which reported KS and cervical cancer.

Documentation Capacity:

Documentation capacity by region was measured in two ways: proportion of sites per region with availability of a range of cancer-related data and mean proportion of patients per region with documentation of a range of cancer-related data.

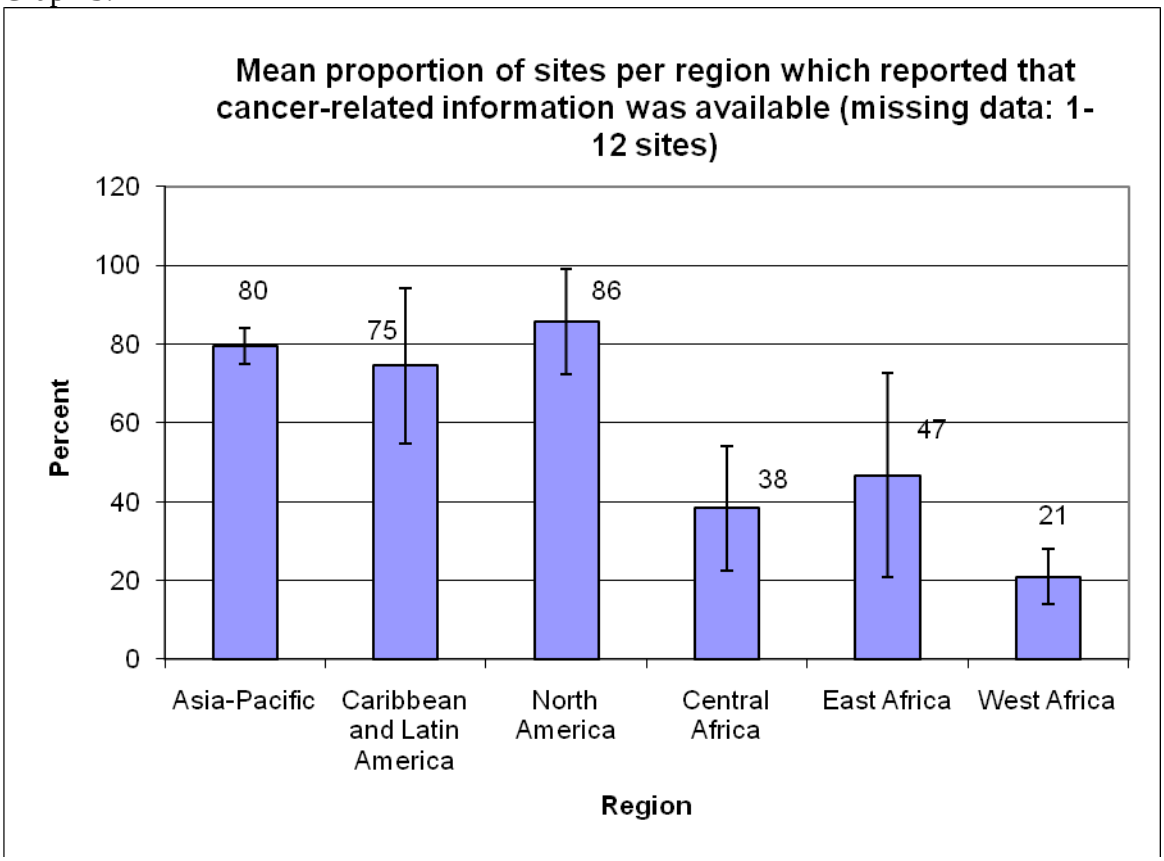
Cancer-related data included information on diagnosis, cancer type, pathology, radiologic data, endoscopic data, behavioral risk factors, co-infections, laboratory results, surgery, chemotherapy, radiotherapy, hormonal therapy, palliative care, date and cause of death.

Sites were asked whether data were available in their unit for the above variables. The average of the proportions of sites per region which reported that specific cancer-related data were collected was then calculated as the mean proportion of sites which reported that cancer-related data was available.

Sites were also asked to estimate the percentage of patients in their units for whom information was collected on the above variables. The means of these estimated percentages of patients for whom cancer-related information was collected were then calculated for each region.

Graph 3 is a summary of the mean proportion of sites per region which reported that cancer-related information was available for their units.

Graph 3.

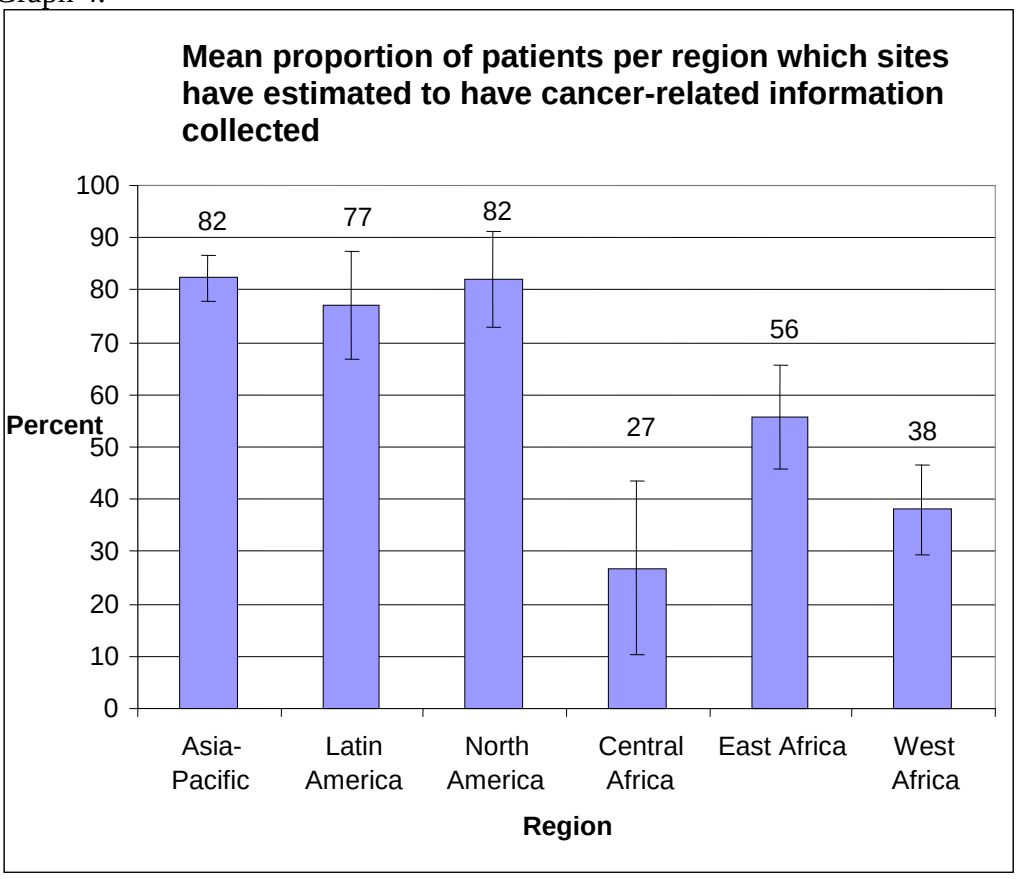


* Black bars represent 95% confidence intervals

As seen in Graph 3, the North American, Caribbean/Latin American and Asia-Pacific regions had the highest mean proportion of sites which reported that data was available in their units on cancer-related information such as diagnosis, surgery, chemotherapy, radiotherapy, hormonal therapy, palliative care and date and cause of death. In contrast, the three African regions had the lowest mean proportion of sites which reported that cancer-related data was available in their units, ranging from 21% to 47%.

Graph 4 is a summary of the mean proportion of patients per region which was estimated by sites to have had cancer-related information collected.

Graph 4.



*Black bars represent 95% confidence intervals

As seen in Graph 4, the mean proportion of patients per region with documentation of cancer-related information was highest for the North American, Caribbean/Latin American and Asia-Pacific regions, ranging from 77-82%. The three African regions reported the lowest mean proportion of patients with documentation of cancer-related data, ranging from the lowest among the Central African sites (27%) to 56% among the East African sites.

Interestingly, despite a low overall mean proportion of 27%, sites from the Central African region reported that a large majority of their patients (70% - 90%) had information collected on behavioral risk factors, co-infections and laboratory results (Data not shown).

Screening:

Ten methods for cancer screening delineated on the survey were mammogram, cervical PAP smear, visual inspection (of cervix) with acetic acid (VIA), prostate-specific antigen

(PSA), anal PAP smear, fecal occult blood test (FOBT), colonoscopy, ultrasound, chest X-ray and alpha-fetoprotein (AFP).

Sites were asked whether these diagnostic methods were used for screening in their units. Three standardized responses were:1- method not available; 2- available, used for diagnosis only and 3- available, used for diagnosis and screening.

Sites which answered 'method not available' were designated as sites without the capacity for such methods. Sites which answered 'available, used for diagnosis only' or 'available, used for diagnosis and screening' were designated as sites with the availability of such methods. The mean proportion of sites with the availability of such methods was then calculated for each region.

