

Collaborative Consortia for the Study of HIV-Associated Cancers: US and Low and Middle Income Country Partnerships (U54)

Office of HIV and AIDS Malignancy

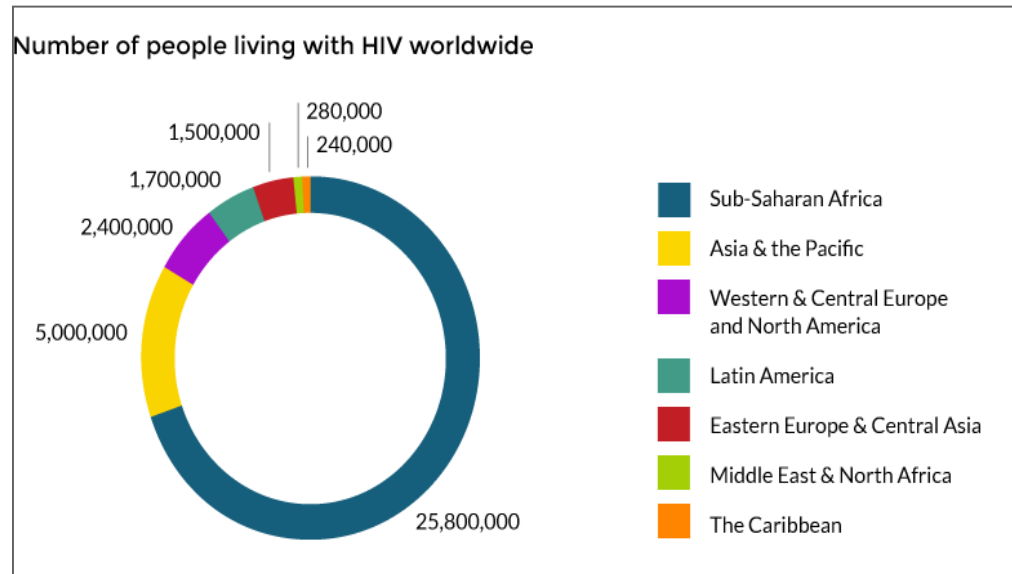
GOAL OF THIS RFA

To support highly meritorious inter-disciplinary multi-project research in HIV-associated malignancies led jointly by U.S. & low and middle income country (LMIC) investigators.

Global Burden of HIV

~36 million persons are infected, most in LMIC

- 25M in Africa
- 5M in Asia
 - 2.5M in India



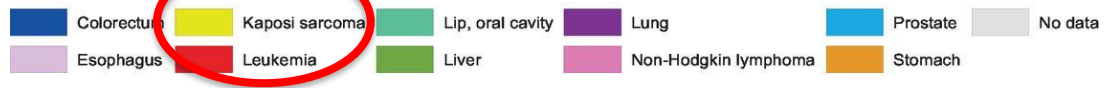
- Mortality from HIV is falling with increased access to antiretroviral therapy (ART).
- HIV-related cancer is a major health problem in LMIC and is expected to be even relatively greater with ART.

Most commonly diagnosed cancers, 2012.

