Where do our research dollars go ...still ?

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"research: careful, systematic, patient study and investigation in some field of knowledge, undertaken to discover or establish facts or principles"
—Webster's dictionary

Introduction

Historical precedents abound proving that "an ounce of prevention is worth a pound of cure". For example, control of "Red River Fever" in Manitoba was achieved by separating the water supply from disposal of sewage carrying the typhoid bacillus. Throughout the world, malaria due to the mosquito-borne parasite was largely controlled by swamp drainage. In neither case was study of the respective offending micro-organism a major contributor to disease control. So it will be with cancer control.

To date, major advances in cancer control have come from epidemiologic research and serendipitous clinical observations. Thus, reduced use of tobacco, reduced exposure to cancer-causing chemicals, radiation, and ultraviolet light, eradication of cancer-causing protozoa and bacteria, and immunization against viruses, have all been effective maneuvers derived from epidemiological studies, and have been very effective in preventing cancer. According to the World Health organization up to 50 per cent of all cancers could still be prevented if we just applied what we know now. As is shown in Table 1, fully 62 per cent of cancer risk is attributable to lifestyle choices, all of which might be changed.

It is true that systemic treatment and screening have made substantial contributions and we must continue these efforts strongly. But we can not afford to keep going in that direction without at the same time making much stronger efforts in prevention. Strategies, based on sound research, must be devised to reverse the factors listed in Table 1.

Given this scenario, our interest has been piqued by the discordance between current directions of cancer research versus the directions in which cancer control solutions are likely to be found. Our initial analysis was largely restricted to the two granting agencies which account for over two thirds of national expenditure on cancer research: the National Cancer Institutes of Canada (NCIC), and the Canadian Institutes of Health Research (CIHR). The NCIC is supported by the Canadian Cancer Society (CCS) which in turn receives voluntary public donations, while the CIHR receives its money indirectly from the public, i.e., through grants from the federal government.

As evidenced in our 2004 Report Card, we found that 70 per cent of cancer research dollars allocated by these agencies went to support studies of the offending organism (the cancer cell) rather than the exogenous factors leading to its creation and external forces driving it to destroy the host. We found that only 13 per cent of the dollars went for prevention research and that the amount of money spent on studies of fruit flies, chickens, and yeast was equivalent to that spent on studies to improve supportive care for cancer patients and survivors.

Three years later we revisit the issue to determine if there has been any change in allocation of research dollars to more closely accord with societal priorities, namely preventing cancer, improving treatment and taking better care of cancer patients and survivors. Or, does research money continue to be allocated according to priorities largely set by the researchers themselves?

Methods

In an attempt to detect changes in patterns of research, we included only the new grants which took effect in 2006, that is, we excluded automatic continued funding of grants into 2006 which had been approved before 2006. Therefore, the total dollar amounts shown will be less than the amounts reported in our previous analysis. The exception to this is the data from the Cancer Research Society (CRS) where the dollars are for new grants awarded for 2005.

In the present study we included additional research agencies, based on the possibility this might affect the picture. Thus, we now account for approximately 80 per cent of new cancer research grants.

We used the same classification of research categories as in the previous report (see sidebar). The classification stipulates that for research to be classified as prevention, diagnosis, or treatment, it must involve humans or material taken directly from humans as tissue or blood

DEFINITIONS

BASIC RESEARCH: studies of cells, bacteria, yeast etc. in tissue culture or in animals. Excluded from this category are *in vitro* studies of blood products or tissues directly removed from humans. Also excluded are studies of human behavior or screening or psychosocial events or mathematical models for epidemiology, risk assessment etc. (see prevention research).

DIAGNOSIS RESEARCH: includes technology development or assessment, marker discovery in a clinical setting, or support of resources related to diagnosis or prognosis. Excluded were screening studies.

TREATMENT-RELATED RESEARCH: includes the testing, development, or clinical application of localized or systemic tumour-directed therapies, or their combinations. Complementary therapy is included if it is tumour directed. Also included were studies of blood products or tissues directly removed from humans in connection with therapy trials. Excluded were all other studies in model systems (see basic research), and psychosocial interventions (see supportive care).

SUPPORTIVE CARE RESEARCH: includes studies in patients undergoing active treatment and aimed at improving quality of life, symptom control, or enhancing patient caregiver interactions and decision-making.

PALLIATIVE CARE RESEARCH: as in supportive care research above but in patients who are no longer on active treatment and who are expected to die soon.

PREVENTION RESEARCH: studies involving epidemiology, demographics, genetics, family studies and risky behaviours in people with no symptoms of cancer, i.e., primary prevention, screening studies, secondary prevention, and studies to prevent recurrence or second primaries in cancer survivors who have completed treatment for their initial primary tumour i.e., tertiary prevention.

products. This is in contradistinction to the definitions in the Common Scientific Outline (CSO), a research classification which places some types of laboratory research in clinical categories even though that research does not involve humans or human material. In our previous study we found that all too frequently laboratory research projects allocated to these CSO categories were only remotely related to clinical problems. As we shall see, that is a critical distinction when comparing our findings with those of others.

In our previous study we also found that a computer scan of the words in the abstract describing the various research projects did not accurately classify each project. Therefore, in the present study to be certain that projects were accurately placed in our classification, we again carefully perused each of the 718 abstracts describing the individual newly-funded projects.