Sites were also stratified by whether available methods were used for either diagnosis only or for diagnosis and screening. The mean proportion of sites for each category was calculated for each region.

Table 3 is a summary of the proportion of sites per region with the capacity for specific diagnostic and screening methods. None of the North American sites answered these questions.

Table 3. Proportion of sites per region which stated that the specific diagnostic and screening method was available in their units

Diagnostic and Screening method	Asia-Pacific (%)	Caribbean and Latin America (%)	Central Africa (%)	East Africa (%)	West Africa (%)
Cervical PAP	95	100	33	75	69
VIA	81	86	22	93	62
Anal PAP	48	33	22	4	31
Mammogram	76	71	10	12	54
FOBT	100	100	33	75	62
Colonoscopy	81	86	11	43	54
Chest X-ray	95	100	44	96	77
Ultrasound	91	86	56	68	69
AFP	100	86	11	43	69
Mean proportion of sites per region	91 (95% CI: 86-96)	88 (95% CI:81-95)	27 (95% CI: 22-32)	57 (95% CI:45-67)	64 (95% CI:60-68)

As seen in Table 3, the mean proportion of sites per region with available cancer diagnostic and screening methods was highest for the Caribbean/Latin American and Asia-Pacific regions with percentages of 88% and 91%, respectively. As mentioned,

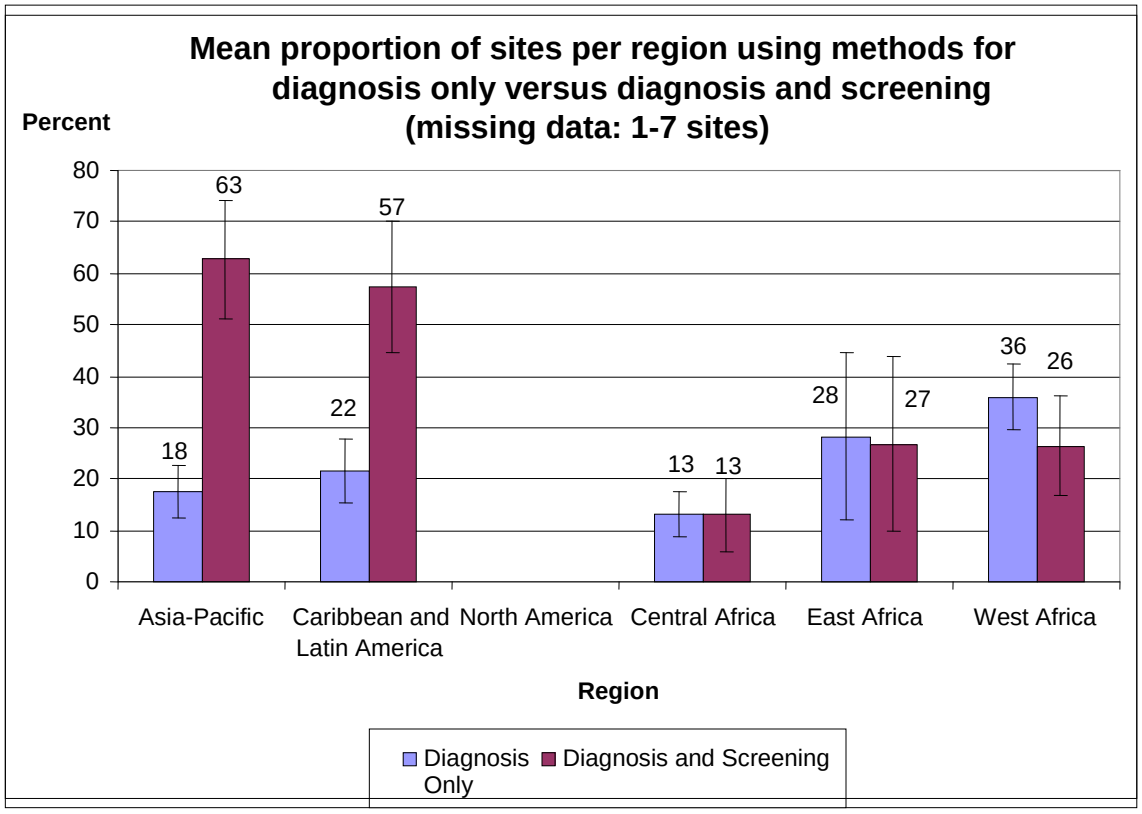
none of the sites from the North American regions answered the questions regarding availability of cancer diagnostic and screening methods.

Central Africa, East Africa and West Africa reported the lowest mean proportions of sites with available screening methods, citing proportions of 27%, 57% and 64%, respectively.

When the diagnostic and screening methods are broken down, among the African regions, the highest proportion of sites reported chest X-ray and ultrasound as available. Except for the Central African region, the lowest proportion of sites reported the anal PAP test as available.

Graph 5 is a summary of the mean proportion of sites per region with available diagnostic and screening methods stratified into 2 categories: 'diagnosis only' or 'diagnosis and screening.' None of the North American sites answered these survey questions.

Graph 5.



* Black bars represent 95% confidence intervals

As seen on Graph 5, when the methods were stratified by whether they were used for diagnosis only or diagnosis and screening, a significantly higher proportion of sites from the Asia-Pacific and Caribbean/Latin America regions reported using the above methods

for diagnosis and screening compared to diagnosis only (63 % , 95% CI: 52 -75 vs. 18% , 95% CI:13-23 and 57%, 95% CI:44-70 vs. 22 %, 95% CI: 16-28 respectively).

However, the three African regions, compared to Asia-Pacific and Caribbean/Latin America, not only reported lower proportions of sites using these methods for either diagnosis only or diagnosis and screening, but diagnosis and screening proportions for the African regions were not significantly different than the diagnosis only proportions.

Diagnosis:

Diagnostic methods included biopsy or fine needle aspiration (FNA), X-ray, computerized tomography (CT) or ultrasound (U/S) and endoscopy. The highest proportion of sites for all regions, except North America which did not answer these survey questions, reported the use of X-ray for diagnosis. The second highest proportion of sites reported the use of biopsy for diagnosis (data not shown).

Sites were asked on the survey to estimate the percentage of the use of the above diagnostic methods for specific cancer types. Graded, fixed responses were: Never, Rarely (0-25%), Sometimes (25-75%), Often (>75-99%) and Always.

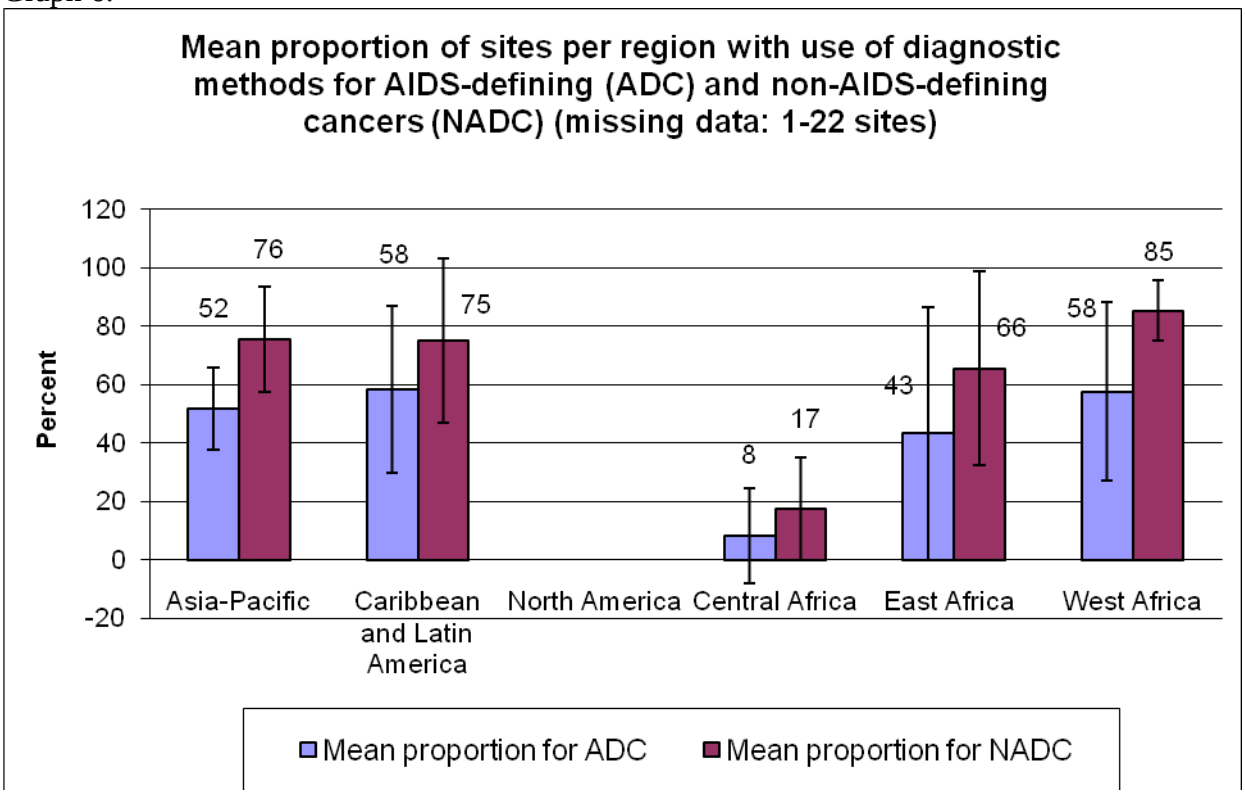
Sites which answered 'never' were categorized as sites which did not use that diagnostic method for that particular cancer type. Sites which answered 'rarely', 'sometimes,' 'often', or 'always' were categorized as sites which did use that diagnostic method for that particular cancer type.

