OVERVIEW
OF
THE SOUTH AFRICAN
CANCER RESEARCH ENVIRONMENT
AS A BASIS FOR DISCUSSIONS
CONCERNING THE ACTIVATION
OF
CARISA
(Cancer Research Initiative of South Africa)

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OVERVIEW OF ONCOLOGY RESEARCH IN SOUTH AFRICA

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1. EXECUTIVE SUMMARY

- Cancer is a highly complex, ubiquitous and devastating disease causing 10 million new diagnoses world-wide per annum. Of these, 6.7 million will succumb and at present there are 24.6 million cancer patients living with cancer and hoping to survive.

- In most countries where cancer surveillance is done, data is collected on incidence (new diagnoses) and mortality (death certificates). A ratio of mortality to incidence, calculated as age standardised rates (ASR), gives a measure of the lethality of a particular cancer. Highly lethal cancers such as liver, pancreas, oesophagus and lung have mortality rates close to the incidence rates while breast, colon and prostate have considerably lower ratios of 0.36, 0.51 and 0.32 respectively.

- When South African mortality data from the MRC Burden of Disease Unit (2000) was studied in relation to incidence data from the National Cancer Registry of the NHLS (1999) it was unexpectedly found that in the case of six out of ten most common cancers (e.g. lung, oesophagus, stomach, Non-Hodgkins lymphoma, liver and bladder) the mortality rates were significantly higher than the incidence rates, which is impossible. In the case of prostate, breast, colorectal and cervical cancers, the mortality rates were lower than the incidence rates - as expected. The unfortunate conclusion from this comparative study is that the National Cancer Registry is not reliable in many cases and probably suffers from large scale under-reporting of cancer in South Africa. It was calculated on the basis of the assumption that South Africa and the World had the same ratio of morbidity to incidence rates of 0.62, that the under-reporting could be as large as 54 507 cases in 1999-2000. If this is indeed so, the annual incidence of new cancer patients in South Africa is not 60 000 as reported by the NCR (1999) but possibly closer to 114 000 p.a.! There are also indications that this under-reporting is more extensive in the Black rather than in the White South African population group and the reasons for this are not clear. It is of considerable importance to find out what the situation is of South Africans with cancer who's cancer diagnoses (if any) do not reach the NCR. It is concluded that mortality data is all that we really have to monitor cancer in South Africa with any degree of certainty. We really do not know for sure what the real incidence of cancer in South Africa is. It is also concluded that in general the cancer surveillance infrastructure in South Africa is not at all optimal and needs concerted attention and extra funding from the health authorities in order to create a reasonable foundation/platform on which to conduct cancer research and control. Without this we can hardly expect to win the war against cancer. One potential remedy supported by the surveillance fraternity is to legislate that all new cancer diagnoses are notifiable to the NCR, irrespective of the technique of diagnosis used, i.e. pathological or clinical.

- In the US progress against cancer is monitored by the National Cancer Institute (NCI) according to at least 21 different criteria such as smoking rates, dietary habits etc. and results are periodically posted on the Internet for all to see. Of these criteria only two, i.e. cancer incidence (which is unreliable) and mortality rate are monitored in South Africa by the NHLS and MRC and not by an NCI because there is no NCI in South Africa. It is assumed that a lack of a detailed Cancer Control Progress Report in South Africa is probably due to the fact that South Africa does not have a definite policy on cancer control but deals with cancer in a fragmented manner. The obvious recommendation is for a visible, functional, dynamic, sustainable, mandated Cancer Control Programme in South Africa that could inspire and unite all the role players in cancer research and cancer control, including NGO's such as CANSA. In most countries Cancer Control Programmes are run by the central Department of Health.

- Comparisons of mortality data in the US and South Africa reveals the important fact that the rates of lung cancer in women and colon cancer in men and women, in South Africa, are between 200 – 300% LOWER than in the USA. Incidence data indicate that these cancers are especially low in Black women, which make them an excellent target for prevention. The question is asked –"*How many extra cancer cases would there be if the common cancers in South Africa reached mortality rates similar to the USA*?" It was calculated that the increase for lung, breast, prostate and colon would be **21 650** cases p.a. It is clear that research aimed at MAINTAINING low cancer rates, as well as lowering HIGH cancer rates such as oesophageal and cervical cancer, could help to prevent thousands of cancer deaths in the future.

- For the first time in 70 years it has now been reported that the mortality of cancer in the USA is decreasing, albeit by only 1% p.a. In South Africa it can be anticipated that the rate will rise as the migration to the cities and life expectancy increases. Cancer is a disease mainly of old age and has now become the No.1 cause of death in the USA.

- As far as the nature of cancer research is concerned, the USA is investing heavily in so-called Molecular Oncology, hoping for new diagnostic techniques and drugs that will significantly reduce the burden of cancer. Much of this is hopeful thinking and the new drugs on the market do not have a dramatic curative effect and cost in the order of $100 000 per patient. Although it is clear that molecular oncology is a potential fountainhead of innovation, it has been proposed that South Africa needs more translation of basic research discoveries into public health processes such as early detection, preventative measures such as vaccination and standardised affordable treatment and palliation. Translation is also needed of all cancer control efforts into legislative policy. It is proposed that basic, applied and translational cancer research form a holistic network or a "cancer continuum"

and that intrinsically there should be synergism between the different role players and certainly not antagonism.

- At present there are 73 cancer research projects being conducted in South Africa at an annual cost of R32 million and there are 12 stakeholders that contribute these funds. The top six contributors are: iThemba Labs, MRC, CANSA, NHLS, BioPAD and the THRIP and INNOVATION funds of the NRF.

- Compared to USA, UK, Germany, Denmark, France and Australia, the cancer research funding in South Africa per head is exceedingly low, i.e. it is only 10 US cents per head per year, whereas the US spends $14.41 (144 –times) and Australia $2.25 (22-times) more than South Africa with less than half the population size in the case of Australia. If South Africa is at all serious about conducting cancer research in order to help prevent a massive escalation of cancer in South Africa during the next 15 years (predicted to increase), then a greater financial commitment is called for from all stakeholders but especially from the top 6 funders, overseas funding agencies and the South African public.

- A CANSA-initiated audit of 10 years of cancer research funded by CANSA from 1994 to 2003, showed an **excellent output** of 570 peer-reviewed publications with an average impact factor of 3.8 at a cost of R28.2 million giving a cost of R50 000 ($8379) per publication which compares extremely well with an overseas cost of $100 000 per publication. There are at present 5 patents from South African cancer research but none of them have lead to commercialisation yet. In 1998-2000 ten cancer research consortiums were assembled of which only 3 remain.

- In general I must conclude, after being involved with cancer in South Africa for 46 years, in one way or another, that the status of cancer research and cancer control in general, in South Africa, has reached a dangerously low level and needs a substantial boost. Nevertheless there is a core of highly dedicated scientists, clinicians, oncologists, paramedics, members of the public and managers at all levels, who are eager to see a renaissance in cancer research in South Africa, which will integrate with and support a comprehensive South African Cancer Control Programme, so that there will also come a day in South Africa when the cancer mortality rate will start to fall –like it is now doing in the USA.

- The hope is that CARISA will be the vehicle and catalyst for the renaissance of cancer research and control in South Africa.

2. ABBREVIATIONS USED:

ASR	Age standardised incidence rate
BioPAD	Biotechnology Partnership and Development
CANSA	Cancer Association of South Africa
CFR	Case fatality Ratio
DOH	National Department of Health of South Africa
DTI	Department of Trade and Industry
iThemba Labs	National Nuclear Accelerator at FAURE
I-ASR	Incidence ASR
IARC	International Agency for research on Cancer
MRC	South African Medical Research Council
M-ASR	Mortality ASR
Mil	millions
NCI	National Cancer Institute (U.S.)
NCR	National Cancer Registry
NHLS	National Health and Laboratory Services
NRF	National Research Foundation
Non-H L	Non-Hodgkins lymphoma
PRF	The Poliomyelitis Research Foundation
PROMEC	Programme for Mycotoxins and Experimental Cancer Research
RSA	Republic of South Africa
SEER	Surveillance Epidemiology and End Results
THRIP	Technology and Human Resources for Industry Programme
UICC	International Union for the Control of Cancer
US, USA	United States of America
WHO	World Health Organisation

3. INTERNATIONAL CANCER SITUATION

Incidence and mortality:

In order to understand the South African cancer environment it is necessary to focus on the international cancer situation so as to gain perspective.

According to Parkin et al. of IARC there were 10.9 million new cancer cases , 6.7 million cancer deaths, and 24.6 million persons living with cancer (within 5 years of diagnosis), in the world, in the year 2002 [1]. The 2002 figures for incidence and mortality of both sexes and the ten most lethal cancers are shown in Table.1.

Table 1. Global Incidence, Mortality and Case Fatality Ratio of the top ten deadliest cancers:

	Site	INCIDENCE					MORTALITY			Ratio
		Males		Females		Total Mil A ***	Males	Females	Total Mil B ***	CFR **** B/A
		Cases	ASR*	Cases	ASR		Cases	Cases		
1	Lung	965241	35.5	386891	12.1	1.35	848132	330786	1.18	0.87
2	Stomach	603419	22.0	330518	10.3	0.93	446052	254297	0.70	0.75
3	Liver	442119	15.7	184 043	5.8	0.63	416882	181439	0.60	0.95
4	Colorectal	550465	20.1	472687	14.6	1.03	278446	250532	0.53	0.51
5	Breast	-	-	1151298	37.4	1.15		410 712	0.41	0.36
6	Oesophagus	315394	11.5	146723	4.7	0.46	261162	124730	0.39	0.38
7	Cervix	-	-	493243	16.2	0.49	-	273505	0.27	0.55
8	Prostate	679023	25.3	-	-	0.68	221002	-	0.22	0.32
9	Non-H L**	175123	6.1	125448	3.9	0.30	98865	72955	0.17	0.57
10	Bladder	273858	10.1	82699	2.5	0.32	108310	36699	0.15	0.31
	Totals mil	4.00		3.37		7.37	2.68	1.93	4.62	0.63
	Percentage	54		46		100	58	42	100	

ASR = Age –standardised incidence rate*
Non-HL = Non-Hodgkin's lymphoma**
Total number of cases in millions***
CFR = Case Fatality Ratio =mortality/incidence. Survival percentage = (1-CFR) x 100****

A number of important insights emerge from Table 1. Firstly, lung cancer remains the most important, world-wide cancer because of the highest incidence (1.35 million), the highest number of deaths (1.18 million) and a very high case fatality ratio of 0.87, i.e. 13% survival. In comparison, breast cancer also has a high incidence but a relatively low case fatality ratio of 0.36, i.e. 64% survival. Secondly, in all cases of genderless cancers, males have on average 16% higher incidence rates than females.

