

## **National Cancer Registry key and current Research Projects**

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### **1. The South African HIV Cancer Match Study (SAM)**

The National Health Laboratory Services (NHLS) laboratories serve over 80% of the South African population and provide the unique opportunity to link longitudinal laboratory HIV data from the NHLS to cancer data from the NCR. This allows for the assessment of cancer risk in HIV-positive people in the era of antiretroviral treatment (ART) availability in South Africa, at national level. The South African HIV Cancer Match Study (SAM) is a probabilistic record linkage study of a national HIV cohort created from HIV laboratory data (CD4 counts, viral load, DNA PCR, HIV diagnostic tests) linked to NCR data for the period 2004 – 2019. The aim of the study is to determine the burden, spectrum and incidence of cancer in HIV positive South Africans in the era of ART in South Africa. Our overarching goal is to inform cancer prevention and control programmes in children and adults living with HIV in the context of the evolving HIV epidemic in South Africa. The SAM study is a collaborative study between the NCR, the International epidemiologic Databases to Evaluate AIDS in Southern Africa (IeDEA-SA) and the Institute of Social and Preventive Medicine at the University of Bern in Switzerland. The SAM study supports several masters and PhD students.

### **2. The Johannesburg Cancer Study (JCS):**

The aims of the Johannesburg Cancer Study are to determine whether risk factors identified for cancers in developed countries apply to Black (African) adult patients attending tertiary public hospitals in Johannesburg, South Africa, and to understand the impact of HIV on cancer risk, with a view to identifying previously unrecognised HIV associated cancers (which may themselves, have an underlying infectious cause).

A total of 25 032 black patients with an incident histologically proven (>95%) cancer of any type were consecutively enrolled between 1995 and 2016. Response rates were >90%. Each patient provided informed consent, lifestyle and demographic information using a structured questionnaire; 19 352 serum samples and 18 973 whole blood samples were stored for genomic analyses.

Results from the study showed the relative importance of several viruses, and leading risk factors on the aetiology of cancer in South Africa using methods similar to a hospital-based case-control study (controls being cancer types unrelated to exposures of interest). This was a practical and valid design in an otherwise logistically difficult setting. This design is recommended in settings where cohort studies are impractical.

Preference is placed on data and sample requests which promote data sharing, equal collaborative opportunities and enhancement of research capacity in South Africa. All requests require local and host institutional ethics, research governance clearance and a collaborative Transfer Agreement.

Table 1. Basic demographic and lifestyle characteristics of cancer patients in the Johannesburg cancer study.

	<b>1995 – 2004 (n=9535)</b>	<b>2005-2016 (n=15497)</b>
<b>Top three cancer types (% of total) – Males (M)</b>	Oesophagus (17.0%), Prostate (11.7%), Lung (10.5%)	Kaposi Sarcoma (13.1%), Oral cavity and pharynx (11.3%), Lung (10.2%)
<b>Top three cancer types (% of total) – Females (F)</b>	Cervix (33.3%), Breast (24.8%), Oesophagus (5.8%)	Breast (33.3%), Cervix (30.8%), Kaposi Sarcoma (4.9%)
<b>Cancers histologically verified</b>	97.4%	98.9%
<b>Cancers ill defined</b>	3.0%	3.5%
<b>% Female</b>	63.7%	68.5%
<b>Median age (years)</b>	52	51
<b>Urban place of birth</b>	46.6%	49.0%
<b>Urban place of residence</b>	87.7%	91.5%
<b>Secondary school leavers</b>	8.1%	20.5%
<b>Using electricity to cook (now)</b>	69.5%	84.2%
<b>Using coal + anthracite to cook (now)</b>	11.1%	2.7%
<b>Using electricity for heating (now)</b>	65.0%	65.7%
<b>Using coal + anthracite for heating (now)</b>	16.8%	11.7%
<b>Smoker (M) – current smokers</b>	40.8%	38.8%
<b>Smoker (F) – current smokers</b>	9.5%	6.0%
<b>Smoker (F) – previous smokers</b>	11.7%	10.0%
<b>Median number of cigs/day (M)</b>	10	8
<b>Median number of cigs / day (F)</b>	5	5
<b>≥ Moderate alcohol drinkers (M) (&gt;200g per week)</b>	48.2%	44.4%
<b>≥ Moderate alcohol drinkers (F) (&gt;200g per week)</b>	17.2%	8.8%
<b>HIV positive (M)</b>	13.3%	33.3%
<b>HIV positive (F)</b>	14.1%	36.0%
<b>Currently using oral contraception only (F only 18-44 years)</b>	5.3%	3.0%
<b>Currently using injectable contraception only (F only 18-44 year)</b>	14.8%	18.0%
<b>Median age at first childbirth (15-54 years as child bearing age)</b>	21	20
<b>Median no of children – (F)</b>	3	3
<b>Median sexual partners</b>	4	4
<b>Language Zulu</b>	24.3%	25.3%
<b>Language Sesotho</b>	19.5%	17.9%
<b>Language Tswana</b>	19.1%	17.5%
<b>Language Xhosa</b>	13.3%	12.1%