Furthermore, the specific cancer types were divided into ADCs and NADCs. For each of the 4 diagnostic methods, the average of the proportions of sites using a particular diagnostic method for KS, NHL and cervical cancer was calculated as the mean proportion of sites using that particular diagnostic method for ADCs The same calculation was performed for each of the 4 diagnostic methods for the NADCs and renamed the mean proportion of sites using that particular diagnostic method for NADCs.

Finally, the mean proportion of sites per region which used any diagnostic method for ADCs was calculated by averaging the mean proportions for all 4 diagnostic methods for ADCs. The mean proportion of sites per region which used any diagnostic method for NADCs was calculated in a similar fashion.

Graph 6. represents the final calculated summary measures for ADCs and NADCs. None of the North American sites answered survey questions regarding the use of cancer diagnostic methods.

Graph 6.



*Black bars represent 95% confidence intervals

As seen in Graph 6, excluding the Central Africa region, nearly a majority of sites have used some method for cancer diagnosis. A low proportion of sites from Central Africa have used cancer diagnostic methods. Although not significant, there appears to be a trend among all regions for a higher proportion of sites to use diagnostic methods for NADCs.

Treatment:

Cancer treatment methods on the survey included chemotherapy, radiotherapy, surgery, hormonal therapy and palliative care. Sites were asked to estimate the percentage of the use of the various treatment methods. Graded responses were: Never, Rarely (0-25%), Sometimes (25-75%), Often (>75%) and Always (100%). Sites which answered 'rarely', 'sometimes', 'often' or 'always' were categorized as sites which used the treatment method of interest. Sites which answered 'never' were categorized as those which did not use the treatment method of interest. None of the sites from the North American region answered survey questions regarding the use of treatment methods.

Table 4 is a summary of the proportion of sites per region which were categorized as having used the particular treatment.

As seen in table 4, excluding the Central Africa region, the mean proportion of sites per region which documented the use of cancer treatment methods was over 50%. On average, 40% of the Central African sites reported the use of cancer treatment methods with the use of palliative care contributing the highest proportion.

Table 4. Proportion of sites per region which have used a treatment method

region	**Asia-Pacific**	**Caribbean and Latin America**	**Central Africa**	**East Africa**	**West Africa**
Chemotherapy	100	86	40	97	70
Radiotherapy	100	71	30	80	30
Surgery	100	71	40	90	80
Hormonal therapy	95	71	10	72	50
Palliative Care	100	86	80	93	60
Mean of all treatment methods	99 (95% CI: 97-100)	77 (95% CI: 70-84)	40 (95% CI:18-95)	86 (95% CI:77-95)	58 (95% CI: 41-75)

The Central African region lags behind the other four regions in terms of tertiary cancer care with the lowest proportion of sites reporting the use of surgery, chemotherapy, radiotherapy and hormonal therapy. The proportion of sites reporting the use of palliative care in the Central African region, however, is comparable to the other regions.

Among the African regions, the proportion of West African sites is lower compared to the East African sites in all aspects of cancer treatment. Among the middle-income sites, the Caribbean/Latin America sites lag behind the Asia-Pacific sites on all treatment variables, although this may be due to the contribution of high-income Australian sites to the Asia-Pacific region.

Discussion:

The distribution of ADCs and NADCs is similar to what has been reported in the literature. A larger proportion of sites from the Asia-Pacific and African regions reported seeing ADCs compared to NADCs among the HIV-positive cancer patients in their units. A large and comparable proportion of sites from North America and Caribbean/Latin America reported finding both ADCs and NADCs among their HIV-positive cancer patients, perhaps reflecting the availability of antiretroviral therapy since 1996 and the ensuing development of NADCs a decade and more later.

Although a significantly higher proportion of sites in East and West Africa reported ADCs compared to NADCs, a large proportion of sites from these regions also reported NADCs among cancer patients in their units (45% in West Africa and 62% in East

Africa). Central Africa reported a small proportion of sites with NADCs as the vast majority of their sites reported finding KS among their cancer patients in their units.

The predominance of ADCs in sub-Saharan Africa compared to Western countries may reflect the approximately 8-year lag in access to ART which the African countries experienced. Even now, though, as seen in our study, as scale-up of ART is in progress, a large proportion of HIV/AIDS sites in the African regions report finding NADCs among their cancer patients.

When specific cancers are examined, the largest proportion of sites for all regions report finding KS, NHL and cervical cancers among their cancer patients. Interestingly, NADCs with effective prevention strategies, such as anal, colon, breast, lung, liver and prostate are also represented among the sub-Saharan sites as well as those of the middle- and high-income regions of Asia-Pacific, Caribbean/Latin America and North America.

Not surprisingly, a larger proportion of sites from North America, Caribbean/Latin America and Asia-Pacific had available cancer-related data in their units compared to the sub-Saharan sites. Sites from the middle- and high-income regions also reported a significantly higher mean proportion of their patients with documentation of cancer-related data.

Perhaps this disparity in documentation of cancer-related information is reflective not only of a lack of documentation, but also a lack of cancer-related resources such as pathology, radiology, surgery and chemotherapy. In the case of Central Africa, despite reporting an overall low mean proportion of patients with cancer care-related data, a majority of sites were still capable of documenting cancer risk factors such as behavioral risk factors and co-infections.

One particular area of cancer care which should be addressed is the disparities in cancer screening between the middle-income regions of Asia-Pacific and Latin America and sub-Saharan Africa. Not only did the former two regions report a significantly higher mean proportion of sites which had diagnostic and screening methods available, a significantly higher proportion of sites from Asia-Pacific and Latin America compared to Africa used these methods for screening purposes.

With a large proportion of African sites, particularly East and West Africa, reporting NADCs among their HIV-infected cancer patients, cancer screening methods must be scaled up and their use for secondary prevention of cancer emphasized. In particular, in East Africa, where antiretroviral therapy is being scaled up and where antiretroviral therapy coverage is generally higher than in West and Central Africa, prevention measures must be in place to address a potential increase in NADCs among people living with HIV/AIDS.

Compared to screening methods, a relatively lower proportion of sites in Asia-Pacific and Caribbean/Latin America reported the use of diagnostic methods for ADCs and NADCs. The finding that the highest proportion of sites from all regions, except North America which did not respond, reported the use of X-ray for diagnosis of NADCs attests to the rudimentary nature of diagnostic methods in low- and middle-income regions.

This lack of valid and reliable diagnostic methodology is important since it may be lead to underreporting of NADCs and an underestimation of HIV-related malignancies during a period of intensive ART scale-up in low- and middle-income countries.

Treatment of HIV-related cancer, including surgery, chemotherapy and radiotherapy are generally available among the sites of Asia-Pacific and Caribbean/Latin America.

Among the African regions, a larger proportion of sites from East Africa compared to West Africa report having used surgery, chemotherapy and radiotherapy for treatment of HIV-related malignancies. In Central Africa, among all treatment methods, only palliative care was reported among a majority of sites.

The above findings are in keeping with a generally lower HIV prevalence in Central and West Africa compared to East and southern Africa (UNAIDS/WHO: 2009 AIDS epidemic update). However, West Africa still contains country-specific HIV epidemics and the political situation and evolving health care systems in Central African countries such as Congo, Rwanda and Burundi remain to be seen as they recover from present and past civil wars (WHO: 2009 AIDS epidemic update) .

Further studies are needed regarding the efficacy of modified chemotherapy and radiotherapy regimes which are suited to low-resource settings which do not have the capacity for highly technological treatment methods and which do not have adequate personnel and resources to address treatment-related complications.

The expansion of ART access and earlier treatment of HIV-infected patients with ART may potentially positively impact the incidence of KS and perhaps NHL in resource-poor settings without the means for chemotherapy treatment (Orem, 2004).

The main limitations of the study are the consequences of missing data. Because of the missing data, accurate statistical inferences could not be made for many of the key variables due to small sample sizes.

There were 39 sites out of a total of 134 IeDEA-participating sites (29%) which did not answer the adult cancer section of the IeDEA site assessment tool. Some of these sites were pediatric HIV/AIDS health care facilities for which the adult cancer section of the survey was irrelevant. However, some of these excluded sites may have been unable to complete the adult cancer section due to a lack of qualified personnel or lack of

information regarding cancer care and treatment. This may have resulted in an overestimation of capacity per region.