The reason for this is not known. Thirdly there is a wide variation in fatality ratios from 0.95 for liver (5% survival) to 0.32 for prostate cancer (68% survival). There are many explanations for differing case fatality ratios and the following factors could all play an important role; successful screening programs and early eradication, accurate early diagnosis, tumour sensitivity for standard surgery, chemo- and radiotherapy protocols and a low metastatic potential. However, all the factors playing a role leading to survival are not yet known. (Generally poor people do not survive as well as the affluent).

Westernised, developed countries had more colorectal, prostate, breast and bladder cancer while developing countries had more stomach, liver, oesophageal and cervical cancers.

PROGRESS REPORT FROM THE UNITED STATES


Harold Varmus

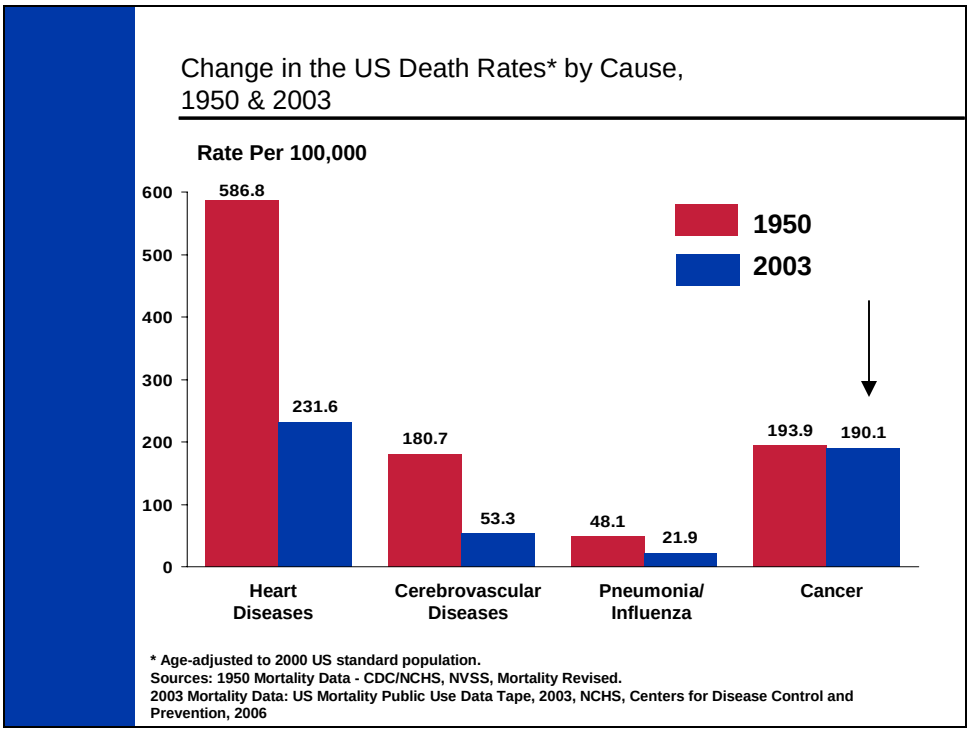
In a recent perspective article in SCIENCE with the title: "*The New Era in Cancer Research*", Nobel Laureate, original discovere of oncogenes, and previous Director of the NIH, Harold Varmus, had the following to say about the international cancer situation:

"The conquest of cancer continues to pose great challenges to medical science. The disease is notably complex, affecting nearly every tissue lineage in our bodies and arising from normal cells as a consequence of diverse mutations affecting many genes. It is also widespread and lethal; currently second most common cause of death in the United States, it is likely to become the most common in the near future.

Despite large federal and industrial investments in cancer research and a wealth of discoveries about genetic, biochemical, and functional changes in cancer cells, cancer is commonly viewed as, at best, *minimally controlled by modern medicine*, especially compared with major other diseases. *Indeed, the age-adjusted mortality rate for cancer is about the same in the 21st century as it was 50 years ago*, whereas the death rates for cardiac, cerebrovascular, and infectious diseases have declined by about two-thirds.[2] "

This dramatic conquest over diseases (other than cancer) is shown below in Fig. 1, which is a teaching slide from the American Cancer Society [3]:

Fig.1. Change in the US death rates by cause.



It can be seen that the age-adjusted mortality rate of about 190 cancer deaths per 100 000 population has not changed significantly since 1950 (arrow). In sharp contrast it is clear that heart disease and cerebrovascular diseases have decreased dramatically by almost two thirds. It is generally agreed that smoking reduction, healthy diets, statins and exercise have contributed significantly to the lowering in the incidence of cardiovascular disease. This lowering is due to physiological changes that take place rapidly. In the case of lung cancer, mutations due to smoking cannot be reversed and it takes decades for the incidence of lung cancer to decrease - essentially through the emergence of new, non-smoking generations. In the US today only 1 in 4 smoke and mortality reduction is imminent

At the American Association for Cancer Research (AACR) Cancer Conference in Washington DC in April 2006, it was announced that **for the first time in 70 years**, the mortality rate for the US had definitely started to drop by a few percentage points[4]. On February 9, 2006, the National Center for Health Statistics announced that the number of annual deaths had fallen for the first time in over 70 years. 556,902 Americans died of cancer in 2003, 369 fewer than in 2002. This decrease in death toll came despite the U.S. population growing 2.9 million from the end of 2002 to the end of 2003.

While the drop in cardiovascular disease incidence has made cancer the leading cause of death in the United States for people under the age of 85 , there are many cancer reduction programmes in the US and it is informative to study the Cancer Progress Report of the National Cancer Institute which is summarised in Table 2 [5]

Table 2: Checklist of progress in the battle against cancer in the US[5]

	ACTIVITY	DETAIL	OUTCOME	VALUE
1	Prevention	Child smokers	7% increase from 28% to 35% 1991-1999	Bad
2	Prevention	Adult smokers	2% decrease from 26% to 24% 1992-1998	Good
3	Prevention	Quitting smoking	5% of daily smokers 1992-1999	Good
4	Prevention	Alcohol	12% decrease 1990-1998	Good
5	Prevention	Fruits	1.3 to 1.5 servings 1989-1996	Good
6	Prevention	Vegetables	3.2 servings to 3.4 1989-1996	Good
7	Prevention	Fats	1% decrease from 34% to 33% 1989-1996	Good
8	Prevention	Obesity	15% increase 1971-1994	Bad
9	Prevention	Physical activity	2% decrease 1990-1998	Bad
10	Prevention	Sun protection	7% decrease 1992-1998	Bad
11	Prevention	Smoking laws	20 more states 1990-2000	Good
12	Prevention	Radon testing	9% increase in homes tested 1991-1998	Good
13	Prevention	Benzene in air	Fall from 3.2 to 1.85 Ug/m^3 1993-1998	Good
14	Early detection	Breast cancer	37% increase in women over 40 having mammograms. 1987-1998	Good
15	Early detection	Cervical screening	5% increase in PAP smears from 74% to 79% in women 18+ 1987-1998	Good
16	Early detection	Colorectal screening	7% increase in adults who had fecal blood test in 2 years 1987-1998	Good
17	Early detection	Colorectal screening	10% increase in sigmoidoscopy from 27% to 37%. Ages 50+ 1987-1998	Good
18	Diagnosis	Incidence –new cases per 100 000	400 to 471.1973-1998	Bad
19	Life after Cancer	Survival (5 years after diagnosis)	12% increase from 50% to 62% 1975-1993	Good
20	Life after cancer	Cost of cancer care	Stable at 4.7% of total US treatment spending. 1963-1995	Good
21	End of life	Mortality	Increase from 198.7 to 202.6 from 1973 - 1998	Bad

4. SOUTH AFRICAN CANCER SITUATION

Incidence, Mortality and Case Fatality ratios.

According to Mqoqi et al. of the National Cancer Registry (NCR) there were **60 343 new cancer cases** in South Africa in 1999 [6]. According to the mortality data of Bradshaw et al. of the Burden of Disease Research Unit of the MRC, there were **65 925 deaths** due to cancers in 2000 [7].

South African cancer incidence and mortality data do not harmonise.

South African cancer incidence (cases and ASR) as well as mortality (only ASR available) rates are presented in Table 3. It can be seen that unfortunately the overall case fatality ratio and survival rates cannot be measured , as was possible in Table 1, because all of the cancer mortality figures except for prostate, breast and cervix were considerably higher (about 200% more) than the cancer incidence figures (See shaded areas in Table 3). **This is completely the wrong way round.** Mortality should logically be lower, and not higher, than incidence. This glaring anomaly between the two independent data sets, from two different institutions, i.e. incidence from the NCR and mortality from the MRC, is most probably due to **under-reporting of cancer incidence.**

Table 3. Top ten cancer sites in South Africa for 1999 and a comparison of male and female ASR values for incidence and mortality.[6]

Cancer Site	INCIDENCE			INCIDENCE			Total cases
	Males			Females			
	Cases	I-ASR*	M-ASR**	Cases	I-ASR	M-ASR	
Breast	-	-	-	5901	33	18	5901
Cervix	-	-	-	5203	29	19	5203
Prostate	3860	34	27	-	-	-	3860
Lung	1738	14	40	721	5	12	2459
Oesophag	1540	11	25	909	6	11	2449
Colo-	1245	10	10	1122	6	7	2367
Bladder	1005	8	9	395	2	2	1400
Stomach	775	6	11	442	3	5	1217
Non-H L	630	4	7	545	3	4	1175
Liver	360	2	12	215	1	5	575
Totals	11153			15453			26606

I-ASR = Incidence: Age –standardised incidence rate per 100 000 of the population*
M-ASR = Mortality: Age –standardised incidence rate per 100 000 of the population**
Grey areas = Where Mortality ASR >> Incidence ASR

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There are serious problems with the South African National Cancer Registry.

In general it can be concluded that the inability to harmonise the incidence data (Cancer Registry) with the mortality data (Burden of Disease) suggests strongly that the National Cancer Registry is seriously flawed by under-reporting. The managers of the NCR are in no way to blame because they are doing sterling work but they can only use the data they get. They have no control over the source of the data. The only way this fundamental flaw could possibly be rectified is to either set up a network of population based cancer registries all over South Africa (very expensive) or advocate for the government to pass legislation necessary to make cancer a notifiable disease, so that no matter where, when or how cancer is diagnosed, such information is sent to the NCR for evaluation and tabulation. At present patient data concerning histological diagnosis and demography are sent to the National Cancer Registry by the NHLS, university, military services and private pathology laboratories, free of charge on a goodwill basis. However, because of patient confidentiality issues some of the contributors have ceased to co-operate with the NCR. Furthermore this registry is a number of years behind (last issue was 1999) and unfortunately does not report any geographic data so that cancer maps of South Africa are not possible. We do not know where the cancer "hot spots" –or "cold spots" - in South Africa are. We do know of instances where thousands were exposed in the past to local carcinogens, i.e. asbestos near Kuruman and aflatoxin-contaminated peanut butter sandwiches at schools in the Eastern Cape. We have no information on cancer incidence near nuclear and industrial facilities. South Africa needs a much better cancer surveillance capability.