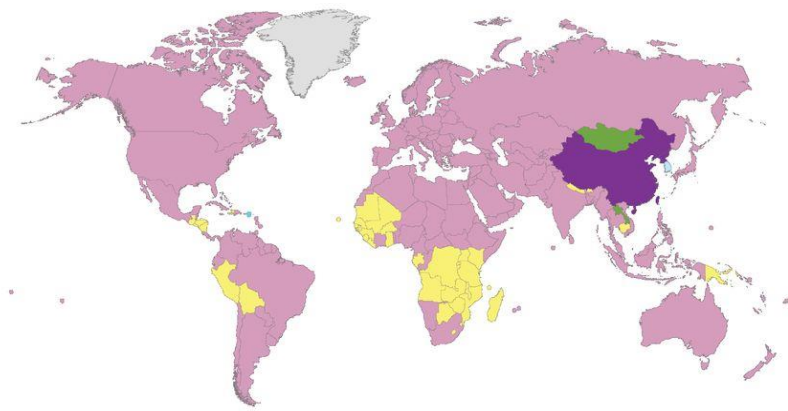
Males



Most common cancer site: males



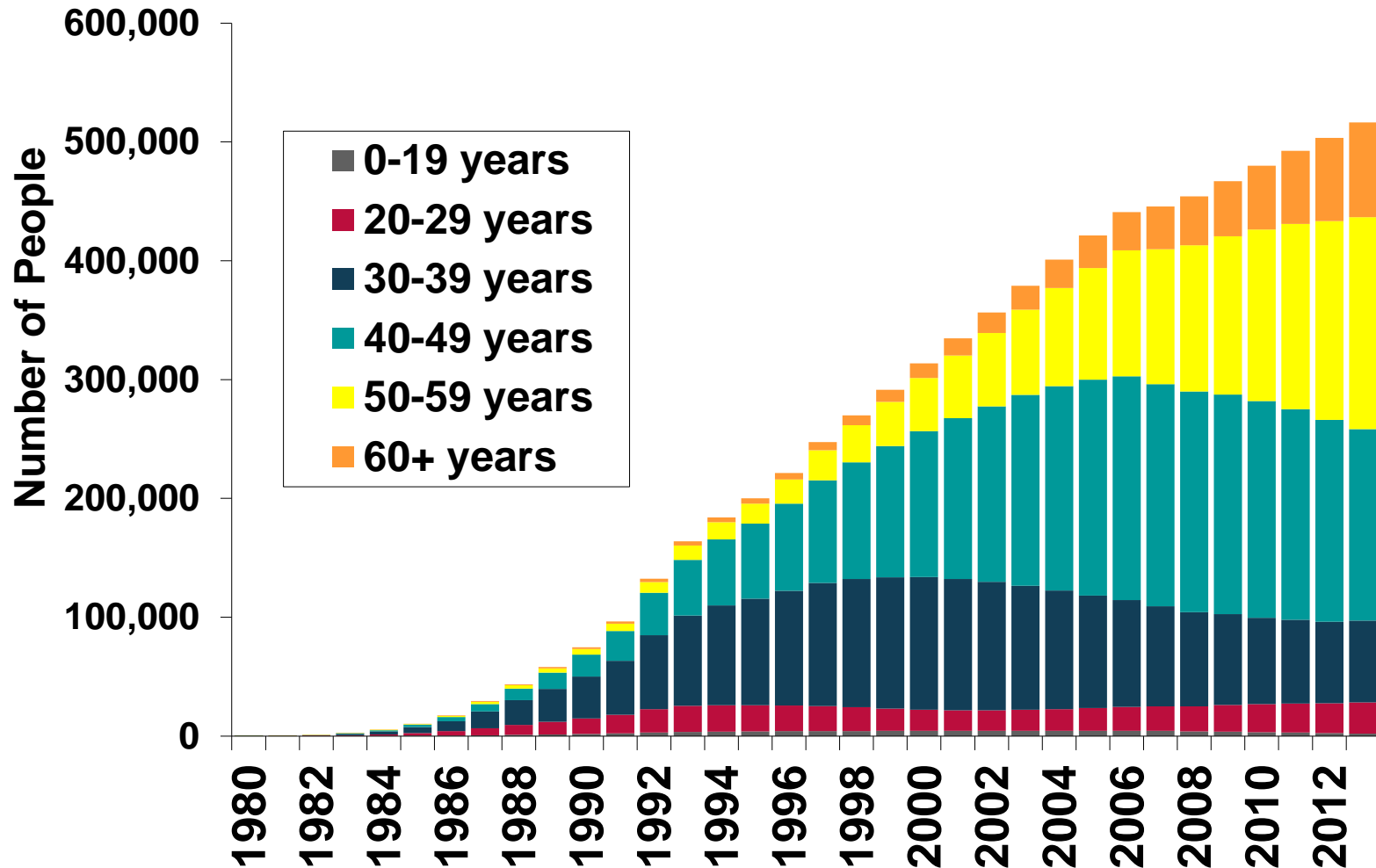
Females



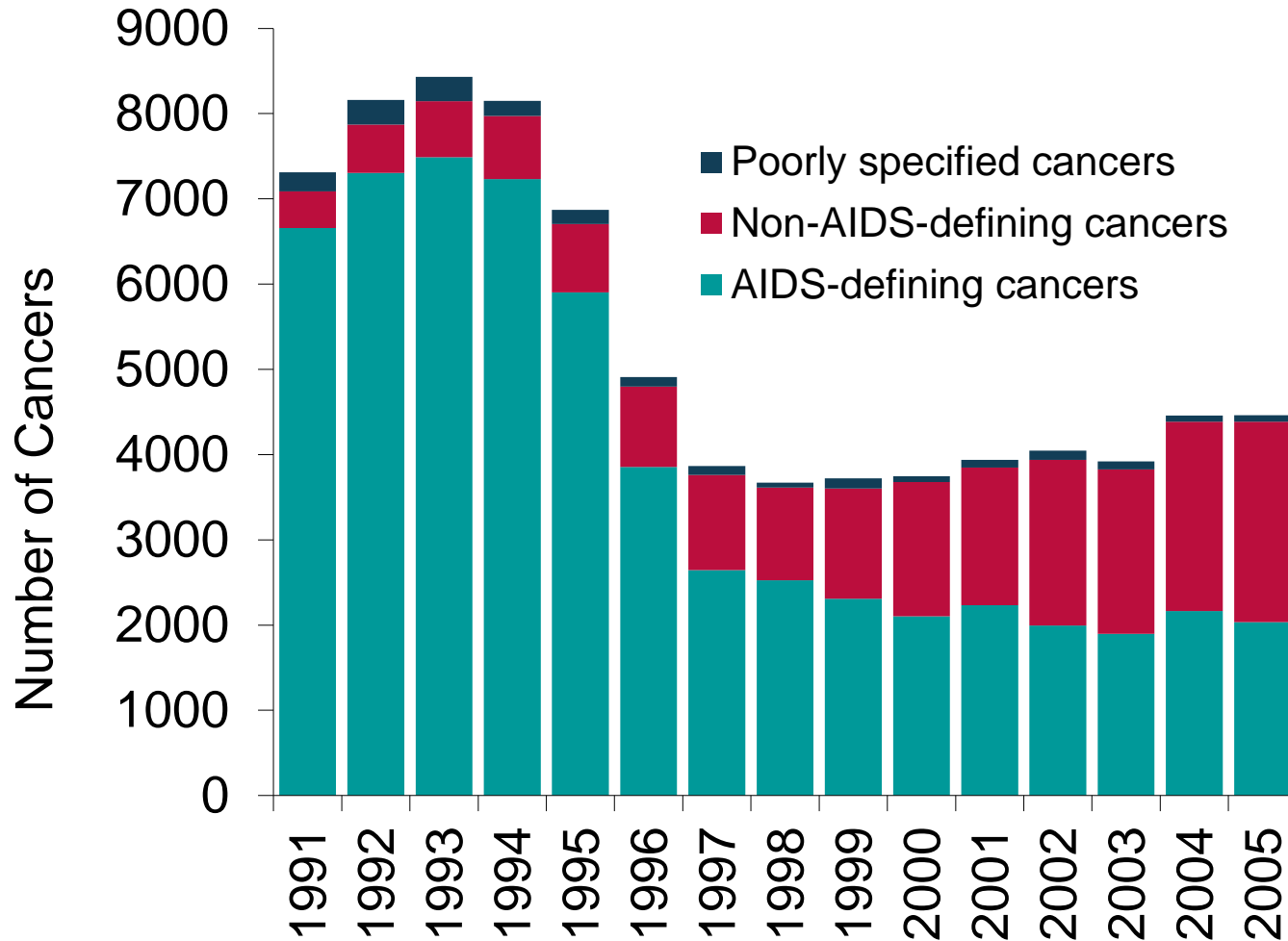
Most common cancer site: females



U.S. AIDS Population, 1980-2013



Total Cancer in U.S. AIDS Population



BSA Subcommittee Recommendations on HIV-Associated Cancers in LMICs

- Improve data on cancer epidemiology
 - Assess burden and types of malignancies in HIV infected persons
- Define factors that influence cancer risk in LMICs
- Define optimal methods for screening and prevention
 - Especially cervical cancer
- Investigate other virally-associated cancers, e.g. oral and liver cancer.
- Identify optimal therapies, taking into account medical infrastructure.

Rationale for U54 Collaborative Consortia in LMIC

- Enable the study of HIV-associated cancers in regions of high incidence
- Ability to study factors affecting differences in incidence, presentation, etc. in various regions
- Ability to study unusual cancers that do not develop in the US (e.g. conjunctival cancer)
- Ability to build capacity so that local researchers and institutions can contribute to this research and future research
- Ability to fund research that will help meet needs of the LMIC



Guech-Ongey et al, IJC, vol 122, 2008

Previous funded Projects

- FY2010-2013 (RFA CA-09-016),
“Developing Research Capacity in
Africa for Studies on HIV-Associated
Malignancies (D43)”
 - 9 awards (total \$4.6 million) per year for 3
years
- FY2014-2018 (RFA CA-13-010),
“Sub-Saharan African Collaborative
HIV and Cancer Consortia (U54)”
 - 8 awards (total cost of \$ 5.4 million) per
year for 5 years



Purpose of RFA

- Fund research projects that address high-priority research questions in HIV associated cancers in LMICs
 - Basic, translational, population, and implementation research conducted in LMICs
- Help increase quality of LMIC institutions to serve as national/regional resources for investigator training and mentoring in cancer research careers
- Builds on U54 RFA CA-13-010, but will not be limited to Africa