All 19 sites of the southern Africa region did not complete the cancer section. Although this does not necessarily introduce bias into the study, we lack rich information from a large region of the African continent with some of the highest HIV prevalences as well as some of the largest antiretroviral treatment programs in the world.

These southern Africa regions may differ significantly from the other African regions in terms of cancer care capacity and these differences (or similarities) may have helped inform health care policy regarding cancer care and treatment for HIV/AIDS patients in low-resource settings, particularly given the aggressive scale up of HAART in South Africa.

In addition to a number of sites which did not respond, some sites which did respond often did not answer all the questions of the cancer section. These missing data are difficult to interpret as to whether they indicate sites with or without such capacity. For example, all the sites of the North American region, most of them well-known academic institutions, did not answer key questions in the cancer diagnosis, screening and treatment sub-sections. In these cases, one can assume that these sites have such capacity but failed to answer the relevant survey questions.

The study investigators and collaborators are in the process of contacting regional directors to encourage their respective site managers to complete the survey. At the recent International AIDS conference in Vienna this summer, in addition to the objectives and study design of the project, a list of sites which had not completed the cancer section of the survey was presented.

Other limitations include the fact that data from the site survey are self-reported. Self-reported data can suffer from recall bias, particularly if estimates are made and responses given without access to documentation.

The questionnaire, although standardized and distributed to all IeDEA-participating sites, has not been validated nor tested for reliability. Internal validity may be jeopardized if survey questions do not accurately measure what was intended to be measured. In addition, questions may not have been interpreted or answered in a standard way across settings and different languages.

External validity may also be questioned since a sample of sites may not be representative of an entire region nor of the country, particularly since over 50% of the sites self-reported as academic medical institutions. Particularly in low-resource settings, academic hospitals are not representative of the majority of HIV/AIDS health care facilities nor of the poor and marginalized HIV-positive population.

Despite these limitations, the many strengths of the study allow these preliminary results to be explored further. The main strength of the study is the ability to pool data from multiple sites around the world into a large single database, allowing for site-level and regional comparisons which have been lacking in the HIV/AIDS epidemiological literature. Because of the nature of the IeDEA consortium with established levels of management, this pooling of data can be done in a cost-effective manner.

In addition, due to the large sample size and the variety of participating sites, policy recommendations based on the results can be made on a population level to improve the care and treatment of HIV/AIDS patients with cancer and to scale up cancer screening for HIV-positive persons, particularly in low-resource settings where cancer usually presents with highly morbid late-stage disease.

Another strength of the study is the use of a standardized questionnaire which was distributed to all IeDEA participating sites. Although interpretation and answering of survey questions may vary across sites and regions, the use of a single survey with the same variables allows for improved data quality which in turn allows for more reliable comparisons among regions.

The adult cancer section of the survey has a breadth and depth of questions covering all aspects of capacity along the cancer care continuum from primary prevention through questions regarding collection of data on behavioral risk factors and co-infections to secondary prevention through questions on the availability of cancer screening methods to tertiary prevention through questions regarding the use of cancer treatment methods. Particularly for low-resource settings, this allows for comments regarding distribution of scarce resources among the three prevention categories.

Recommendations;

With the large scale-up of antiretroviral treatment in low- and middle-income countries, particularly in sub-Saharan Africa, and the emerging epidemiological evidence of NADCs in these regions, strategies for increasing the capacity to document, screen, diagnose and treat HIV-related malignancies must be established.

An increase in capacity does not necessarily entail costly maneuvers. For example, even though the majority of resource-poor sites in the Central African region did not have cancer-related data, still, 70-90% of their patients had documentation of behavioral risk factors and co-infections. This level of data collection should be extended to all areas of cancer care, whether such care is available or not, in order to accurately record gaps in resources along the cancer care continuum.

In addition, documentation of cancer risk factors can help tailor site-level primary prevention efforts, such as smoking cessation, alcohol and drug use and risky sexual behavior.

Cost-effective screening methods, such as VIA for cervical cancer and fecal occult blood tests (FOBT) for colon cancer are available and can be scaled up for HIV-infected patients, even in low-resource, rural settings and particularly in sub-Saharan Africa and Asia where invasive cervical cancer is the most common malignancy in women regardless of HIV status.

Ultrasounds for screening of hepatocellular cancer in HIV-positive patients may not be feasible in low-resource settings, but Hepatitis B vaccination can certainly be increased as has been successfully implemented in China. Research on the effectiveness of the HPV vaccine for primary prevention of cervical cancer in low- and middle-income countries can proceed alongside introduction of the vaccine in clinical settings.

Given the uncertainty of the effect of HAART on long-term partial immune suppression and the persistence of oncogenic viruses, Hepatitis B and HPV vaccination are all that more important for people living with HIV/AIDS.

Capital and human resources for diagnostic cancer methods, particularly biopsy and pathology, should be increased in order to avoid under ascertainment of HIV-related malignancies and to accurately report epidemiological trends of ADCs and NADCs in low- and middle-income countries. Global consortiums such as IeDEA can establish standardized case reporting systems which will allow for valid comparisons among different HIV-positive cohorts (Sasco, 2010). In addition, sentinel sites can be established in low-resource settings not only for data collection, but also as sites for capacity-building in the methods and training of cancer diagnosis in HIV-positive patients.

Scale-up of cancer treatment methods in low- and middle-income countries should not include complicated chemotherapy regimens. On the contrary, standard of care regimens in high-income countries must be effectively adapted to low-resource settings to allow for a paucity of trained oncologists and supportive measures to care for treatment-related complications. Inexpensive but standardized and effective palliative care regimens should be routine in low-resource settings which often care for patients presenting with advanced stage and incurable cancers.

Implementation of early initiation of ART for HIV-positive individuals in low-resource settings may have a large impact on ADCs such as KS and perhaps NHL.

In addition, national efforts must be underway to improve and expand HIV surveillance systems and population-based cancer registries to allow for large linkage studies which will result in more reliable epidemiological data on HIV-related cancers, as has been done in North America, Europe and Australia and as has been shown to be feasible in low-income countries such as Uganda. Valid epidemiological evidence on ADCs and NADCs in low- and middle-income countries will lead to more targeted and effective cancer prevention and treatment strategies for people living with HIV/AIDS.

Appendix I. International epidemiologic Databases to Evaluate AIDS (IeDEA) Site Assessment Tool

IeDEA
International epidemiologic Databases to Evaluate AIDS

Site Name*_____

Address: _____
street

_____
city/district state/province postal code

_____
country

If the care and treatment program at this facility part of a larger network (e.g., AMPATH, MTCT-Plus, FACES, etc), please list the network name here: _____

	Name	Contact Number	Email
Primary contact			
Data manager			

CANCER SECTION:

D. CANCER. Please answer these cancer-related questions about HIV patients treated at this facility. "UNIT" refers to the cancer care location for persons with HIV.

No.	QUESTIONS AND INSTRUCTIONS	RESPONSES	SKIPS
	Questions D01—D10 are about case ascertainment of cancer cases, including sources of cancer data, their validity, and completeness.		
D01	How would you describe your unit? Circle the number(s) for the best response(s).	Individual medical clinic ☐ Group of medical clinics ☐ Center from a multi-site study ☐ Academic hospital ☐ Other hospital (local, non teaching, etc.) ☐ Other, Please describe: _____	
D02	**Please indicate the type of patients seen in your unit by choosing the approximate percentage of all patients seen in your unit for each category listed below:**		

HIV patients	☐0%	☐ 1-25%	☐ 26-49%	☐ 50-75%	☐> 75%
Cancer patients	☐0%	☐ 1-25%	☐ 26-49%	☐ 50-75%	☐> 75%
Infectious Disease	☐0%	☐ 1-25%	☐ 26-49%	☐ 50-75%	☐> 75%
Surgical patients	☐0%	☐ 1-25%	☐ 26-49%	☐ 50-75%	☐> 75%
Other: _____	☐0%	☐ 1-25%	☐ 26-49%	☐ 50-75%	☐> 75%
Other: _____	☐0%	☐ 1-25%	☐ 26-49%	☐ 50-75%	☐> 75%
Other: _____	☐0%	☐ 1-25%	☐ 26-49%	☐ 50-75%	☐> 75%
Other: _____	☐0%	☐ 1-25%	☐ 26-49%	☐ 50-75%	☐> 75%
Other: _____	☐0%	☐ 1-25%	☐ 26-49%	☐ 50-75%	☐> 75%

D03	What is the earliest year your unit begin collecting cancer data? Specify year.	*Specify year below.* _____ Unknown	9
D04	What is the most recent year for which your unit collected cancer data? Specify year.	*Specify year below.* _____ Unknown	9

D05 **A list of several common cancer types in HIV-patients is provided in the table below. Please estimate the % each cancer type is seen in your unit among all cancers diagnosed. Space is provided at the end of the table if needed for additional cancer types that are common to HIV-infected patients in your unit.**