Up to 50% of lung, oesophageal and liver cancer may not be diagnosed histologically at all.

Table 3 shows that in the case of lung, oesophageal and liver cancer the mortality ASR's are more than double that of the incidence ASR. This is highly abnormal and could only mean that in the case of at least 50% of these three cancers no histological diagnosis were made due to late presentation, logistical insufficiencies or other reasons such as only making clinical diagnoses in order to reduce costs. A more worrying possibility is that the missing incidence data could partially have been due to non-presentation of about 50% of the patients with these cancers. It is most important to find out the exact reasons why the incidence figures of these cancers are so low compared to the mortality figures. In the case of liver cancer the mortality ASR is six-times that of the incidence ASR in males. This is the biggest anomaly of all and could be due to ready clinical diagnosis due to macroscopic appearance of this cancer, facile blood tests and the inherent danger of taking a histological biopsy from the liver. It could also be due to non-presentation of patients due to the generally know fact that cures for liver cancer hardly exist (Case fatality ratio = 0.95, i.e. 5% survival).

5.PROGRESS REPORT FROM SOUTH AFRICA

Cancer incidence and mortality:

The only available data for a Cancer Progress Report from South Africa is the incidence and mortality ASR's from the NCR (1999)[6] and Burden of Disease Report[7] which are compared to data of the World (2002)[1] and the USA (2002)[8] in Table 4.

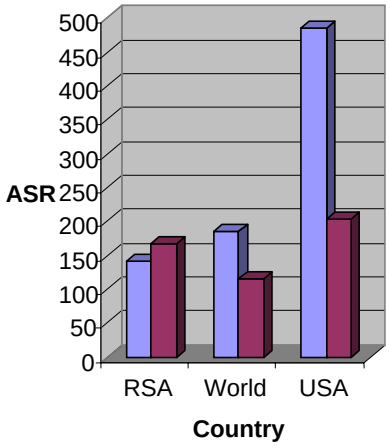
Table 4. Comparison of ASR incidence rates in men and women in South Africa, the world and the USA

Country	SOUTH AFRICA		WORLD		UNITED STATES	
	Incidence A*		Incidence A***		Incidence A****	
Gender	Males	Females	Males	Females	Males	Females
ASR	148	135	209	161	558	412
Average	142		185		485	
	Mortality B**		Mortality B***		Mortality B	
Gender	Males	Females	Males	Females	Males	Females
ASR	184	152	138	92	242	164
Average	168		115		203	
Ratio of B/A	1.18		0.62		0.42	

Pages 86-87 Reference 6* Pages 182-183 Reference 7** Table 1 Reference 1***
Tables I-4, I-5 & I-6 Reference 9****

Fig. 2: Graphic presentation of the comparison of cancer incidence and mortality rates in South Africa, the World and the USA.

Incidence (cases/100 000) indicated by left columns and mortality by columns on the right



It can be seen in Fig.2 that in the World and the USA cancer incidence is higher than mortality – as it should be. In South Africa mortality is higher than incidence, signalling a problem. In order for the mortality/incidence ratio to be the same in South Africa as in the world (Ratio = 0.62), an **extra 54 507 cancer diagnoses** would need to be made p.a.(Appendix 2) This implies that the cancer surveillance in South Africa by the NCR covers only **52%** of the cancer population or that the survival percentage is lower than the world average of 55% – or both.

Nevertheless, it is disturbing that in South Africa we have no available data to monitor the progress of all our efforts against cancer with any certainty except for age adjusted incidence of mortality.

Deeper analysis of the mortality data shows that for most cancers the mortality rates are similar to the rest of the world except for female lung cancer and male and female colon cancer compared to the USA - as is shown in Table 5.

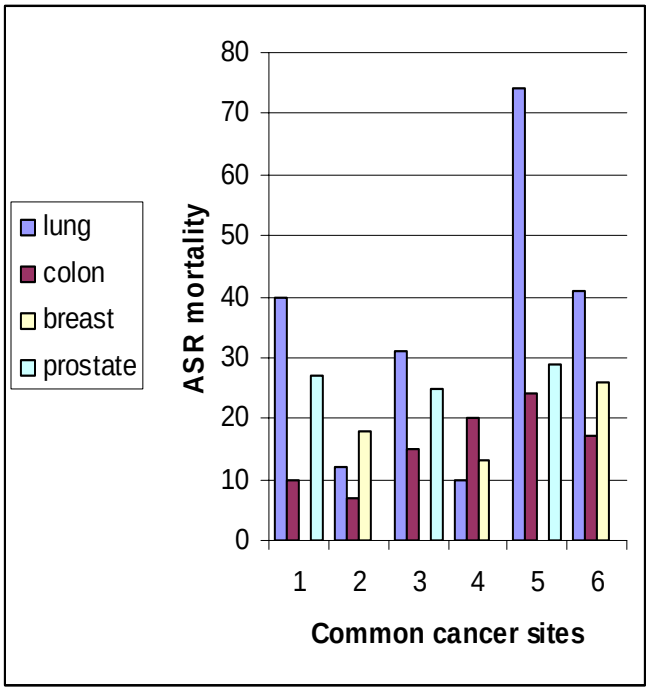
Table 5: Mortality rates of common cancers in South African, World and USA males and females.

	RSA		World		USA	
	Males	**Females**	**Males**	**Females**	**Males**	**Females**
Lung	40	12	31	10	74	41
Breast		18		13		26
Prostate	27		25		29	
Colon	10	7	15	20	24	17

The shaded areas indicate the the "golden opportunities" of the best target cancers for preventative intervention in order to maintain low mortality rates.

The data in Table 5 are presented graphically in Fig.3

Fig.3 Mortality rates of common cancers in South African, World and USA males and females



Groups:

1. RSA Males
2. RSA Females
3. World Males
4. World Females
5. USA males
6. USA females

Fig.3 shows that cancers with lowest mortality in RSA vs. USA are RSA males & female colon and RSA female lung. Breast and prostate are close to world and USA rates.

Conclusion: Mortality data is more compatible with World and USA data compared to incidence data that creates the impression of far greater differences in incidence rates compared to the World and USA. This impression is most probably erroneous except for colon and lung in the Black population group where the mortality figures are also significantly lower.

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Assuming that the data from the burden of disease studies is reasonably reliable, the question can be asked –"*How many extra cancer patients would there be if the common cancers in South Africa reached mortality rates similar to the USA*?" Table 6 and 7 contain data aimed at answering this question.

Table 6. Potential for increased number of cancer cases in South Africa.

Cancer site	**RSA :A**		**USA:B**		**Difference:B-A**	
	Mortality cases ASR		**Mortality cases ASR**		**Mortality cases ASR**	
	Males	**Females**	**Males**	**Females**	**Males**	**Females**
Lung	40	12	74	41	34	29
Breast		18		26		8
Prostate	27		29		2	
Colon	10	7	24	17	14	10
				Totals	50	47

The data in Table 6 can be used to calculate the increased number of cancer mortalities in South Africa if the ASR of year 2000 increased to that of the ASR in the USA for year 2003. This calculation is shown in Table 7.

Table 7. Calculation of the increased number of cancer mortalities in South Africa

Cancer Site	**Increased ASR units*** **A**	**Population size**** **B**	**Sum of A x B** **AxB**
Lung	31	450	13 950
Breast	8	225	1 800
Prostate	2	225	500
Colon	12	450	5 400
		Total	**21 650**

Difference between ASR mortality for RSA year 2000 and USA year 2002 *

RSA population = 45 000 000. ASR is per 100 000. For males + females average ASR multiplies with 450 while for male or female only ASR multiplies with 50% of population, i.e. 225.**

Using only mortality data, Tables 6 and 7 show that compared to the USA South Africa has **21 650** less cancer patients per capita in terms of lung, breast, prostate and colon cancer.

From this it is concluded that the biggest opportunity for preventing cancer in South Africa lies with lung cancer which is **"under-represented"** by **13 950** patients per year of the whole population.

From Table 7 it is clear that the main opportunity for cancer prevention in South Africa lies with maintaining the low cancer mortality rate in Black women. This rate is **342%** lower than the rate for Black women in the USA.

Indices for cancer control reporting in South Africa:

The data presented here support the hypothesis that the NCR data is unreliable and probably significantly under-reported especially in terms of the Black population group of South Africa. Unfortunately the morbidity data of the Burden of Disease report of the MRC is not differentiated into race groups because if it was, this would be an alternative source of information to test the hypothesis that the NCR data was biased towards surveillance of cancers in the White group rather than in the Black group. These uncertainties regarding the veracity of the NCR lead to the conclusion that mortality data is more reliable for monitoring the South African cancer situation. This being the case, the following parameters can be presented for ongoing progress monitoring in the struggle against cancer in South Africa.

- General cancer mortality ASR (Available)
- Mortality rate of lung cancer in Black females
- Mortality rate of colon cancer in Black males
- Mortality rate of colon cancer in Black females
- Mortality rate of cervical cancer (Available)
- Mortality rate of oesophageal cancer (Available)
- Smoking in high school children especially Black girls
- Smoking in Black women –metropolitan areas
- Smoking in Black women – rural areas

6. INTERNATIONAL CANCER RESEARCH SITUATION

There is no obvious source of information concerning all cancer research projects in the world and what the current, dominant research themes, results and applications are. Nevertheless, by attending the international conference of the American Association for Cancer Research (AACR) in Washington DC during April 2006 and reading seminal articles in leading international journals a degree of contectualisation is possible. What follows should be regarded to some extent as eclectic.

The rise of Molecular Oncology:

The May 26th 2006 issue of **SCIENCE** (Journal of the American Association for the Advancement of Science - AAAS) contains a special section on the ***"Frontiers in Cancer Research"***[2]

According to articles in this issue of **SCIENCE** the main topic in current international cancer research is - **the rise of molecular oncology.**

This is defined by Harold Varmus as follows:

"Understanding the genetic and biochemical mechanisms by which cancers arise and behave is now widely believed to portend improvements in the way we detect, classify, monitor, and treat these diseases"

The key concept is that molecular research will come up with the most important answers and most of the work is directed at better therapy, i.e. less toxic and more specific treatments.

Cancer prevention is hardly mentioned at all.

