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OPINION PIECE

South African National Cancer Prevention Services

PA Goldberg, M Muchengeti, I Buccimazza, F Malherbe, N Mbatani, A van Wyk, R Ramesar

On behalf of the SANCaPS Group

Corresponding author, email: *paul1144@iafrica.com*

The South African National Cancer Prevention Services (SANCaPS) comprises a group with clinical, epidemiological, and oncological skills, established to fill the need for comprehensive and holistic cancer prevention. The primary objective of this collective effort is the translation of laboratory research into primary preventative medicine. A secondary aim is to stimulate ongoing research. Significant work on inherited colorectal cancer has been conducted in the Western and Northern Cape for over two decades. Established processes and protocols are already in place to identify and manage at-risk individuals. Consequently, it is logical to expand this work to a national level. This approach will help build the necessary infrastructure for future expansion into other cancer types. A step in this direction has been taken by the SANCaPS group who have advised that the data processing component should be associated with the National Health Laboratory Service (NHLS) Corporate Data Warehouse (CDW) and the National Cancer Registry. This choice is informed by the fact that all cancer histopathology reports, whether from the public or private sector, pass through the CDW. This setup enables the identification of inherited cancers. The primary objective is to identify family members at high risk for developing cancers in the future. The National Registry has the legislative framework to provide the services SANCaPS require.

Several strategies are required for primary prevention of cancer and must take into account national circumstances.[1] Vaccination against hepatitis B has the potential to decrease the occurrence of hepatocellular carcinoma, while vaccination against human papillomavirus may reduce the incidence of cervical carcinoma and, hopefully, squamous cell carcinomas in the anogenital and oropharyngeal regions.[1] The greatest risk factor for the development of most cancers is age. South Africa has a very young population.[2] It is, therefore not surprising that currently, the incidence of many cancers is relatively low compared to first-world countries.

The mortality from cancers can be reduced by education, high-quality and accessible health care and by population screening programmes.[3] Screening programmes for cancers are well established in high-income countries (HIC) but less so in low- to middle-income countries (LMIC). There are no national screening programmes for any cancer in South Africa. Colorectal cancer, for instance, is the third most common cancer in males and females combined, yet the incidence is less than 10 per 100 000[4] compared with 40 per 100 000 in HIC. A national population screening programme will only become efficient when there is an ageing population at risk of contracting the disease, and increased funding becomes available for preventative medicine.

Clinical and cost-effective screening has shown to be feasible in the small proportion of cancers that have an inherited predisposition.[5] Data reporting the proportion of cancers where inherited mutations contribute to their cause arise from studies in HIC. Between 5-10% of breast, 10% of ovarian and 6% of colon cancers have a germline component. There is increasing evidence that these figures might not apply to LMICs. The population pyramids in LMICs are very different from those in high-income ones.[6] The population in the former group is far younger, with a very small proportion of elderly people. It would not be surprising if inherited cancers account for a higher proportion of the cancer disease burden in LMICs, as the relatively few elderly individuals means fewer sporadic cancers. There is some evidence to support this premise. Work in Nigeria,[7] Uganda, and Cameroon[8] has demonstrated a high proportion of *BRCA1* and *BRCA2*-related breast cancer (11%).[9] There is evidence from three South African studies that the incidence of inherited colorectal cancers may well be 3-5 times higher in South Africa than in HICs.[10-12]

Cancers related to germline mutations tend to occur earlier in life than sporadic ones. The impact of the loss of a young breadwinner parent from these cancers is likely to have a far greater effect on families with young children, than the elderly who die from sporadic cancers. Individuals at high risk of developing germline-associated cancers can be identified and offered strategies to reduce the risk of mortality at a young age. Work in South Africa has shown that surveillance colonoscopy adds a median of 20 years of additional life in individuals at high risk due to an *h*MLH1 mutation.[13]

Since nearly all pathology reports for cancer cases, whether from the public or private sector, pass through the NHLS CDW before reaching the National Cancer Registry, it should theoretically be possible to identify all colorectal cancer reports based on ICD-10 and/or SNOMED codes. However, at present, there is a lack of standardisation in the reporting of colorectal cancer by pathologists in South Africa. The reporting formats range from narrative, where

essential data may occasionally be omitted, to synoptic protocols. Even when synoptic protocols are employed, there is a lack of standardisation across laboratories. Typically, the data within a pathology report is captured in a single data field, making it challenging to extract specific pathology parameters. Over the last 15 years, minimum dataset colorectal cancer reports have been verified and introduced by many countries as a recommendation. This solves the variability of quality and standardises the terminology used. We have drawn up a minimum colorectal cancer dataset based on that developed by the International Collaboration on Cancer Reporting.[14] A standardised pathology report format with drop-down menus and required fields has been developed and is currently undergoing testing in the NHLS laboratories. The pathology data in this report format will be captured in discrete data fields to enable easy extraction of specific pathology parameters.