Features of the RFA

- **Grants will encompass 3 research projects and 2 mandatory cores**
 - Research projects can include epidemiological, social behavioral, basic, translational and clinical studies
 - Clinical trials are excluded, but clinical research is permitted
 - Application should have multiple projects that address a central theme
- **Mandatory Cores**
 - Administrative and Coordinating
 - Mentoring and Career Development
- **Optional Cores**
 - Technical Cores required for the proposed studies
 - Clinical/Translational (patient recruitment, sample acquisition, study design, IRB approval)
 - Epidemiology/Biostatistics (statistical support)
 - Laboratory (pathology, virology, immunological assays)

Additional Features of RFA

- Developed in collaboration with the NCI CGH and FIC
- Applications can either be submitted by an LMIC or US institution
- **Limited to countries that are not funded under the previous U54 RFA (CA-13-010)**
 - Uganda, Rwanda, Kenya, Botswana, Tanzania, and Malawi
- Demonstrate equal and shared partnership between the LMIC & U.S. co-applicants
- LMIC institutions should provide evidence of institutional commitment
 - e.g. financial support, space, protected time for clinicians, and faculty positions
- Budget should support research and career development in LMICs for young investigators (but no degree training)
- Request up to \$600,000 direct costs per year for 5 years
- Requested set aside \$2.2M. Anticipate 2 to 3 awards

Examples of Possible Research Areas

- Determine the role of sequence variations of causative oncoviruses (i.e. HBV, HCV, HPV and KSHV)
- Evaluation of co-factors for various HIV-associated tumors (e.g. malaria, other infectious co-factors)
- Studies of the pathogenesis of tumors that are unusual outside of certain LMIC (like conjunctiva cancer)
- Development of pathological and immunohistochemical tools
- Evaluating treatment-associated toxicities, optimal supportive care, and overall survival
- Studies to identify strategies to improve the integration of HIV and cancer care

Some Ways that US Partnerships can Enhance HIV Malignancy Research in LMIC

- Quality of data:
 - Improve existing cancer registries
 - Improve systematic HIV data capture on cancers
 - Reliable and consistent meta-data on treatment and outcome
- Assistance in tissue/specimen banking
- Improve pathology for diagnosis and research
 - Novel technologies for resource-limited settings
- Link novel scientific collaboration to unique needs and investigator training and mentoring
- Help translate research training to better patient care

Examples of Research in Ongoing Sub-Saharan/U.S. U54 Consortia

➤ H2U Consortia (Makere and Johns Hopkins)

- Hepatocellular carcinoma (HCC) case-control study
- HCC screening study
- Biomarkers including virologic and aflatoxin biomarkers

➤ University of Botswana/Penn Research Consortium of HPV related Cervical Cancer

- Study HPV/HIV epidemiology, pathogenesis, behavioral, clinical, immunologic risk factors
- Identify optimal therapeutic options in HIV+ women with cervical cancer

➤ Malawi Cancer Consortium (University of Malawi/UNC Lineberger CCC)

- HIV-cancer record linkage study using the Malawi National Cancer Registry
- Elucidate subsets of HIV-KS to improve outcomes
- Elucidate circulating and gene expression profiles that correlate with outcome in HIV-NHL

Examples of Early Outcomes from Ongoing U54 Collaborative Consortia

- **Moi Teaching and Referral Hospital, Moi University, Kenya and Academic Model Providing Access to Healthcare (AMPATH) consortium**
 - Developed platforms for HPV typing, cryotherapy, and LEEP in order to conduct studies on risk factors for HPV infection and dysplasia
 - Developed biorepository for cervical specimens at KEMRI
- **University of Malawi College of Medicine UNC: Malawi Consortium**
 - Improved pathology allowing characterization of lymphoproliferative disorders including identification of multicentric Castleman disease (Gopal et al., *Lancet* 2014).

Evaluation Criteria for the RFA

➤ Metrics to evaluate RFA

- Number of applications received
- Quality of applications (score range) and number funded
- Diversity of thematic areas (epidemiology, pathology, basic, clinical studies behavioral sciences, and implementation science)
- Institutional commitment provided
- Geographic areas represented
- Number of grants received that leverage other existing resources (NIH or non-NIH supported)

➤ Ultimate evaluation of RFA's impact

- Quality of research conducted, publications, capacity building, and contributions to global health.

The NIH Office of AIDS research (OAR) has approved this FOA as “high priority”, AIDS research, meaning that we have permission to use our AIDS funds for it.



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