The main aspects of **Molecular Oncology** were reported top be the following:

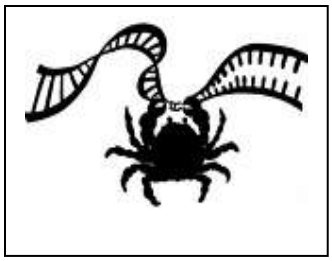
- **Genetic basis of cancer**

  Mutations are now recognised to be the fundamental lesions driving cancer.

  When certain normal genes are mutated they become oncogenes that drive cancer. The inactivation of suppressor genes also drive cancer.

  There are 350 different genes involved in driving cancer

  Germ line mutations associated with cancer have been found in 66 genes.



- **Hallmarks of cancer**

  Acquisition of self-sufficient signals for growth

  Capacity for extended proliferation

  Resistance to growth-inhibiting signals

  Ability to evade cell death signals

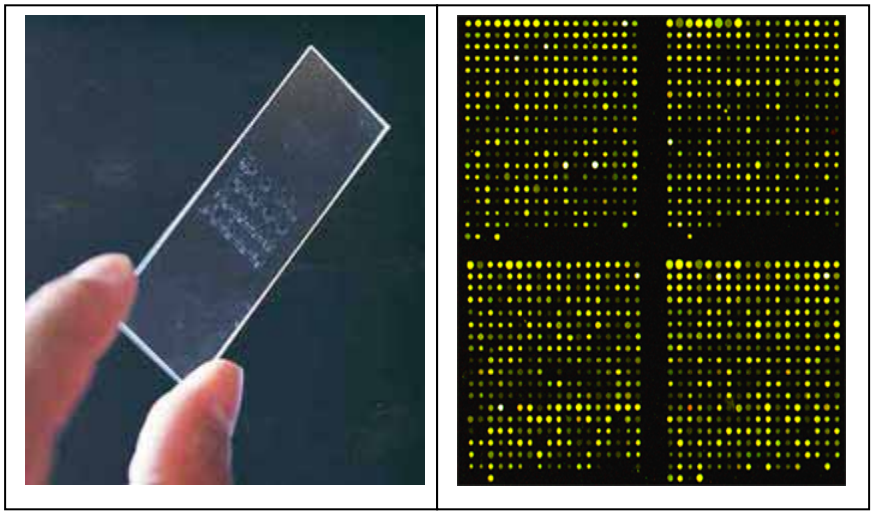
  Potential for tissue invasion and metastasis

  Power to induce blood-vessel formation
  (angiogenesis)

- **Classification of tumours based on DNA and RNA**

  Use is made of microarrays which can screen thousands of genes on one slide.

  Uncertain art practised in a few academic centres



- **Development of reliable new biomarkers for the detection of tumours.**

  Based on evidence of changes in the structure or production of certain proteins in specific cancers -this has yet to occur

- **Development of novel, high-affinity ligands for imaging.**

- **Oncogene dependence**

  Unexpected discovery that interfering with oncogenes can lead to apoptosis (programmed cell death). (In simple terms, the cancer cell is addicted to its oncogenes and if they are inactivated the cancer cell commits suicide.)

  Development of therapeutic agents that interfere with major oncogenes such as KRAS and MYC

- **Mutational Repertoire of different cancer cells**

  The Cancer Genome Atlas (TCGA) initiative of the NIH intends to sequence 1000-2000 genes (exons only) in various cancer cells in order to plot the various "roadmaps" of cancer at the molecular level. The relative importance of each oncogene will also be determined and this knowledge is hoped to facilitate better drug development.

- **Deciphering mechanisms of resistance and developing multi-agent treatment protocols.**

  One of the biggest problems in chemotherapy of cancer is the development of resistance as has occurred with the new drug Gleevec (Imatinib) which blocks the BCR-ABL tyrosine kinase and dramatically inhibits clonal expansion of pluripotent hematopoietic stem cells that underlies CML. It is hoped that multi-agent protocols, as in the case of HIV proliferation will also be highly successful in treating certain cancers.

- **Better characterisation of tumour stem cells which are the ultimate target of therapy**.

  There is a growing awareness that only a few percent of cells in a tumour are stem cells which are most likely to be resistant to treatment. New drugs should be tested against stem cells.

Non-molecular Oncology:

Varmus also recognises other developed, improved and widely used means to control cancer over and above the promise of molecular oncology and lists the following:

- **Strategies for prevention such as smoking cessation programmes**

- **Vaccination against cancer-promoting viruses such as hepatitis B and papilloma viruses.**

- **Methods for detection of premalignant lesions and early cancers such as:**

  PAP smears
  Mammography
  Colonoscopies

PAP smear

- **Neurotrophic medications to control the ancillary symptoms of cancer, most obviously pain and nausea**

- **Growth factors to blunt the side-effects of cytotoxic treatments such as anemia and leucopenia.**

- **Psychosocial methods for managing the response of patients and families to the diagnosis and treatment of cancers.**

- **To this list could also be added prevention strategies involving healthy lifestyles with reference to:**

- Diet
- Physical exercise
- Avoidance of obesity
- Avoidance of excessive sunlight while obtaining sufficient sunlight for optimal synthesis of vitamin D
- Avoidance of exposure to oncogenic viruses and carcinogens such as aflatoxin

The UICC and Cancer Research:

http://www.uicc.org/index.php?id=1257&L=0

Unlike the philosophy of molecular oncology portending (foreshadowing) improvements in cancer control, the UICC has a philosophy of governments implementing cancer control programmes immediately with existing strategies of evidence-based early detection, prevention, treatment and patient care.

National cancer control planning

Responding to the challenge of cancer burden

Current cancer patterns reflect the way we live, and global trends for cancer burden are on the rise, both in developed and developing countries.

Today, cancer causes almost 7 million deaths every year, corresponding to 12.5% of deaths worldwide. Close to 11 million people are diagnosed with cancer every year, a figure estimated to rise to a staggering 16 million by 2020.

Cancer risk factors such as tobacco smoking, unhealthy diet and physical inactivity, exposure to infections and carcinogens, and longer life expectancy all contribute to these rising trends. And yet, through research we know that by making appropriate lifestyle choices, up to one-third of all cancers could be prevented; through early detection and effective treatment, lethal consequences could be avoided in another third; further, pain relief and palliative care would increase the quality of life of cancer patients, even in low-resource settings.

Cancer control is a public-health approach aimed at reducing the burden of cancer in a population. Planning integrated, evidence-based and cost-effective interventions throughout the cancer continuum (from research to prevention, early detection, treatment, palliative care) is the most effective way to tackle the cancer problem and reduce the suffering caused to patients and their families.

In response to the enormous burden of cancer, countries around the world are developing or have already developed national cancer plans. These plans are based on a systematic review of the cancer burden of the nation and the scientific base regarding what has proven effective in decreasing the burden. The plans identify the priorities and specific actions that a nation should take to reduce its cancer burden.

Most nations, however, have yet to begin a systematic national cancer planning effort and many are just becoming aware of the opportunity to do so. Where governments are concentrating on other immediate health priorities, NGOs can play a critically important role in increasing public and leadership awareness of the cancer problem and in developing effective partnerships that can take on the responsibility of cancer planning.

The WHO and cancer Research

http://www.who.int/cancer/en/

The WHO has a cancer control/research philosophy very similar to that of the UICC, as outlined below:

WHO cancer control programme

Cancer is a public health problem worldwide. It affects all people: the young and old, the rich and poor, men women and children

Cancer is the uncontrolled growth and spread of cells that may affect almost any tissue of the body. Lung, colorectal and stomach cancer are among the five most common cancers in the world for both men and women. Among men, lung and stomach cancer are the most common cancers worldwide. For women, the most common cancers are breast and cervical cancer.

More than 11 million people are diagnosed with cancer every year. It is estimated that there will be 16 million new cases every year by 2020. Cancer causes 7 million deaths every year—or 12.5% of deaths worldwide.

We now know enough about the causes of cancer to prevent at least one-third of all cancers. Cancer is largely preventable: by stopping smoking, providing healthy food and avoiding the exposure to carcinogens. Information is also available that would permit the early detection and effective treatment of a further one-third of cases. Some of the most frequent cancer types are curable by surgery, chemotherapy or radiotherapy. The chance of cure increases substantially if cancer is detected early. There are effective strategies for the relief of pain and the provision of palliative care to all patients and their families, even in low resource settings.

- promotion and strengthening of comprehensive national cancer control programmes;
- building international networks and partnerships for cancer control;
- promotion of organized, evidence-based interventions for early detection of cervical and breast cancer;
- development of guidelines on disease and programme management;
- advocacy for a rational approach to effective treatments for potentially curable tumours;
- support for low-cost approaches to respond to global needs for pain relief and palliative care.

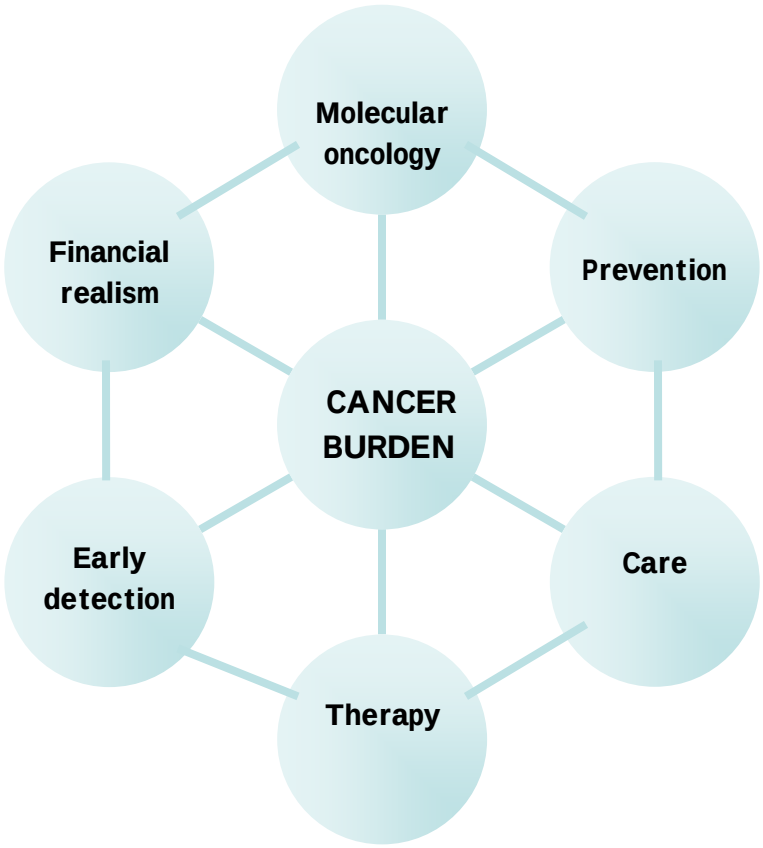
Cancer control is a public health approach aimed at reducing causes and consequences of cancer by translating our knowledge into practice. WHO's work towards the prevention and control of cancer focuses on these major areas:

The Cancer Programme is a key activity within the Department of Chronic Diseases and Health Promotion.