Estimate the percentage that each of the following cancer types is found among all people with cancer in your unit. If needed, list other cancer types commonly seen in your unit. (Select one answer that most applies for each type of cancer):					
Anal	☐0%	☐1-5%	☐6-20%	☐20-75%	☐> 75%
Breast	☐0%	☐1-5%	☐6-20%	☐20-75%	☐> 75%
Cervix	☐0%	☐1-5%	☐6-20%	☐20-75%	☐> 75%
Colorectal	☐0%	☐1-5%	☐6-20%	☐20-75%	☐> 75%
Head and Neck	☐0%	☐1-5%	☐6-20%	☐20-75%	☐> 75%
Hodgkin's Disease	☐0%	☐1-5%	☐6-20%	☐20-75%	☐> 75%
Non-Hodgkin's Lymphoma	☐0%	☐1-5%	☐6-20%	☐20-75%	☐> 75%
Kaposi's Sarcoma	☐0%	☐1-5%	☐6-20%	☐20-75%	☐> 75%
Leukemia (Bone Marrow)	☐0%	☐1-5%	☐6-20%	☐20-75%	☐> 75%
Liver	☐0%	☐1-5%	☐6-20%	☐20-75%	☐> 75%
Lung	☐0%	☐1-5%	☐6-20%	☐20-75%	☐> 75%
Penis	☐0%	☐1-5%	☐6-20%	☐20-75%	☐> 75%
Prostate	☐0%	☐1-5%	☐6-20%	☐20-75%	☐> 75%
Stomach	☐0%	☐1-5%	☐6-20%	☐20-75%	☐> 75%
Other: _____	☐0%	☐1-5%	☐6-20%	☐20-75%	☐> 75%
Other: _____	☐0%	☐1-5%	☐6-20%	☐20-75%	☐> 75%
Other: _____	☐0%	☐1-5%	☐6-20%	☐20-75%	☐> 75%
Other: _____	☐0%	☐1-5%	☐6-20%	☐20-75%	☐> 75%
Other: _____	☐0%	☐1-5%	☐6-20%	☐20-75%	☐> 75%

D06 **Estimate the percentage (%) of the use of tissue sampling (biopsy or fine needle aspiration) in the diagnosis or staging of each of the following cancer types in your unit. If needed, list other cancer types commonly seen in your unit. Space is provided at the end of the table for a listing of additional cancer types that are common to HIV-infected patients in your unit.**

Estimate the percentage that each of the following cancer types is found among all people with cancer in your unit. If needed, list other cancer types commonly seen in your unit. (select one answer that most applies for each cancer type):					
Anal	☐0%	☐ 1-5%	☐ 6-20%	☐ 20-75%	☐> 75%
Breast	☐0%	☐ 1-5%	☐ 6-20%	☐ 20-75%	☐> 75%
Cervix	☐0%	☐ 1-5%	☐ 6-20%	☐ 20-75%	☐> 75%
Colorectal	☐0%	☐ 1-5%	☐ 6-20%	☐ 20-75%	☐> 75%
Head and Neck	☐0%	☐ 1-5%	☐ 6-20%	☐ 20-75%	☐> 75%
Hodgkin's Disease	☐0%	☐ 1-5%	☐ 6-20%	☐ 20-75%	☐> 75%
Non-Hodgkin's Lymphoma	☐0%	☐ 1-5%	☐ 6-20%	☐ 20-75%	☐> 75%
Kaposi's Sarcoma	☐0%	☐ 1-5%	☐ 6-20%	☐ 20-75%	☐> 75%
Leukemia (Bone Marrow)	☐0%	☐ 1-5%	☐ 6-20%	☐ 20-75%	☐> 75%
Liver	☐0%	☐ 1-5%	☐ 6-20%	☐ 20-75%	☐> 75%
Lung	☐0%	☐ 1-5%	☐ 6-20%	☐ 20-75%	☐> 75%
Penis	☐0%	☐ 1-5%	☐ 6-20%	☐ 20-75%	☐> 75%
Prostate	☐0%	☐ 1-5%	☐ 6-20%	☐ 20-75%	☐> 75%
Stomach	☐0%	☐ 1-5%	☐ 6-20%	☐ 20-75%	☐> 75%
Other:	☐0%	☐ 1-5%	☐ 6-20%	☐ 20-75%	☐> 75%
Other: ______	☐0%	☐ 1-5%	☐ 6-20%	☐ 20-75%	☐> 75%
Other:	☐0%	☐ 1-5%	☐ 6-20%	☐ 20-75%	☐> 75%
Other: ______	☐0%	☐ 1-5%	☐ 6-20%	☐ 20-75%	☐> 75%
Other:	☐0%	☐ 1-5%	☐ 6-20%	☐ 20-75%	☐> 75%

D07

Estimate the percentage of the use of <u>radiograph (X-ray)</u> in the diagnosis or staging of each of the following cancer types in your unit. If needed, list other cancer types commonly seen in your unit. (Select one answer that most applies for each cancer type):					
Breast	☐Never	☐Rarely (0-25%)	☐Sometimes (25-75%)	☐Often (>75-99%)	☐Always
Colorectal	☐Never	☐Rarely (0-25%)	☐Sometimes (25-75%)	☐Often (>75-99%)	☐Always
Head and Neck	☐Never	☐Rarely (0-25%)	☐Sometimes (25-75%)	☐Often (>75-99%)	☐Always
Hodgkin's Disease	☐Never	☐Rarely (0-25%)	☐Sometimes (25-75%)	☐Often (>75-99%)	☐Always
Non-Hodgkin's Lymphoma	☐Never	☐Rarely (0-25%)	☐Sometimes (25-75%)	☐Often (>75-99%)	☐Always
Liver	☐Never	☐Rarely (0-25%)	☐Sometimes (25-75%)	☐Often (>75-99%)	☐Always
Lung	☐Never	☐Rarely (0-25%)	☐Sometimes (25-75%)	☐Often (>75-99%)	☐Always
Stomach	☐Never	☐Rarely (0-25%)	☐Sometimes (25-75%)	☐Often (>75-99%)	☐Always
Other: ______	☐Never	☐Rarely (0-25%)	☐Sometimes (25-75%)	☐Often (>75-99%)	☐Always
Other:	☐Never	☐Rarely (0-25%)	☐Sometimes (25-75%)	☐Often (>75-99%)	☐Always
Other: ______	☐Never	☐Rarely (0-25%)	☐Sometimes (25-75%)	☐Often (>75-99%)	☐Always
Other: ______	☐Never	☐Rarely (0-25%)	☐Sometimes (25-75%)	☐Often (>75-99%)	☐Always
Other: ______	☐Never	☐Rarely (0-25%)	☐Sometimes (25-75%)	☐Often (>75-99%)	☐Always

D08

Estimate the percentage of the use of <u>radiograph (ultrasound or computerized tomography)</u> in the diagnosis or staging of each of the following cancer types in your unit. If needed, list other cancer types commonly seen in your unit. (Select one answer that most applies for each cancer type):

Breast	☐Never	☐Rarely (0-25%)	☐Sometimes (25-75%)	☐Often (>75-99%)	☐Always
Cervix	☐Never	☐Rarely (0-25%)	☐Sometimes (25-75%)	☐Often (> 75-99%)	☐Always
Colorectal	☐Never	☐Rarely (0-25%)	☐Sometimes (25-75%)	☐Often (> 75-99%)	☐Always
Head and Neck	☐Never	☐Rarely (0-25%)	☐Sometimes (25-75%)	☐Often (> 75-99%)	☐Always
Hodgkin's Disease	☐Never	☐Rarely (0-25%)	☐Sometimes (25-75%)	☐Often (> 75-99%)	☐Always
Non-Hodgkin's Lymphoma	☐Never	☐Rarely (0-25%)	☐Sometimes (25-75%)	☐Often (> 75-99%)	☐Always
Liver	☐Never	☐Rarely (0-25%)	☐Sometimes (25-75%)	☐Often (> 75-99%)	☐Always
Lung	☐Never	☐Rarely (0-25%)	☐Sometimes (25-75%)	☐Often (> 75-99%)	☐Always
Prostate	☐Never	☐Rarely (0-25%)	☐Sometimes (25-75%)	☐Often (> 75-99%)	☐Always
Stomach	☐Never	☐Rarely (0-25%)	☐Sometimes (25-75%)	☐Often (> 75-99%)	☐Always
Other: ____________	☐Never	☐Rarely (0-25%)	☐Sometimes (25-75%)	☐Often (> 75-99%)	☐Always
Other: ____________	☐Never	☐Rarely (0-25%)	☐Sometimes (25-75%)	☐Often (> 75-99%)	☐Always
Other: ____________	☐Never	☐Rarely (0-25%)	☐Sometimes (25-75%)	☐Often (> 75-99%)	☐Always
Other: ____________	☐Never	☐Rarely (0-25%)	☐Sometimes (25-75%)	☐Often (> 75-99%)	☐Always
Other: ____________	☐Never	☐Rarely (0-25%)	☐Sometimes (25-75%)	☐Often (> 75-99%)	☐Always