Identifying FAP is not difficult because of obvious multiple adenomas at endoscopy. Mismatch repair gene abnormalities are more difficult to detect. While there are histological clues, these are subjective and require careful examination. Either immunohistochemical testing for mismatch repair proteins or polymerase chain reaction for microsatellite instability are mandatory requirements for all colorectal cancer histopathology reports in many HIC. The SANCaPS group has recommended that these should be mandatory within our environment; however, it should initially be limited to tumours in individuals below 60 years of age for cost reasons. With this restriction, the SANCaPS group estimates that three colorectal cancers per day at a national level will need further investigation. Computer software that allows for the automatic importation of the data from histopathology reports, seamless generation of pedigrees, and the provision of follow-up records for surveillance, cancer development in family members, surgery, and survival is not currently available. Most international services seem to rely on multiple entry systems, which require repetitive input of similar data. We are currently surveying international units with the aim of establishing international cooperation to develop the software that can fulfil these needs. In the interim, we will need to continue using multiple programmes that are currently in place. Staff will need to be employed to implement these goals. They will include genetic counsellors, data-managers, and data-capturers.

In South Africa and other LMICs many patients with inherited cancers are treated similarly to non-inherited cancers. Identification and management of family members at risk is often overlooked. In some institutions, the inherited potential is identified, and genetic testing is performed at international laboratories, incurring high costs. Protocols for mutation identification with a panel of known common mutations are available locally and are significantly cheaper. Only families with an obvious dominant inherited pattern and a significant number of at-risk family members will be selected for sequencing for unknown mutations. This needs to be standardised nationally.

Once the systems for identifying and managing family members at high risk for developing colorectal cancers have been established, we plan to expand this to the management of other cancers.

Approximately 40-60% of females with mismatch repair gene mutations develop endometrial cancers at a young age. Ovarian neoplasms are less common (10–15%), but with *BRCA1* mutations, between 39–46% and with *BRCA2* mutations between 11–17% develop ovarian neoplasms by the age of 70 years.[12] It is difficult to identify endometrial and ovarian neoplasms early. Some international units recommend prophylactic hysterectomy and bilateral oophorectomy once a family has been completed. We are currently investigating the role of regular high-definition ultrasound as a screening tool.

Some breast units in South Africa routinely perform mutation testing on patients with breast carcinoma who fulfil criteria for genetic testing according to current guidelines. Predictive testing is offered to all unaffected family members after genetic counselling, if a genetic mutation is detected in a proband. Unaffected family members who test positive for the genetic mutation are offered initial surveillance or risk-reducing surgery, depending on their age at detection of the mutation and the type of mutation. Other units do not offer these services as part of routine management. This needs to be standardised nationally.

Conclusion

The risk factors for cancer, including age and inherited mutations, vary across regions and populations. Vaccination, early detection and standardised pathology reporting are key elements for cancer-reducing strategies. The establishment of SANCaPS represents a significant step towards addressing these challenges using inherited cancers as the starting point. SANCaPS is currently unfunded and purely voluntary. It is in the process of forming a not-for-profit company and raising funds. As we move forward, prioritising the identification as well as management of high-risk individuals, developing specialised software, and expanding our efforts to encompass various cancer types will be crucial in our mission to reduce the burden of inherited cancers.

We would like to invite people who are interested in being involved in the SANCaPS initiative to email info@sancaps.co.za.