7. A HOLISTIC APPROACH TO CANCER RESEARCH AND CONTROL

According to Varmus, successful control of cancer will require more than just new technologies, whether molecularly based – or not. It also calls for elimination of disparities in care – and in access to care – that are based on racial and economic factors. Possible holistic schemes of the cancer research (and control) environment are presented here for consideration.

Fig. 4 Model A: HOLISTIC NETWORK



Important features:

1. All aspects of the scheme are both control measures or research fields.

2. All aspects are linked to each other and should be aimed at reducing the cancer burden

3. Molecular oncology supports early detection, prevention and therapy with new insights, techniques and products.

4. Prevention involves a wide spectrum of activities from health promotion to vaccines, drugs, supplements, sun creams and condoms.

5. Early detection involves PAP smears, sigmoidoscopy, mammography, PSA-blood test, imaging with CT, MRI and PET as well as new imaging and molecular technologies being developed

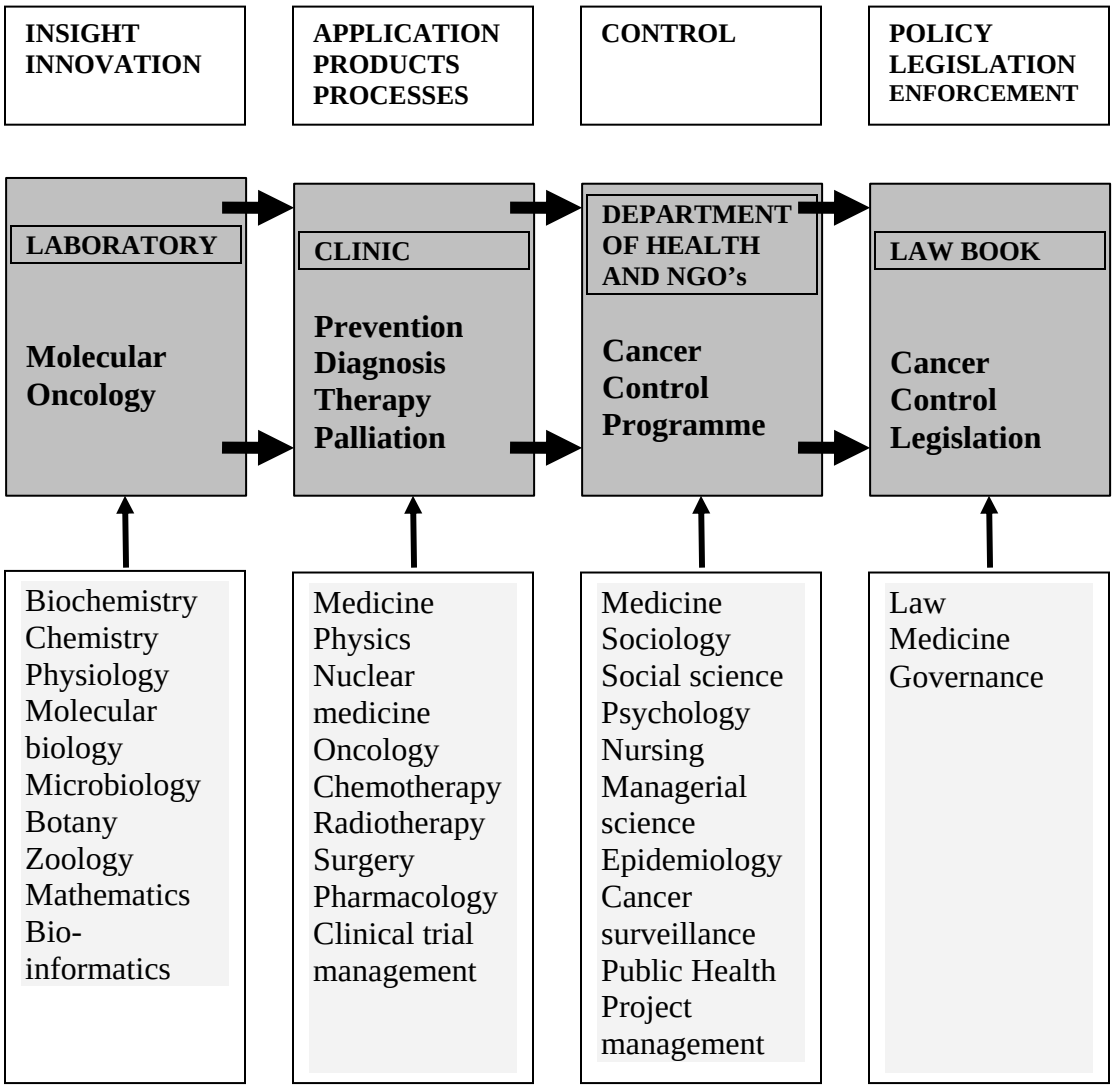
6. Treatment involves standard chemotherapy, radiotherapy, surgery and experimental drugs including anti-oncogene drugs such as tyrosine kinase inhibitors (Imatinib, Dasatinib), HER2 binders (Trastuzamab/Herceptin, Lapatinib) as well as new antiangiogenic drugs (Bevacizumab).

7. Personalised treatment based on the gene profile of the tumour before and after treatment.

8. Cancer research and control should be affordable (financial realism). (The average cost of molecularly targeted cancer treatments has increased from $20 000 per patient per year to about $100 000 per patient per year.)

9. Care involves psychosocial support after diagnosis, pain and nausea control during therapy.

FIG. 5 Model B: CANCER CONTINIUM or Translation from MOLECULES to LAWS.



Important Features:

1. Molecular oncology, mainly in the laboratory, leads to new insights, technologies and products enhancing prevention, diagnosis, therapy and palliation in society and in clinics.

2. Prevention, diagnosis, therapy and palliation are important parts of cancer control programmes

3. Cancer control programmes lead to sustainable and enforceable legislation.

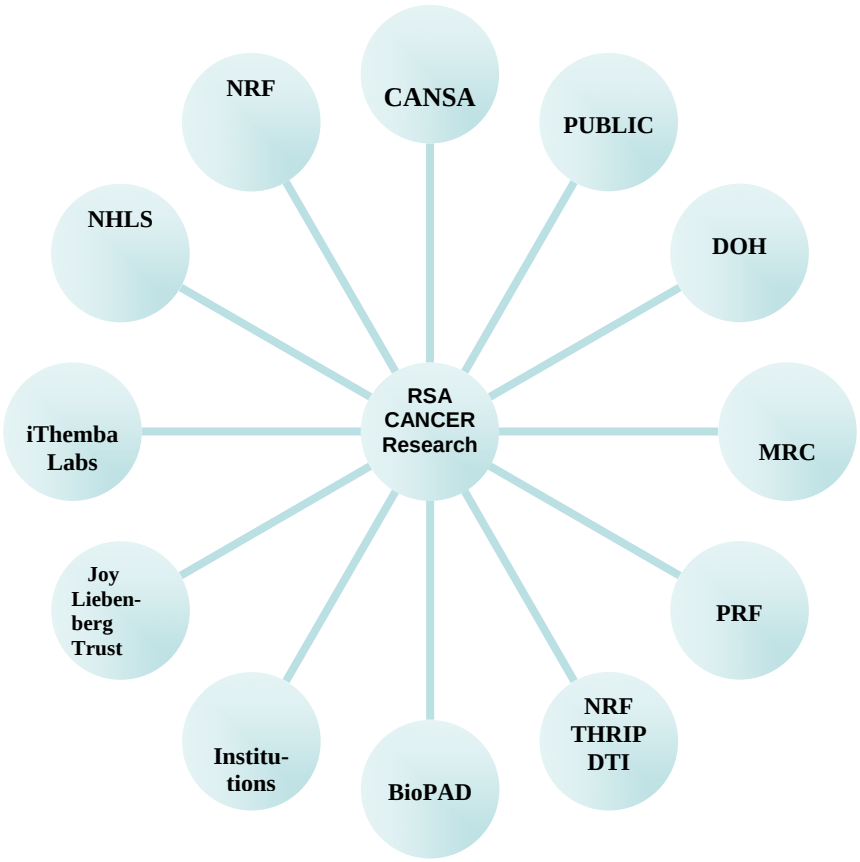
4. Sustainable enforceable legislation (eg. Anti-smoking laws) affect the whole population and help to reduce the burden of cancer on a large scale.

8.THE SOUTH AFRICAN CANCER RESEARCH SITUATION

8.1 The Stakeholders:

There are at least 10 stakeholders in South African cancer research, i.e. Cancer Association of South Africa (CANSA), Medical Research Council (MRC), National Research Foundation (NRF), Technology and Human Resources for Industry Programme (THRIP), Department of Trade and Industry (DTI), Biotechnology Partnership and Development (BioPAD), South African Department of Health (DOH), National Health Laboratory Services (NHLS) , The Poliomyelitis Research Foundation (PRF), iThemba Labs (National Accelerator Centre), Joy Liebenberg Trust, Universities and the public for donating funds for research and taking part in research projects.