D09

Estimate the percentage of the use of <u>endoscopic procedures (e.g., upper aerodigestive endoscopy, colonoscopy, cystoscopy, bronchoscopy)</u> in the diagnosis or staging of each of the following cancer types in your unit. If needed, list other cancer types commonly seen in your unit. (Select one answer that most applies for each cancer type):

Anal	☐Never	☐Rarely (0-25%)	☐Sometimes (25-75%)	☐Often (> 75-99%)	☐Always
Cervix	☐Never	☐Rarely (0-25%)	☐Sometimes (25-75%)	☐Often (> 75-99%)	☐Always
Colorectal	☐Never	☐Rarely (0-25%)	☐Sometimes (25-75%)	☐Often (> 75-99%)	☐Always
Head and Neck	☐Never	☐Rarely (0-25%)	☐Sometimes (25-75%)	☐Often (> 75-99%)	☐Always
Lung	☐Never	☐Rarely (0-25%)	☐Sometimes (25-75%)	☐Often (> 75-99%)	☐Always
Stomach	☐Never	☐Rarely (0-25%)	☐Sometimes (25-75%)	☐Often (> 75-99%)	☐Always
Other: ____________	☐Never	☐Rarely (0-25%)	☐Sometimes (25-75%)	☐Often (> 75-99%)	☐Always
Other: ____________	☐Never	☐Rarely (0-25%)	☐Sometimes (25-75%)	☐Often (> 75-99%)	☐Always
Other: ____________	☐Never	☐Rarely (0-25%)	☐Sometimes (25-75%)	☐Often (> 75-99%)	☐Always
Other: ____________	☐Never	☐Rarely (0-25%)	☐Sometimes (25-75%)	☐Often (> 75-99%)	☐Always
Other: ____________	☐Never	☐Rarely (0-25%)	☐Sometimes (25-75%)	☐Often (> 75-99%)	☐Always

D10

Please estimate the percentage of patients in your unit for whom you collect the following information (0- 100%) and in which form is this information stored (check all that apply):		
Information on:	**% of patients in your unit for whom you collect this information (0- 100%)**	**In which form is this information stored (check all that apply):**
Cancer diagnoses (as Yes/No)		☐ Paper medical chart kept by patient ☐ Paper medical chart kept by unit ☐ Electronic data
Specific cancer types		☐ Paper medical chart kept by patient ☐ Paper medical chart kept by unit ☐ Electronic data
Histopathology		☐ Paper medical chart kept by patient ☐ Paper medical chart kept by unit ☐ Electronic data
Radiologic information		☐ Paper medical chart kept by patient ☐ Paper medical chart kept by unit ☐ Electronic data
Computerized tomography		☐ Paper medical chart kept by patient ☐ Paper medical chart kept by unit ☐ Electronic data
Endoscopic information		☐ Paper medical chart kept by patient ☐ Paper medical chart kept by unit ☐ Electronic data

Questions D11- D13 are about common risk factors for cancer, including behaviors such as smoking, alcohol use, sexual behavior and co-infections.

D11 Please check the boxes in the table below for risk factors which may be collected within your unit.

Behavior/Other risk factors	Do you collect any information for this behavior?	If yes,do you normally ask about the frequency and/or quantity?
Cigarette smoking	☐Yes; ☐ No	☐Yes; ☐ No
Pipe smoking	☐Yes; ☐ No	☐Yes; ☐ No
Tobacco chewing	☐Yes; ☐ No	☐Yes; ☐ No
Wood burning stove	☐Yes; ☐ No	☐Yes; ☐ No
Alcohol consumption	☐Yes; ☐ No	☐Yes; ☐ No
Lifetime or recent # of sex partners	☐Yes; ☐ No	☐Yes; ☐ No
Same sex or opposite sex partner preference	☐Yes; ☐ No	
Snuff	☐Yes; ☐ No	☐Yes; ☐ No
Illicit/illegal injection drug use	☐Yes; ☐ No	☐Yes; ☐ No
Marijuana/cannabis	☐Yes; ☐ No	☐Yes; ☐ No
Illicit/illegal non-injection drug use	☐Yes; ☐ No	☐Yes; ☐ No
Family history of cancer	☐Yes; ☐ No	

D12 **Please check the boxes in the table below for co-infections/laboratory measures which may be collected within your unit.**

Co-infection or laboratory measure	Do you collect any information for this co-infection or laboratory measure?	If yes, what is the method of diagnoses (select all that apply):
KSHV	☐Yes; ☐ No	☐Serology ☐ PCR
Hepatitis B	☐Yes; ☐ No	☐Serology ☐ PCR
Hepatitis C	☐Yes; ☐ No	☐Serology ☐ PCR
Epstein-Bar virus	☐Yes; ☐ No	☐Serology ☐ PCR
HPV	☐Yes; ☐ No	☐Serology ☐ PCR
HTLV-1	☐Yes; ☐ No	☐Serology ☐ PCR
H. pylori	☐Yes; ☐ No	☐Serology ☐ PCR
Malaria	☐Yes; ☐ No	☐Serology ☐ PCR
TB	☐Yes; ☐ No	

D13

Please estimate the percentage of patients in your unit for whom you collect the following information (0- 100%) and in which form is this information stored (check all that apply):		
Information on:	**% of patients in your unit for whom you collect this information (0- 100%)**	**In which form is this information stored (check all that apply):**
Behavior/Other risk factors		☐ Paper medical chart kept by patient ☐ Paper medical chart kept by unit ☐ Electronic data
Co-infections		☐ Paper medical chart kept by patient ☐ Paper medical chart kept by unit ☐ Electronic data
Laboratory measures		☐ Paper medical chart kept by patient ☐ Paper medical chart kept by unit ☐ Electronic data

	Is this diagnostic method used for cancer screening in your unit?	If diagnostic method is available, indicate the main reason someone may not use this method. *Please check the box beside all that apply.*	
D14	**Mammograms** ☐ Method not available ☐ Available, used for diagnosis only ☐ Available, used for diagnosis and screening	☐ High cost to the patient ☐ Logistics (e.g. patient lives far away from closest facility.) ☐ High waiting time to receive test ☐ Other_____ ☐ Don't Know ☐ NA	
D15	**Prostate-specific antigen** ☐ Method not available ☐ Available, used for diagnosis only ☐ Available, used for diagnosis and screening	☐ High cost to the patient ☐ Logistics (e.g. patient lives far away from closest facility.) ☐ High waiting time to receive test ☐ Other_____ ☐ Don't Know ☐ NA	

	Is this diagnostic method used for cancer screening in your unit?	If diagnostic method is available, indicate the main reason someone may not use this method. *Please check the box beside all that apply.*	
D16	**Cervical Pap smear** ☐ Method not available ☐ Available, used for diagnosis only ☐ Available, used for diagnosis and screening	☐ High cost to the patient ☐ Logistics (e.g. patient lives far away from closest facility.) ☐ High waiting time to receive test ☐ Other_____ ☐ Don't Know ☐ NA	
D17	**Gynecologic exam (visual inspection only with ascetic acid)** ☐ Method not available ☐ Available, used for diagnosis only ☐ Available, used for diagnosis and screening	☐ High cost to the patient ☐ Logistics (e.g. patient lives far away from closest facility.) ☐ High waiting time to receive test ☐ Other_____ ☐ Don't Know ☐ NA	
D18	**Anal Pap smear** ☐ Method not available ☐ Available, used for diagnosis only ☐ Available, used for diagnosis and screening	☐ High cost to the patient ☐ Logistics (e.g. patient lives far away from closest facility.) ☐ High waiting time to receive test ☐ Other_____ ☐ Don't Know ☐ NA	
D19	**Ultra sound** ☐ Method not available ☐ Available, used for diagnosis only ☐ Available, used for diagnosis and screening	☐ High cost to the patient ☐ Logistics (e.g. patient lives far away from closest facility.) ☐ High waiting time to receive test ☐ Other_____ ☐ Don't Know ☐ NA	
D20	**Occult blood in stool** ☐ Method not available ☐ Available, used for diagnosis only ☐ Available, used for diagnosis and screening	☐ High cost to the patient ☐ Logistics (e.g. patient lives far away from closest facility.) ☐ High waiting time to receive test ☐ Other_____ ☐ Don't Know ☐ NA	
D21	**Colonoscopy** ☐ Method not available ☐ Available, used for diagnosis only ☐ Available, used for diagnosis and screening	☐ High cost to the patient ☐ Logistics (e.g. patient lives far away from closest facility.) ☐ High waiting time to receive test ☐ Other_____ ☐ Don't Know ☐ NA	

D22	**Chest x-ray** ☐ Method not available ☐ Available, used for diagnosis only ☐ Available, used for diagnosis and screening	☐ High cost to the patient ☐ Logistics (e.g. patient lives far away from closest facility.) ☐ High waiting time to receive test ☐ Other_____ ☐ Don't Know ☐ NA	
D23	**Alpha-fetoprotein blood test** ☐ Method not available ☐ Available, used for diagnosis only ☐ Available, used for diagnosis and screening	High cost to the patient ☐ Logistics (e.g. patient lives far away from closest facility.) ☐ High waiting time to receive test ☐ Other_____ ☐ Don't Know ☐ NA	
D24	Are data regarding these diagnostic methods available for your unit? *Please circle the number of the best response.*	☐Yes ☐ No	