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Supplementary Table

Title	Initials	full names	Surname	Orcid	Affiliation	role	email	input
Dr	AP	Alessandro Pietro	Aldera	https://orcid.org/0000-0002-9615-1692	Division of Anatomical Pathology, University of Cape Town and JDW Pathology Inc, Cape Town	Anatomical pathologist	alessandro.aldera@uct.ac.za	Minimum dataset colorectal
Ms	U	Ursula	Algar	https://orcid.org/0000-0002-3408-3348	Familial colorectal cancer Unit of the Colorectal Unit of the Division of General Surgery, Groote Schuur Hospital and University of Cape Town, Cape Town, South Africa	Genetics nurse	ursula.algar@uct.ac.za	patient coordinatory
	G	Gloseije	Bazolana				gloseijeb@nicd.ac.za	
Prof	BD	Brendan Dirk	Bebington		Wits Donald Gordon Medical Centre, School of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa	colorectal surgeon	brendanbebington@gmail.com	Lead: Gauteng
Dr	T	Trevor	Bell	https://orcid.org/0000-0003-2630-7513	National Institute of Communicable Diseases, National Health Laboratory Services	Principal Health Data Analyst, NICD	TrevorB@nicd.ac.za	set up NHLS systems
Prof	M	Marc	Blockman	https://orcid.org/0000-0001-7240-8812	Department of Internal Medicine, Groote Schuur Hospital and University of Cape Town	ethicist	marc.blockman@uct.ac.za	Ethics
Prof	P	Philippus	Bornman			HPB surgeon	philippus.bornman@uct.ac.za	none yet
Dr	J	Jaco	Botes		Division of Surgery, Faculty of Medicine & Health Sciences, Tygerberg Campus	surgeon, bioinformatics	jacobotes@sun.ac.za	Bioinformatics
Prof	ABT	Adam Brunette	Boutall	https://orcid.org/0000-0002-6413-5890	Colorectal Unit of the Division of General Surgery, Groote Schuur Hospital and University of Cape Town, Cape Town, South Africa	colorectal surgeon	boutall@icloud.com	
Dr	I	Ines	Buccimazza	https://orcid.org/0000-0002-5399-3101	Department of Surgery, Nelson R Mandela School of Medicine, University of KwaZulu-Natal, Durban	Breast surgeon	ines.buccimazza@gmail.com	Lead: Breast surgery KZN
Ms	S	Sinead	Cameron-Mackintosh	https://orcid.org/0000-0001-6705-8766	Simply Genetics	Genetic councillor	sinead.cameron-mackintosh@alumni.uct.ac.za	Councilling systems
Dr	WC	Wenlong Carl	Chen	https://orcid.org/0000-0002-3248-4906	National Cancer Registry, National Health Laboratory Service, Johannesburg, South Africa, Strengthening Oncology Services Research Unit, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa, Sydney Brenner Institute for Molecular Bioscience, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa	IT specialist	WenlongC@nicd.ac.za	IT dashboards and AI NHLS
Dr	JP	Peter	Cruse		Head of Healthcare, Henley Business School Africa	Anatomical pathologist	petercruse@gmail.com	Fund raising
	G	Gillian	Dusterwald		Family Colorectal Cancer Clinic, Groote Schuur Hospital and the University of Cape Town, Cape Town, South Africa	Genetic councillor	geneticcounsel@gmail.com	Councilling systems
Ms	C	Cassandra	Ferreire	https://orcid.org/0000-0002-7386-0752	Data Manager IQVIA		cassandra.ferreira@iqvia.com	data management
Prof	PA	Paul Adrian	Goldberg	https://orcid.org/0000-0003-1612-7519	Colorectal Unit of the Division of General Surgery, Groote Schuur Hospital and University of Cape Town, Cape Town, South Africa	colorectal surgeon	paul.goldberg@uct.ac.za	lead
	S	Shaun	Grimett			IT specialist national cancer warehouse	shaun.grimett@nhls.ac.za	IT management NHLS
Dr	M	Michael	Klipin	https://orcid.org/0000-0003-0269-9161	Head, Division of Biomedical Informatics, Wits Health Consortium. Honorary Lecturer Department of Surgery, University of the Witwatersrand	surgeon, bioinformatics		Bioinformatics
Dr	GF	Francois	Malherbe	https://orcid.org/0000-0001-8910-6925	Division of General Surgery, Groote Schuur Hospital and the University of Cape Town, Cape Town, South Africa	Breast Surgeon	francois.malherbe@uct.ac.za	Lead: Minimum dataset breast cancer
	E	Ephraim	Mashaba		Central Data Warehouse, National Health Laboratory Service, Johannesburg, South Africa	IT specialist	ephraim.mashaba@nhls.ac.za	IT management NHLS