Fig.6 Stakeholders in cancer research in South Africa



Roles of the Stakeholders:

The different stakeholders in South African cancer research play different roles as indicated in Table.8

Table 8. Roles of stakeholders in South African cancer research

	Stakeholder	Role in cancer research
1	**CANSA**	Fund research projects Evaluate research projects Prioritise research Invest and allocate public donations for research Evaluate research output
2	**MRC**	Fund research projects Evaluate research projects Prioritise research Allocate government funds
3	**BioPAD**	Fund research and development projects towards commercialisation Evaluate research projects Prioritise research
4	**DOH/NHLS**	Fund National Cancer Registry Conceptualise, research and promulgate legislation
5	**NRF/THRIP/DTI**	Fund research projects (NRF) Evaluate research projects Fund existing projects leading to a novel process or product (THRIP funded by the DTI)
6	**PRF**	Fund research projects involving oncogenic viruses
7	**Joy Liebenberg Trust Fund**	Fund cancer prevention related research. Administered by ABSA
8	**Universities/institutions**	Employ researchers and fund laboratories. Partially fund research projects Create intellectual property Create new knowledge
9	**Members of the Public**	Donate funds for cancer research. Take part in clinical trials Take part in cancer control interventions
10	**iThemba Labs**	Proton & neutron therapy Production of isotopes for imaging

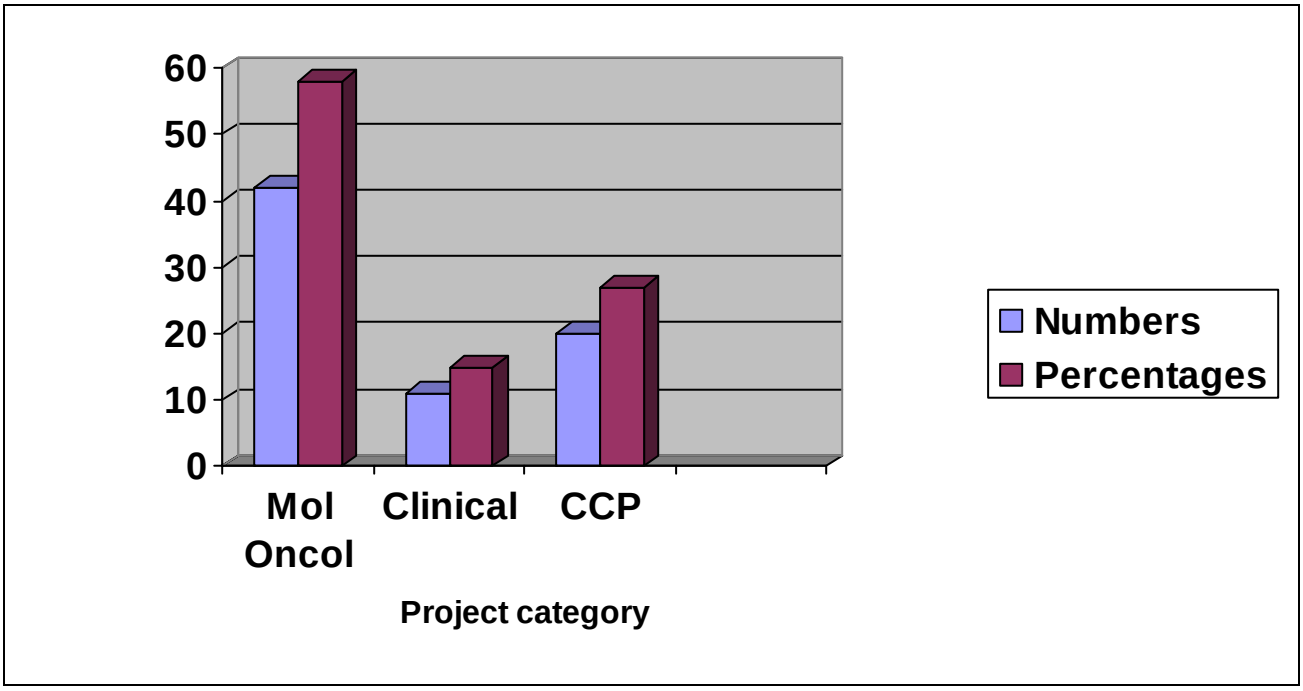
8.2 Research Projects:

According to available information there are a total of at least 73 cancer research projects being conducted in South Africa during 2006.

Information concerning the principal investigator, institution and tile of research project are contained in Appendix 1.

The cancer research projects can be categorised in terms of molecular oncology (Mol Oncol), clinical aspects (Clinical) and cancer control aspects (Control) as shown in Fig.7.

Fig.7 Comparison of the number of research projects involving molecular oncology (mol oncol), clinical research (clinical) and cancer control programme (CCP) aspects such as epidemiology.



There were 42(58%) molecular oncology projects, 11(15%) clinical projects and 20(27%) cancer control projects. Compared the cancer control, there are twice as many molecular oncolgy cancer research projects, while clinical projects are half as many as control projects, i.e. there is a 4: 2: 1 relationship.

The dominant status of molecular oncology could be due to the belief that fundamental innovations leading to early detection, prevention, therapy and palliation will come from biochemical studies. A Ph.D project involving molecular oncology can also be executed in a few years at a reasonable expense, while clinical and control research, such as clinical trials and interventions, often need more time and funds.

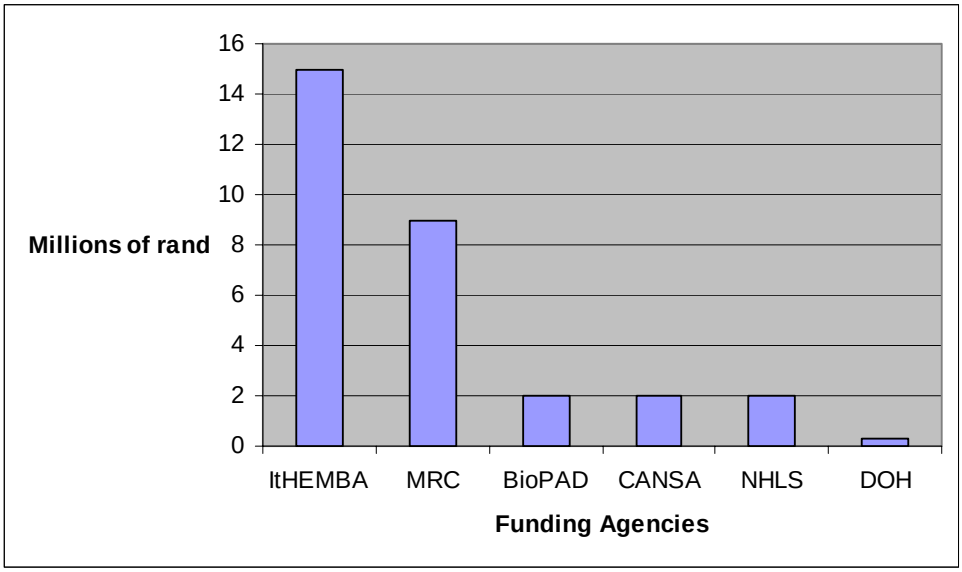
8.3 Funding of cancer research in South Africa:

The total funding for cancer research in South Africa for 2006 is reflected in Table. 10 and Fig. 8

Table 10. Funding of cancer research in South Africa

	Funder	Amount (millions of RSA Rands)
1	**CANSA**	R2.7
2	**MRC-self initiated projects**	R1.2
3	**MRC-Unit projects**	R7.7
4	**THRIP**	R1
5	**BioPad**	R2
6	**NHLS**	R2
7	**DOH**	R0.3
8	**NRF: Innovation Fund**	?
9	**iThemba**	R15
	TOTAL	**R32**

Fig. 8 Funding of cancer research in South Africa



Comparison of cancer research funding:

At the original founding meeting of CARISA at the MRC on the 16th and 17th of February, 2004, the 29 participants listed **resources** (funding, manpower, knowledge) as the main strategic issue facing cancer research. Information is now readily available on the funding of cancer research in the US, EU countries and Australia. A reasonable way to present data for comparisons is to calculate the spending per capita as US dollars [9,10]. Such a comparison is shown in Table 11 and Fig.14

Table 11. Comparison of direct spending on cancer research[9,10]

Country	Funding Body	Funding allocated to cancer research and infrastructure	Total estimated funding	Population	US Dollars invested per head of population
United States	**NCI** **ACS**	3982.8M 168.6M	$4151.4M	288M	$14.41
United Kingdom		$499M	$499M	60M	$8.32
Germany		$463	$463	82M	$5.65
Denmark		$26M	$26	5.4M	$4.8
France		$256M	$265	61M	$4.34
Australia	**NHMRC** **State Cancer Councils**	23M 19.8M	$42.8M	19M	$2.25
South Africa	**All**	R32 M	$4.6M	45 M	$0.1

Fig 9. Comparison of spending on cancer research in the US, EU countries, Australia and South Africa in terms of US$ per person.

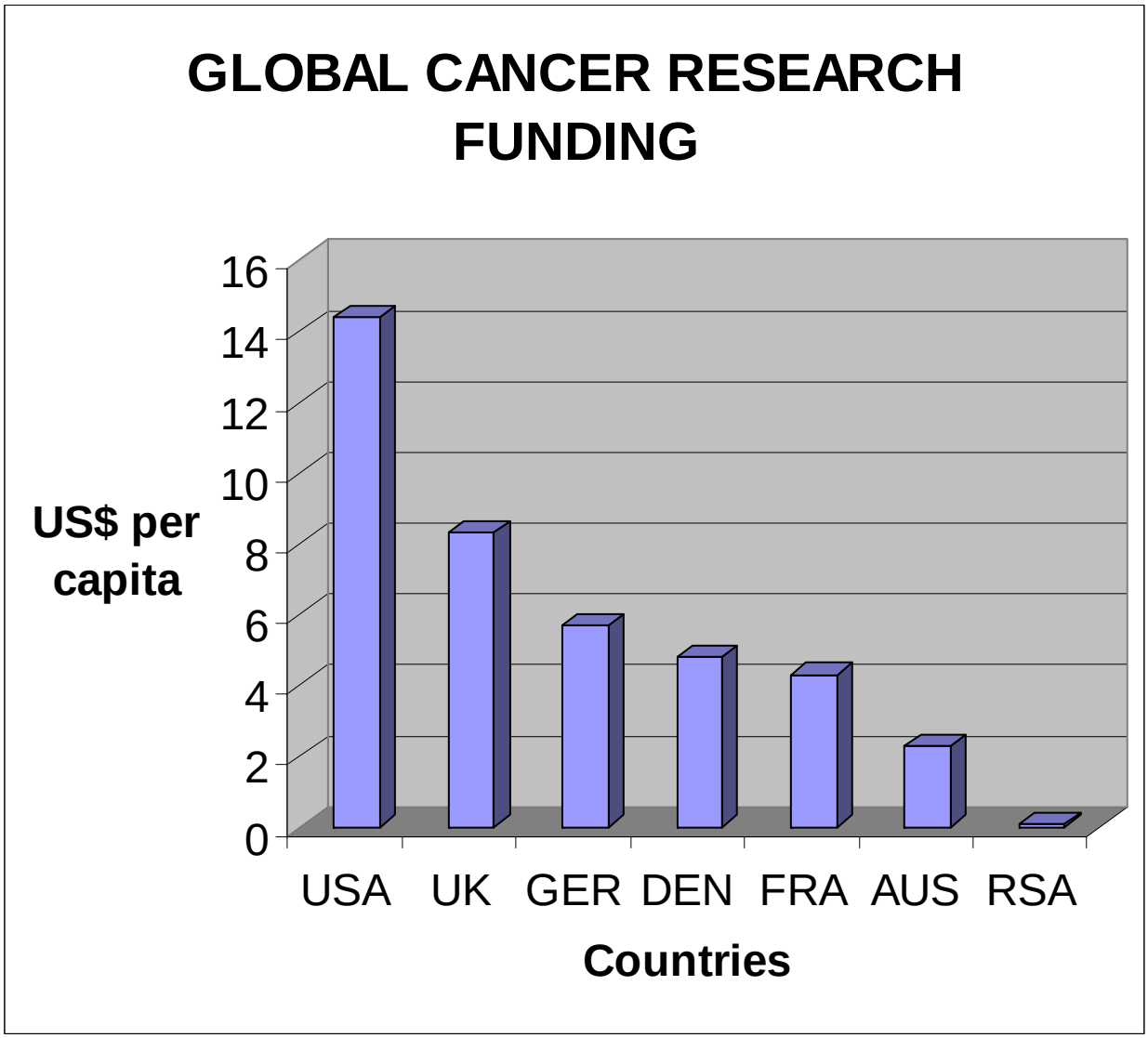


Table 12: Comparison of cancer research spending in US dollars per person and as a percentage of the USA spending in dollars [9,10]

	US	UK	GER	DEN	FRA	AUS	RSA
Country	**United States**	**United Kingdom**	**Germany**	**Denmark**	**France**	**Australia**	**South Africa**
US$/person	**14.4**	**8.3**	**5.7**	**4.8**	**4.3**	**2.3**	**0.1**
Percentage where USA=100	**100**	**58**	**40**	**33**	**30**	**16**	**0.7**

8.4 Patents from cancer research:

The following patents have resulted from cancer research funding in South Africa.