	Questions D25-D41 refer to available data on cancer treatments and outcomes among your cohort members. ***Please check the box next to the best response.***		
D25	Are data regarding chemotherapy available for your unit?	☐Yes ☐ No	
D26	Are data regarding radiotherapy available for your unit?	☐Yes ☐ No	
D27	Are data regarding surgery available for your unit?	☐Yes ☐ No	
D28	Are data regarding comfort care (e.g., antiemetic or other supportive therapy) available for your unit?	☐Yes ☐ No	
D29	Are data regarding palliative care (e.g., analgesic therapy and other treatment modalities when cure can no longer be attempted) available for your unit?	☐Yes ☐ No	
D30	Are data regarding hormonal therapy available for treatment of prostate and breast cancer available for your unit?	☐Yes ☐ No	
	Please rate how strongly you agree or disagree with following statements:		
D31	Estimate the percentage of the use of chemotherapy for cancer patients that need it.	☐ Never ☐ Rarely (0<25%) ☐ Sometimes (25%<75%) ☐ Often (75% > but not always) ☐ Always (100%)	

D32	Please select the main reason someone with cancer may not receive chemotherapy if they need it.	☐ High cost to the patient ☐ Logistics (e.g. patient lives far away from closest facility.) ☐ High waiting time to receive test ☐ Other_____ ☐ Don't Know	
D33	Estimate the percentage of the use of radiotherapy for cancer patients that need it.	☐ Never ☐ Rarely (0<25%) ☐ Sometimes (25%<75%) ☐ Often (75% > but not always) ☐ Always (100%)	
D34	Please select the main reason someone with cancer may not receive radiotherapy if they need it.	☐ High cost to the patient ☐ Logistics (e.g. patient lives far away from closest facility.) ☐ High waiting time to receive test ☐ Other_____ ☐ Don't Know	
D35	Estimate the percentage of the use of surgery for cancer patients that need it.	☐ Never ☐ Rarely (0<25%) ☐ Sometimes (25%<75%) ☐ Often (75% > but not always) ☐ Always (100%)	
D36	Please select the main reason someone with cancer may not receive surgery if they need it.	☐ High cost to the patient ☐ Logistics (e.g. patient lives far away from closest facility.) ☐ High waiting time to receive test ☐ Other_____ ☐ Don't Know	
D37	Estimate the percentage of the use of palliative care for cancer patients that need it.	☐ Never ☐ Rarely (0<25%) ☐ Sometimes (25%<75%) ☐ Often (75% > but not always) ☐ Always (100%)	
D38	Please select the main reason someone with cancer may not receive palliative care if they need it.	☐ High cost to the patient ☐ Logistics (e.g. patient lives far away from closest facility.) ☐ High waiting time to receive test ☐ Other_____ ☐ Don't Know	
D39	Estimate the percentage of the use of hormonal therapy for all prostate and breast cancer patients that need it.	☐ Never ☐ Rarely (0<25%) ☐ Sometimes (25%<75%) ☐ Often (75% > but not always) ☐ Always (100%)	
D40	Please select the main reason someone with prostate or breast cancer may not receive hormal therapy if they need it.	☐ High cost to the patient ☐ Logistics (e.g. patient lives far away from closest facility.) ☐ High waiting time to receive test ☐ Other_____ ☐ Don't Know	

D41

Please estimate the percentage of patients in your unit for whom you collect the following information (0-100%) and in which form is this information stored (check all that apply):

Information on:	% of patients in your unit for whom you collect this information (0- 100%)	In which form is this information stored (check all that apply):
Surgery		☐ Paper medical chart kept by patient ☐ Paper medical chart kept by unit ☐ Electronic data
Chemotherapy		☐ Paper medical chart kept by patient ☐ Paper medical chart kept by unit ☐ Electronic data
Radiotherapy		☐ Paper medical chart kept by patient ☐ Paper medical chart kept by unit ☐ Electronic data
Hormonal therapy		☐ Paper medical chart kept by patient ☐ Paper medical chart kept by unit ☐ Electronic data
Comfort care		☐ Paper medical chart kept by patient ☐ Paper medical chart kept by unit ☐ Electronic data
Palliative care		☐ Paper medical chart kept by patient ☐ Paper medical chart kept by unit ☐ Electronic data

	Questions D42-D44 relate to the collection of mortality data on cancer patients in your facility		
D42	Are data available for date of death for cancer patients in your unit?	*Please check the box next to the best response.* ☐ Yes ☐ No	
D43	Are data available for cause of death for cancer patients in your unit?	*Please check the box next to the best response.* ☐ Yes ☐ No	
D44	Please indicate sources of mortality data from the following list (circle the number(s) for all that apply):	☐ Medical records ☐ Administrative databases ☐ Death certificates ☐ National mortality databases ☐ Other. Please describe: _____	

Appendix 2. List of 95 sites whose responses to adult cancer section of IeDEA site assessment tool were used for analysis

Site ID	Site name	Site city	Site Country
Asia-Pacific region			
AHOD	The Alfred Hospital	Melbourne	Australia
AP01	Beijing Ditan Hospital	Beijing	China
AP02	Chiang Mai University - Pediatrics	Muang	Thailand
AP03	Chiang Rai Regional Hospital	Muang	Thailand
AP05	HIV-NAT, Thai Red Cross AIDS Research Centre - Adult		Thailand
AP06	Hospital Likas	Kota Kinabalu	Malaysia
AP08	Institute of Infectious Diseases	Pune	India
AP09	International Medical Center of Japan	Shinjuku-ku	Japan
AP10	Khon Kaen University	Muang	Thailand
AP11	National Centre for HIV/AIDS, Dermatology and STD, Social Health Clinic (NCHADs)	Russey Keov	Cambodia
AP12	National Yang-Ming University	Taipei	Taiwan
AP13	Pediatric Institute, Hospital Kuala Lumpur	Wilayah	Malaysia
AP15	Queen Elizabeth Hospital	Hong Kong SAR	China
AP16	Ramathibodi Hospital	Bangkok	Thailand
AP17	Research Institute for Tropical Medicine	Muntinlupa City	Philippines
AP18	Sanglah Hospital	Denpasar	Indonesia
AP19	Siriraj Hospital, Mahidol University		Thailand
AP20	Sungai Buloh Hospital	Selangor	Malaysia
AP21	Tan Tock Seng Hospital	Tan Tock Seng	Singapore
AP22	University Malaya Medical Centre	Kuala Lumpur	Malaysia
AP23	Yonsei University College of Medicine	Seoul	Korea
AP25	Ching Mai University - Adult	Maug	Thailand
AP27	Cipto Mangunkusumo General Hospital - Adult	Central Jakarta	Indonesia
Database)	Gold Coast Sexual Health Clinic	Miami	Australia
RPA	RPA Sexual Health	Camperdown	Australia
St Vincents	St Vincent's Hospital, Sydney	Darlinghurst	Australia
Latin America region			
CCASA01	Argentina	Buenos Aires	Argentina
CCASA02	Brazil	Rio de Janeiro	Brazil
CCASA03	Chile	Santiago	Chile
CCASA04	Haiti	Port-au-Prince	Haiti
CCASA05	Honduras	Tegucigalpa	Honduras

CCASA06	Instituto Nacional de Ciencias MÃ©dicas y NutriciÃ³n, Salvador ZubirÃ¡n	Tlalpan	Mexico
CCASA07	Peru	San Martin de Porres	Peru
Central Africa region			
CAE01	LimbÃ© Provincial Hospital in Cameroon	Limbe	Cameroon
CAF01	AmoCongo-Kasavubu	Kinshasa	Congo
CAF02	AmoCongo-Ndjili	Kinshasa	Congo
CAF03	AmoCongo-Ozone	Kinshasa	Congo
CAF04	AmoCongo-Kenya	Lubumbashi	Congo
CAF05	AmoCongo-Tabacongo	Lubumbashi	Congo
CAF06	AmoCongo-Matadi	Matadi	Congo
CAF07	Military Hospital of YaoundÃ©	Yaounde	Cameroon
CAF08	Hopital General de YaoundÃ©	Yaounde	Cameroon
CAF10	Burundi CNR-Adult	Bujumbura	Burundi
East Africa region			
EA01	Chulaimbo Sub District Hospital	Kisumu West	Kenya
EA02	Pandipieri	Kisumu	Kenya
EA03	Family Health Options Kenya (Kisumu)	Kisumu East	Kenya
EA04	Moi Teaching and Referral Hospital	Eldoret	Kenya
EA05	Mt. Elgon	Mt. Elgon	Kenya
EA06	Kabarnet District Hospital	Baringo	Kenya
EA07	Iten	Keiyo	Kenya
EA08	Teso District Hospital	Teso	Kenya
EA09	Webuye District Hospital		Kenya
EA10	Khunyangu Sub District Hospital	Busia	Kenya
EA11	Turbo Health Centre	Uasin Gishu	Kenya
EA12	Amukura	South Teso	Kenya
EA13	Busia District Hospital	Busia	Kenya
EA14	Uasin Gishu District Hospital	Uasin Gishu	Kenya
EA15	Burnt Forest AMPATH Clinic	Eldoret East	Kenya
EA16	Mosoriot Health Centre	Nandi North	Kenya
EA17	Kitale District Hospital	Kitale	Kenya
EA18	Kapenguria District Hospital	West Pokot	Kenya
EA19	Lumumba	Kisumu	Kenya
EA20	Tuungane Youth Centre	Kisumu	Kenya
EA21	Port Victoria District Hospital	Bunyala	Kenya
EA22	Naitiri Health Centre	Bungoma North	Kenya
EA23	New Nyanza Provincial Hospital	Kisumu	Kenya