Title	Initials	full names	Surname	Orcid	Affiliation	role	email	input
	N	Natalie	Mayat		National Institute of Communicable Diseases, National Health Laboratory Services		nataliem@nicd.ac.za	
Dr	N	Nomonde	Mbatani	https://orcid.org/0000-0001-8826-5182	Department of Obstetrics and Gynaecology, University of Cape Town, South Africa	Gynaecologist	nomonde.mbatani@uct.ac.za	Lead Gynae minimum datset
Prof	J	Jennifer	Moodley	https://orcid.org/0000-0002-9398-520	School of Public Health and Cancer Research Initiative, Faculty of Health Sciences, University of Cape Town	Research	jennifer.moodley@uct.ac.za	research
Dr	M	Mazvita	Muchengeti	https://orcid.org/0000-0002-1955-923X	National Cancer Registry, National Health Laboratory Service, Johannesburg, and School of Public Health, University of the Witwatersrand, Johannesburg and South African DSI-NRF Centre of Excellence in Epidemiological Modelling and Analysis (SACEMA), Stellenbosch University, South Africa.	Director National cancer registry	mazvitam@nicd.ac.za	Manager National cancer registry
Prof	C	Clement	Penny	https://orcid.org/0000-0003-4429-5712	Chairperson, Human Research Ethics Committee, Medical; and Wits/MRC Common Epithelial Cancer Research Centre, University of the Witwatersrand	Ethicist	clement.penny@wits.ac.za	Ethics
Prof	Y	Yvonne	Perner	https://orcid.org/0000-0002-3569-6867	Division of Anatomical Pathology, School of Pathology, Faculty of Health Sciences, University of the Witwatersrand and NHLS	Anatomical pathologist	yvonne.perner@nhls.ac.za	Past head pathology Wits
Prof	K	Komala	Pillay	https://orcid.org/0000-0003-1971-900X	Professor and Head, Department of Pathology, University of Cape Town and National Health Laboratory Services	Anatomical pathologist	komala.pillay@uct.ac.za	Lead Anat path Expert group
Prof	R	Rajkumar	Ramesar	https://orcid.org/0000-0001-5688-1634	Director: MRC Precision and Genomic Medicine Research Unit (Unit Director), Division of Human Genetics, (Prof/ HoD), Faculty of Health Sciences, University of Cape Town and National Health Laboratory Service (HoD), Groote Schuur Hospital , Cape Town, South Africa	Genetist	raj.ramesar@uct.ac.za	Lead: Human Genetics
Dr	G	George	Rebello	https://orcid.org/0000-0002-0654-7598	JDJ Diagnostics Durban and the Division of Human Genetics, University of Cape Town, Cape Town, South Africa	IT specialist	george.rebello@uct.ac.za	Bioinformatics
Dr	B	Barbara	Robertson		Radiation Oncology, University of Cape Town and Groote Schuur Hospital	oncologist	barbara.robertson@uct.ac.za	Oncology
Dr	E	Elvira	Singh	https://orcid.org/0000-0003-1259-2122	National Cancer Registry, National Health Laboratory Service, Johannesburg	Past director of National cancer registry		
Dr	A	Abraham	Van Wyk	https://orcid.org/0000-0002-0946-2434	Division of Anatomical Pathology, Tygerberg Hospital, National Health Laboratory Service, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa, Department of Pathology, Faculty of Medicine and Health Sciences, University of Stellenbosch, Cape Town, South Africa	Anatomical pathologist	abrievanwyk@gmail.com	Lead: Minimum colorectal dataset
Dr	H	Helena	Vreede	https://orcid.org/0000-0002-6644-6027	Division of Chemical Pathology, Department of Pathology, Faculty of Health Sciences, University of Cape Town, Cape Town, South Africa, Department of Clinical Pathology, Groote Schuur Hospital Laboratory, National Health Laboratory Service, Cape Town, South Africa	Chemical pathologist	helena.vreede@nhls.ac.za	design of minimum dataset reports
Prof	R	Reubina	Wadee	https://orcid.org/0000-0002-5981-4450	Department of Anatomical Pathology, National Health Laboratory Services and the University of the Witwatersrand	Anatomical pathologist	reubina.wadee@nhls.ac.za	Head Pathology Wits and gynae minimum dataset
Dr	J	Jenny	Edge			Breast surgeon	dr@jennyedge.co.za	Breast surgeon WITS
Dr	K	Kirsten	Fearnhead			Anatomical pathologist	kirsty@drkf.co.za	Private pathologist minimum datset
Dr	c	Caroline	Nel			Anatomical pathologist		Breast pathologist
Dr	E	Eunice	van den Berg			Anatomical pathologist		Breast pathologist