At present there are at least 5 patents:

Table 13. Patents from cancer research in South Africa.

	PATENT	AUTHORS	Number
1	*Oral immunization with papillomavirus virus-like particles*	Rose; Robert C. (Dansville, NY); *Williamson*; Anna-Lise (Cape Town, ZA); Rybicki; Edward P. (Cape Town, ZA)	6,153,201
2	*A multimeric self-cleaving ribozyme construct.*	Patrick Arbuthnot and Marc Weinberg	Patent accepted by South African patent office October 2004
3	*The invention relates to a method of inhibiting Hepatitis B Virus replication with a multimeric hammerhead ribozyme.*	Patrick Arbuthnot	South African Patent number 2004/08825
4	A self-cleaving RNA expression cassette.	Patrick Arbuthnot, Marc Weinberg, Abdullah Ely and Sergio Carmona.	PCT/IB2004/002816 National filings (USA and RSA) carried out on 1 March 2006
5	*MDR resistance treatment and novel pharmaceutically active riminophenazines*	Medlen; Constance Elizabeth (Pretoria, ZA); *Anderson*; Ronald (Pretoria, ZA); O'Sullivan; John Francis (Dublin, IE)	June 9, 1998 5,763,443

8.5 Conferences:

Cancer research conferences funded entirely by CANSA were held in 1979, 1980, 1982 and 1997. There were no conference fees and all bona fide cancer researchers in South Africa were invited to attend free of charge, except for students who had to pay their own S&T expenses.

8.6 Consortiums:

During 1997 CANSA decided to double expenditure on cancer research and at the same time create a raft of consortiums to address cancer problems of national priority. Researchers were invited to tender for these funds by writing comprehensive proposals.

During the Research Committee meetings of CANSA in 1997/8/9 it was decided to initiate 10 new cancer research consortiums. Details of these consortiums are indicated in Table 14:

Table 14: Details of CANSA cancer research consortiums:

	Consortium	Mission	Status
1	Primary liver cancer	Aetiology & pathogenesis	Ongoing
2	New anti-cancer drugs	Discovery &preliminary testing	Ongoing with development funding from BioPAD
3	Colon cancer	Genetics, diagnosis, prevention, surgery	Ongoing
4	HPV vaccine	Vaccine development	Discontinued Funded by NRF Innovation Fund
5	Stress and cancer	Measurement, coping	Discontinued
6	Breast cancer	Biology, genetics, treatment	Discontinued
7	Oesophageal cancer	Biology, aetiology,early diagnosis	Discontinued
8	Prostate cancer	Epidemiology	Discontinued
9	Apoptosis	Biochemistry, activators from indigenous medicinal plants	Discontinued
10	Cancer epidemiology	Aetiology, incidence	Discontinued

Reasons for discontinuation were the following:

- Principal investigator leaving the country
- Principal investigator changing research field
- Much larger funding required
- Lack of productivity

8.7 Ten year audit of CANSA funded research projects:

In 2004 CANSA decided to retrospectively analyse the funding and productivity of all funded research projects over a ten year period from 1994 to 2003.

This study has been completed and is in manuscript form prior to submission for publication. The main findings of the study were the following:

OUTCOME OF THE AUDIT OF 10 YEARS OF CANCER RESEARCH FUNDED BY CANSA: 1994-2003

- 129 researchers from 10 institutions in South Africa.
- 192 projects
- **570 peer-reviewed publications which could be found in PubMed**
- CANSA spent R28.2 million (2000 value) – equal to $4.8 million (2000 value)
- **The mean Impact factor of all of the publications was 3.8**
- **The number of publications per $1 million was 119 and the cost of a publication was US $8 379 (RSA R49 436)**
- **According to international publications the CANSA sponsored researchers did exceptionally well in terms of the relatively low cost per publication (r50 000 vs. R700 000) and Impact Factor (3.8 vs. 3.2 for US oncology publications from EU countries)**
- During the 10 years grantees published from 0 to 79 publications.
- Thirty six percent of the grantees did not publish a single paper
- In order to prevent this lack of productivity a tri-partite legally-binding agreement is being drafted, to be signed by CANSA, grantees and their institutions, before a project starts, stating that the absence of publications after 4 years, without valid reasons, will necessitate the full refunding of the grant to CANSA by the institution

9. Cancer control matrix for research, health promotion and advocacy:

At the original Cancer Workshop 16-17 February 2004 at the MRC, it was decided that a useful format for conceptualising cancer research opportunities in South Africa could be to construct a matrix consisting of major cancers on the x-axis and cancer control categories on the Y-axis as shown below in Fig.

Table 15. Cancer research and control matrix[11]

	Breast	Cervix	Prostate	Lung	Colon	Oesopha-geal	Liver	Kaposi's	Lym-phoma	Head & Neck (Mouth, oro-pharynx)
Numbers of cancer deaths in 2000	3062	3424	2411	7173	2446	5803	2692	Not listed as such	1018	1464
Ranking as cause of cance death	4	3	7	1	6	2	5		12	10
Process:										
Primary Preven-tion	Genetic counsel-ling	HPV vaccine		Anti-smo-king	Genetic counsel-ling	Health promo-tion	Hepatitis B Vaccine Anti-aflatoxin measures	Health promo-tion Safe sex	Health pro-motion Safe sex	Health promo-tion Anti-smoking
Secon-dary Preven-tion		PAP	PSA			Brush biopsy				Dentists
Treat-ment	Clinical Trials Drug discovery	Smit Tube Drug discovery	Drug discovery Hormone trials. Distinction between Aggressive, non-aggressive types re surgery	Drug dis-covery	Drug dis-covery	Drug dis-covery Radia-tion schedules	Drug dis-covery Radia-tion schedules	Drug dis-covery Radiation schedules	Drug dis-covery Radiation schedules	Drug dis-covery Radiation schedules
Pallia-tion		Search for cost effective schedules								
Demo-graphics	+	+	+	+	+	+	+	+	+	+
Advo-cacy										
Audit		Bloch study Only 20% have had PAP smear					Peanut butter story			

10. SWOT Analysis:

(N.B. These are the independent opinions of the author)

Strengths:

- Proven high quality and productivity of South African cancer researchers
- Proven low cost of peer-reviewed articles in high impact journals
- South Africa a natural laboratory for cancer research with 4 different population groups, developed and underdeveloped areas with widely differing cancer incidence rates.
- Proven role models for successful translation along the cancer continuum e.g. from molecular studies on hepatitis C in the etiology of primary liver cancer leading to legislation for vaccination against hepatitis C antigen - thus sealing the end of primary liver cancer in South Africa
- Relatively low cost of clinical trials
- Growing biotechnology base that can act synergistically with cancer research (molecular oncology, early diagnosis, drug development).
- CARISA

Weaknesses:

- Cancer not a national priority, consequently cancer research not a national priority
- No established Cancer Control Programme policy at the DOH
- Extremely low funding from MRC and other stakeholders compared to international standards
- No National Cancer Institute
- Inadequate and dysfunctional National Cancer Registry
- Lack of population based cancer registries
- Insufficient funding for individual cancer research projects
- No cohesive organisation for cancer researchers

- Sporadic cancer research conferences
- Lack of cancer research fellowships and bursaries
- Lack of long-term strategic, integrated planning of research
- Lack of cancer research lead programmes with a few exceptions
- No significant overseas funds for cancer research
- Lack of commitment and vision to test new South African anti-cancer drugs, preventive vaccines and diagnostic devices in South Africa due to high cost.
- No follow-through on the development of a South African papilloma virus vaccine after prototypes were established.
- Very few overseas cancer research experts visiting South Africa

Opportunities:

- CARISA
- EU cancer research funding
- Development of new drugs
- Very low incidence of colon cancer in South African Blacks (etiology, prevention, role of maize meal?)
- Very low lung cancer incidence in South African Black females (smoking prevention)
- Etiology of oesophageal cancer – HPV, diet, mycotoxins
- NIH cancer research co-operation/funding
- South Africa to become a leader in developing countries in Africa re cancer control and cancer control research
- South Africa to become a world leader in affordable cancer clinical trials
- South Africa to become a world leader in viral oncology (etiology, pathogenesis, vaccines, prevention)

- For DOH to declare cancer a notifiable disease

Threats:

- The philosophy that cancer is a problem of rich, developed countries and not really important in underdeveloped countries.

  (In the US cancer is now the No.1 cause of death (>50% of mortality), while in South Africa only about 20% of mortality is due to cancer. Nevertheless, the WHO, UICC, IARC have warned that over the next 15 years cancer will increase alarmingly by 50% to a yearly total of 15 million cases, i.e. an increase of 5 million extra cases p.a. mainly in underdeveloped countries. South Africa cannot afford to be complacent about cancer. Apart from cervical and oesophageal cancers, other cancers have markedly lower incidence rates in South Africa's Black population group. However without an adequate Cancer Control Programme policy, cancer incidence rates could double in South Africa. This will place a tremendous burden on already burdened oncology services especially in the public sector.).

- Cancer research momentum in South Africa decreases even further due to young scientists going overseas and promising scientists electing not to do cancer research mainly due to problems of national commitment, very poor funding and the uncertainty of cancer research as a career choice.

- Due to a lack of national commitment attempts to develop South African anti-cancer products are abandoned and are imported from elsewhere.