EA27	Ocean Road Cancer Institute(ORCI)	Kala	Tanzania
EA28	Tumbi Special Hospital CTC	Kibaha Coast	Tanzania
EA29	Masaka Healthcare Centre	Masaka	Uganda
EA30	Mujha Care Ltd	Kampala	Uganda
EA31	Mbale Regional Hospital	Mbale	Uganda
EA32	Mbarara Regional Referral Hospital - Mbarara University, Immune Suppression Syndrome Clinic	Mbarara	Uganda
EA34	Infectious Disease Institute (IDI)	Kampala	Uganda
North America region			
NA_ACCORD01	Case Western Reserve University	Cleveland	USA
NA_ACCORD02	Johns Hopkins University	Baltimore	US
NA_ACCORD04	Southern Alberta Cohort	Calgary	CANADA
NA_ACCORD05	University of Alabama at Birmingham	Birmingham	USA
NA_ACCORD06	University of North Carolina	Chapel Hill	USA
NA_ACCORD07	University of Washington	Seattle	USA
NA_ACCORD08	Vanderbilt University	Nashville	USA
West Africa region			
WA01	SMIT Abidjan	Abidjan	Cote d'Ivoire
WA02	CHU Yopougon	Abidjan	Cote d'Ivoire
WA04	Centre mÃ©dical de suivi des donneurs de sang (CMSDS)	Abidjan	Cote d'Ivoire
WA05	MTCT PLUS	Abidjan	Cote d'Ivoire
WA06	CEPREF	Abidjan	Cote d'Ivoire
WA07	CENTRE HOSPITALIER UNIVERSITAIRE PEDIATRIQUE CHARLES DE GAULLE (CHUP-CDG)	OUAGADOUGOU	Burkino Faso
WA08	CENTRE INTEGRE DE RECHERCHES BIOCLINIQUE D'ABIDJAN (CIRBA)	ABIDJAN	Cote d'Ivoire
WA09	CENTRE DE RECHERCHE CLINIQUE ET DE FORMATION (CRCF)	DAKAR	Senegal
WA10	UNIVERSITY OF ABUJA TEACHING HOSPITAL (UATH)	GWAGWALADA	Nigeria
WA13	CENTRE DE PRISE EN CHARGE DU VIH HOPITAL DU POINT G	BAMAKO	Mali
WA15	CENTRE NATIONAL HOSPITALIER UNIVERSITAIRE HKM	COTONOU	Benin
WA16	UNIVERSITY OF BENIN TEACHING HOSPITAL	Benin City	Nigeria
WA17	GenitoUrinary Medicine Clinic, Medical Research Council (UK) Laboratories	Fajara	Gambia
WA18	Gabriel TourÃ©	Bamako	Mali
WA21	CNHU/HKM	COTONOU	Benin

Appendix 3. List of 39 sites which did not complete adult cancer section of IeDEA site assessment tool

Site ID	Site name	Site city	Site country
Asia-Pacific			
AP04	Cipto Mangunkusumo General Hospital - Pediatric	Jakarta	Indonesia
AP07	Hospital Raja Perempuan Zainab II	Kota Bharu	Malaysia
AP14	Penang Hospital		
AP26	HIV-NAT, Thai Red Cross AIDS Research Centre - Pediatric		Thailand
Central Africa			
CAE02	Kibuye Hospital		
CAE03	Muhima Hospital		
CAE04	RWISA		
CAF09	Children's Hospital of YaoundÃ©		
CAF11	Burundi CNR-Pediatric		Burundi
CAF12	Kalembelembe Pediatric Hospital		
East Africa			
EA26	MOROGORO	Morogoro	Tanzania
EA33	San Raphael/St. Francis Hospital, Nsambya	Kampala	Uganda
North America			
NA_ACCORD03	Ontario HIV Treatment Network		Canada
NA_ACCORD09			
West Africa			
WA03			
WA11	CENTRE HOSPITALIER NATIONAL D'ENFANTS ALBERT ROYER	Dakar	Senegal
WA12	HOPIATL DE JOUR DU CENTRE HOSPITALIER UNIVERSITAIRE - YALGADO OUEDRAOGO	OUAGADOUGOU	Burkino Faso
WA14	UPEIV-HIA	Cotonou	Benin
WA19	Korle Bu Teaching Hospital		
WA20	Service de pÃ©diatrie, HÃ´pital Gabriel TourÃ©		
Southern Africa			
sa_51173	Khayelitsha	Sea Point, 8050	South Africa
sa_51403	Newlands Clinic	Harare	Zimbabwe
sa_51404	CorpMed Medical Centre	Lusaka	Zambia
sa_51405	Gugulethu ART Programme	Cape Town, 7925	South Africa
sa_51406	Helen Joseph Hospital Themba Lethu Clinic	Johannesburg, 2041	South Africa
sa_51407	Independent Surgery	Gaborone	Botswana
sa_51408	Lighthouse Trust Clinic	Lilongwe	Malawi
sa_51409	Masiphumelele - Desmond Tutu HIV Centre	Cape Town	South Africa
sa_51410	Cato Manor, Umkhumbane Clinic	Congella, 4013	South Africa
sa_51412	Paediatric Day Hospital	Maputo	Mozambique
sa_51413	Perinatal HIV Research Unit (PHRU)	Johannesburg, 1864	South Africa

sa_51414	Tygerberg Hospital	Tygerberg, 7505	South Africa
sa_51418	SolidarMed Mozambique	Pemba	Mozambique
sa_51432	Coronation, University of the Witwatersrand	Johannesburg	South Africa
sa_51433	Free State provincial ARV roll-out	Mowbray, 7700	South Africa
sa_51434	Chris Hani Baragwanath Hospital, Harriet Shezi Clinic	Soweto	South Africa
sa_51435	McCord Hospital	Durban, 4001	South Africa
sa_51436	Red Cross Children Hospital	Cape Town, 7701	South Africa
sa_51437	Solidarmed Zimbabwe	Jerera	Zimbabwe

Appendix 4. List of key variables and their corresponding survey questions, variable categories and units of measure

Question on survey	Variable category	Key Variable	Measure
D01	Facility characteristic	Type of site	Individual clinic/Group of clinic/multi-site center/academic hospital
D05		Cancer types	AIDS-defining/non-AIDS defining Organ-specific cancers
D11-D12, D24-D30, D42-D43	Documentation capacity	Availability of data on: (Yes/No)	1 diagnostic methods 2 chemotherapy treatment 3 radiotherapy treatment 4 surgery 5 comfort care 6 palliative care 7 hormonal therapy 8 date of death 9 cause of death 10 behavioral risk factors 11 co-infections
D10, D13, D41		Proportion of patients with documentation of: (percent)	1 cancer diagnosis 2 cancer type 3 histopathology 4 radiologic information 5 computerized tomography (CT) information 6 endoscopic information 7 behavioral risk factors 8 co-infections 9 laboratory measures

			10 surgery 11 chemotherapy 12 radiotherapy 13 hormonal therapy 14 comfort care 15 palliative care
D14-D23	Screening Capacity	Availability of: (Yes/No)	1 mammogram 2 prostate-specific antigen (PSA) 3 cervical PAP smear 4 visual inspection with acetic acid (VIA) 5 Anal PAP smear 6 Ultrasound 7 Fecal occult blood test of stool (FOBT) 8 Colonoscopy 9 Chest X-ray 10 Alpha-fetoprotein (AFP)
		Method used for diagnosis only or diagnosis and screening	1 mammogram 2 prostate-specific antigen (PSA) 3 cervical PAP smear 4 visual inspection with acetic acid (VIA) 5 Anal PAP smear 6 Ultrasound 7 Fecal occult blood test of stool (FOBT) 8 Colonoscopy 9 Chest X-ray 10 Alpha-fetoprotein (AFP)
D06-D09	Diagnostic Capacity	Use of: (Yes/No)	1 tissue sampling (biopsy or FNA) 2 radiograph (X-ray) 3 radiograph

			(ultrasound or CT) 4 endoscopy
D31-D40	Treatment Capacity	Use of :(Yes/No)	1 chemotherapy 2 radiotherapy 3 surgery 4 palliative care 5 hormonal therapy

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