\*Note these figures are illustrative- comprising crude estimates in both potential cases and controls

### **3. Evolving Risk Factors for Cancers in African Populations (ERICA-SA) study:**

Lifestyle, infection, genetic susceptibility and cancer in South Africa: development of research capacity and an evidence base for cancer control.

<http://www.mrc.ac.za/intramural-research-units/evolving-risk-factors-cancers-african-populations-erica-sa>

In response to the growing burden of cancer, we established the (SA-MRC Funded) Johannesburg Cancer Study (JCS) at the National Cancer Registry (NCR) in 1995 and collected lifestyle information, serum and blood for DNA extraction from about 20,000 consecutive black patients with an incident cancer. This is now by far the largest epidemiological study in Africa that has collected lifestyle information together with biobanked serum and blood for DNA extraction. This study will investigate three areas:

#### 1) Lifestyle risk factors in broad range of cancer types

In developed countries, these cancer related risks have changed significantly over time. Since the mid-1990s to recent years, several of these risk factors (e.g. smoking, snuff, indoor pollution and hormonal factors) have also changed in prevalence in South Africa. These changes require re-evaluation of each risk factor to measure their evolution and relative importance over time. The JCS recruited patients in a continuous fashion over a 21-year period, from 1995 until 2016, a historical record of such changes in lifestyle factors over time is now available. The sample size of 25 032 patients, a first of its kind in Africa, allows for detailed (re)investigation of the evolving risk factors for cancers.

#### 2) Infectious agents in cancer

Contributions of infection to cancer causality will be investigated on a broad scale. Identifying the interplay between environmental factors (lifestyle and infections) against a yet to be described genetic profile of this population will lead to accurate prioritisation of each exposure. Moreover, this will provide an evidence base for further research into causation and translation into targeted cancer control programmes.

#### 3) Genetic susceptibility to common African cancers

Little is known about the contribution of common genetic variants to leading cancer types such as breast, oesophageal or cervical cancer risk in Africa, and the few studies that have been conducted have been hampered by small sample sizes and the small number of variants tested

for association. This is in stark contrast to progress in European and Asian populations, where genome-wide association studies (GWAS) have identified substantial numbers of associated genes or loci which are revealing some of the key molecular pathways involved in cancer. The study aim is to identify genes and genetic variants which alter cancer risk.

#### **4. Men of African Descent and Carcinoma of the Prostate Network (MADCaP):**

<https://www.madcapnetwork.org/>

Cancer of the prostate (CaP) is the leading cancer among men in sub-Saharan Africa (SSA). A substantial proportion of these men with CaP are diagnosed at late (usually incurable) stages, yet little is known about the aetiology of CaP in SSA.

The NCR hosts one of seven SSA centres, partnering with the Centre for Proteomics and Genomics Research (CPGR, Cape Town) and five US centres to study the genetics and epidemiology of CaP in SSA. This study developed and implemented standardized collection of epidemiological questionnaire data, medical record data and bio-samples across seven centres. Genomic data isolated from whole blood will be used in genome-wide association studies (GWAS) to identify common risk variants for CaP in SSA.