- The National Cancer Registry can collapse.

- Both principal investigators of the largest research consortiums (Primary Liver Cancer and New Drug Discovery) are reaching retirement age and the future of these lead projects is uncertain.

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10. **Cancer research in Australia: A survey of cancer researchers.**

    www.ncci.org.au/pdf/researchReview.pdf

11. **http://www.sahealthinfo.org/cancer/index.htm**

12. Appendix 1:

Current cancer research projects in South Africa- 2006

Principal investigator, institution and title of cancer research project.

	Principal Investigator	Institution	Project Title	Funder Category
	SELF-INITIATED PROJECTS – CANSA (14)			
1	Dr O A Ayo-Yusuf	UP	Effects of life skills training on tobacco use and oral health of adolescents in Limpopo province SA.	CANSA Control
2	Prof G Brown	UCT	Role of dectin-1 in beta-glucan mediated ant-cancer immunotherapy.	CANSA Molecular
3	Prof W Gelderblom	Promec Unit MRC	Cancer modulating properties of SA herbal teas (rooibos and honeybush).	CANSA Molecular
4	Prof A Joubert	UP	Differential cellular mechanisms and gene expression profiles of 2-methoxy-17B- estradiol and estradiol metabolites in a breast cancer cell line and non-tumourigenic epithelial breast cell line.	CANSA Molecular
5	Prof M Kew	WITS	Aetiology and pathogenesis of hepatocellular carcinoma in SA blacks.	CANSA Molecular Clinical
6	Dr V Leaner	UCT	The role of nuclear transport proteins in the development of cancer.	CANSA Molecular
7	Prof W Marasas	Promec Unit MRC	Population based cancer registry in the Eastern Cape	CANSA Control
8	Prof W Marasas	Promec Unit MRC	Diet & other risk factors associated with oesophageal cancer in Transkei	CANSA Control
9	Prof C Medlen	UP	Project developmental and experimental chemotherapy of multidrug resistant cancer.	CANSA Molecular
10	Dr N Mqoqi	NHLS	National Cancer Registry	CANSA Control
11	Dr E Murray	UCT	IBCSG and Atlas studies to improve treatment of early breast cancer (breast cancer databases	CANSA Clinical
12	Prof I Parker	UCT	Cancer epidemiology and the establishment of a hospital based cancer registry at Groote Schuur Hospital	CANSA Control
13	Prof G Wessels	US	Cape Town population based cancer registry pilot project.	CANSA Control
14	Dr P Willem	NHLS	Fra3B, FHIT and WWOX in SA megaloblatic anemia and oesophageal cancer	**CANSA** Molecular
	SELF-INITIATED PROJECTS – MRC (21)			

15	Dr J Burke	**WITS**	Characterisation of the protein-protein interactions between redox proteins and stress-activated kinases: Implications for apoptosis and cancer	**MRC Molecular**
16	Prof T Coetzer	**NHLS**	The role of Bcr-Abl in telomere dynamics	**MRC Molecular**
17	Prof M.Davies-Coleman	**RHODES**	The search for marine natural products active against oesophageal cancer	**MRC Molecular**
18	Dr G Hanekom.	**UCT**	Development of a diagnostic multiplex real-time PCR assay for breast cancer	**MRC Molecular Clinical**
19	Prof C Heyns	**US**	Molecular genetics of prostate cancer in South African subpopulations	**MRC Molecular Clinical**
20	Dr A.Hunter	**UCT**	The pro-apoptotic potential of tumour cells after irradiation by selective environmental and metabolic intervention	**MRC Molecular**
21	Dr A Joubert	**UP**	The regulatory role and mechanisms of 2-methoxy-17B-estradiol,a selectively anti-mitogenic steroid with anti-tumour potency	**MRC Molecular**
22	Dr R Lalloo	**UWC**	Cape The life course approach to the aetiology of head and neck cancer	**MRC Control**
23	Dr A Louw.	**US**	Sex hormone binding globulin (SHBG) in breast cancer patients receiving tamoxifen	**MRC Molecular**
24	Prof L.Louw	**UFS**	A lipid model for adenomatous colon cancer: Fatty acid profiles for cancer patients	**MRC Molecular**
25	Prof L.Louw	**UFS**	Mitogen-activated protein kinase signalling pathways in colon cancer	**MRC Molecular**
26	Prof G Maritz	**UWC**	The effect of maternal nicotine exposure on fetal and neonatal lung Cytochrome P450: A long-term study to investigate possible increased sensitivity of lung tissue of the offspring to selected carcinogenic substances	**MRC Molecular**
27	Prof C Medlen	**UP**	An in vitro investigation of the anti-tumour properties of Sutherlandia frutescens	**MRC Molecular**
28	Prof S.Moore	**US**	Mutational analysis of susceptibility loci in RET and EDNRB genes in MEN syndromes, familial medullary thyroid carcinoma and congenital neuronal dysganglionoses in the diverse South African population	**MRC Molecular**
29	Dr F Moore	**US**	Regulation of Cytosolic 5'	**MRC**

			Nucleotidase isoform Type II (cN-II) by AMP-activated protein kinase-mediated phosphorylation: Implications for purine nucleoside therapy of haematological malignancies	**Molecular**
30	Prof T Nyokong	**RHODES**	Development of drugs for photodynamic therapy of cancer (1)	**MRC Molecular**
31	Dr B.Odhav	ML Sultan Technikon	Chemoprotective actions of natural products on cultured human cells exposed to aflatoxins	**MRC Molecular**
32	Prof A Paterson	**NHLS**	The molecular pathology of colorectal carcinoma in young patients of South African origin	**MRC Clinical**
33	Dr S Roux	**NMMU**	An investigation into the anti-diabetic effects of catechins found in Sutherlandia frutescens and Pterocarpus marsupium	**MRC Molecular**
34	Dr S Songca	**UL MEDUNSA**	Oligomeric Porphyrins for Photodynamic Therapy	**MRC Molecular**
35	Prof E.Wilson	**UCT**	The biology of prostate stem cells	**MRC Molecular**
	MRC RESEARCH UNIT PROJECTS			
	UNIT	**PROJECT:**		
	Visit http://www.mrc.ac.za/research/ourresearch.htm for more details			
36	**EXERCISE SCIENCE AND SPORTS MEDICINE RESEARCH UNIT** **Prof Tim Noakes** **UCT**	• The role of exercise training in the rehabilitation of patients with peripheral vascular disease. • Other chronic diseases (diabetes mellitus, osteoporosis, rheumatological conditions, fibromyalgia, hypertension, hyperlipidaemia, renal failure, chronic obstructive airways disease, **cancer patients**)		
37	**BURDEN OF DISEASE RESEARCH UNIT** **Dr Debbie Bradshaw** **MRC**	• Estimation of the Burden of Disease (which includes mortality due to cancer).		
38 **39**	**THE HEALTHPROMOTION RESEARCH AND DEVELOPMENT GROUP** **Prof Priscilla Reddy** **MRC**	• Ways to prevent – and cease – tobacco usage; • The needs and experiences of unpaid voluntary and involuntary care-givers		
39 **40** **41** **42** **43** **44**	**CANCER EPIDEMIOLOGY RESEARCH GROUP** **Dr Lara Stein**	• Epidemiology of Cancer in Africa • Cancer among current and ex-employees of Rossing Uranium Mine, Namibia. • The South African National Cancer Registry 1988-1997: • Cancer Patterns among kidney transplant recipients in		

45 **46** **47**	**NHLS**	South Africa • Cancer Epidemiology study • Herpesviruses and haematological malignancies • Tobacco Mortality Study • Epidemiology of HHV8 • Epidemiology of Human Papillomavirus (HPV)
48	**CHRONIC DISEASES OF LIFESTYLE UNIT** **Prof Krisela Steyn** **MRC**	• To undertake public health research, which addresses whereby healthy lifestyles, early diagnosis, and cost-effective management of these diseases and their risk factors can be promoted in the South African population
49 **50** **51** **52** **53** **54** **55** **56** **57** **58** **59**	**PROMEC UNIT** **Prof Wally Marasas** **MRC**	• Biochemical action of food-borne toxins • Risk assessment related to the use of indigenous plants for medicinal purposes • Transkei cancer registry • Cancer epidemiology • Mechanisms of carcinogenesis • Biomarkers/early diagnosis • Dietary modulation • Cancer prevention • Long-term effects of food-borne toxins and carcinogens in experimental animals • Synergistic interaction • Investigations into the in vitro production of mycotoxins and carcinogens
60	**SOUTH AFRICAN TRADITIONAL MEDICINES RESEARCH UNIT** **Prof Peter Smith** **UCT**	• Isolation and characterisation of anticancer and cytotoxic compounds from plants used by tradtional healers
61 **62** **63** **64** **65** **66** **67** **68** **69**	**OESOPHAGEAL CANCER RESEARCH GROUP** **Prof I Parker** **UCT**	• The role of dietary fatty acids in cancer prevention • Human papilloma virus types associated with oesophageal cancer in the Transkei region of the Eastern Cape • Antimutagenic, antiproliferative and cancer modulating properties of SA herbal teas • Diet and duodenal-gastric-oesophageal reflux: its possible role in the pathogenesis of oesophageal cancer. • Genetic mutation and genes involved in tumour metastasis • Genetic polymorphisms in drug metabolising genes • Search for candidate genes by differential display RT-PCR • Search for candidate genes by comparative genomic hybridization • Cancer registration in the Transkei region of the Eastern

		Cape
70	**HUMAN GENETICS RESEARCH UNIT** **Prof Rajkumar Ramesar** **UCT**	• Human cancer genetics
71 **72** **73** **74**	**iThemba Labs**	• Proton therapy-clinical treatment protocols • Neutron Therapy-Clinical Treatment Protocols • Radiation Biology Investigations into radiation /drug interaction and cancer cell radiosensitivity. Also molecular mechanisms that influence radiotherapy outcome • iThemba LABS also do research in the development and production of radioactive isotopes for the detection and treatment of cancers. This include modern short half life short range radioactive implants as well Positron Emission Tomography (PET) Isotopes. Example: Excitation functions for the production of 82Sr by proton bombardment of natRb at energies up to 100 MeV.

Appendix 2:

CALCULATION OF CANCER INCIDENCE DEFICIT IN SOUTH AFRICA

1. Incidence of 142 is too low.
2. 142 for 45 million is 63 900
3. Assume mortality rate of 168 is right
4. Assume RSA has ratio = world= 0.62
5. Then 168/X = 0.62
6. Then X =271 (Higher than World, less than USA).
7. If incidence 142 gives 60 000 incidence then 271 gives 271/142 X 60 000 = 114,507 which is 54 507 more than current total.