Results

Table 2 shows the agencies included in the present study, the total dollar amounts allocated for new grants and the percentages allocated to each category of research. The pie charts in Figure 1 compare the overall distribution of grant funding from the previous study with the present study. There appears to have been no overall material change in allocation of research dollars since the last study three years ago. Most of the money continues to go for basic research. However, some important details deserve attention.

Table 3 compares the percentage of funding allocated to each research category by NCIC and CIHR, the two largest agencies included in the previous period, with the present period. There has been a significant shift in the allocation by the NCIC: proportionately more money was allocated to treatment and prevention research in 2006 compared to 2003. The figures for CIHR have changed relatively little from the previous analysis, except for a modest decline in per cent of new dollars allocated for prevention and a slight increase for diagnostic research.

Many of the dollars allocated by NCIC for treatment research are given to the NCIC Clinical Trials Group (NCIC-CTG), which conducts large clinical trials testing various methods of cancer control. At the time of this analysis 46 of 50 ongoing trials were testing innovative cancer treatments, three were testing supportive care strategies, and one large trial was testing an agent to prevent breast cancer.

Also noteworthy is the program of the Ontario Institute for Cancer Research (OICR), an entity supported by the Ontario government. The focus of this agency is supposed to be on prevention, early detection, diagnosis, and treatment. Nevertheless, Table 2 indicates that almost two thirds of the new grant money awarded in 2006 was for basic research as we have defined it, i.e., it did not directly involve humans or human tissue or blood.

Discussion

As has been succinctly stated in the report of the Canadian Cancer Research Alliance (CCRA), "The burden of disease is

only one factor that drives the direction of research. Scientific opportunity, the introduction of new technologies, the researchability of a tumour type, the size and level of expertise in the research community, and the strategic priorities of research funders all shape the direction research will take."[1] Given the results of the present survey of research dollar allocation, and the one undertaken three years ago, it would appear that the factors driving research continue to be predominantly those of the researchers themselves.

Regarding scientific opportunity, it is not as if we do not know what was contributing to the cancer epidemic. As shown in Table 1, 62 per cent of cancers can be attributed to smoking, inappropriate diet, lack of exercise and resulting obesity, excessive use of alcohol and unprotected sun exposure. The problem is how to apply this knowledge.

TABLE 1 **RISK FACTORS FOR CANCER**
(PER CENT ATTRIBUTABLE RISK)

Diet	24%
Tobacco	22%
Genetic predisposition	20%
Infections	10%
Family history	8%
Alcohol	6%
Occupation	6%
Obesity	5%
Physical inactivity	4%
Sunlight	1%
Environment	1%
Ionizing radiation	<1%

Despite the evidence indicating which factors promote cancer, the research priorities of CIHR do not appear to have changed by 2006, the emphasis on research of the offending organism continues. Changes in research allocation have been relatively minor and could simply have been due to the vagaries of year-over-year comparisons.

It should be noted that the CIHR recently announced that $10-million will be allocated over five years to research which will enable Canadians to "better detect, treat, and survive cancer". This is most welcome and is an improvement over the previous announcement of $2.4-million over six years. The most recent grant is worth 7.5 cents per Canadian per year, compared to the previous grant of one cent per Canadian per year. Meanwhile, the allocation for new basic research by CIHR is in the order of $2.61 per Canadian per year.

Of note is the fact that a relatively small amount ($300,000) was allocated for studies which cannot reasonably be related to cancer. One might regard this amount as trivial, and perhaps due to an internal administrative error in reporting. But the fact remains that it is larger than that allocated by CIHR for research in palliative care of cancer patients ($187,000).

Hopefully, since the 2006 grant period, the CIHR has continued to change its research emphasis in a material way. If so, we look forward to documenting that change in future analyses.

In contrast to the relatively small changes in CIHR funding, the NCIC appears to be refocusing its efforts in a major fashion. According to the results shown in Table 3, considerably more emphasis is being placed on treatment and prevention compared to previous grant periods. The increase from 16 per cent to 39 per cent in grants allocated for treatment research is particularly noteworthy. Grants for treatment research have traditionally flowed to the NCIC-CTG. This consortium of Canadian clinical researchers continues to be strongly led. It is in the first rank of international clinical cancer research groups and the results of their research change cancer treatment policies worldwide. Up to this point, the NCIC-CTG has emphasized tests of new cancer therapies, only four of the 52 active trials are in prevention and supportive care. Hopefully, these categories will receive increased emphasis.

The NCIC and the Canadian Cancer Society (CCS) have recently entered a new era of collaboration as evidenced by the 10 year strategic plan of NCIC noted on the CCS/NCIC websites. According to the plan, "NCIC will take informed risks in developing new programs that…improve cancer control." NCIC is also "…proposing to undertake, among other activities, an expanded version of the Canadian Cancer Statistics publication and the creation of a policy paper series on priority topics in cancer control to be developed in consultation with CCS." NCIC does not propose to assume the responsibilities of governments, but will advocate for governments to do their jobs. This welcome change in strategy could have a major impact on cancer control in Canada.

Special mention should be made of the program of the Ontario Institute for Cancer Research (OICR). As noted earlier, despite its mandate, most of the money has gone for studies which we have categorized as basic research. However, even though the newly-funded studies are conducted in non-human model systems, most of the abstracts describe research which is sharply focused on solving clinical problems in humans. This is in contradistinction to the more fundamental themes in the other agencies' basic research portfolios. Furthermore, OICR is already participating in prevention research via grants awarded prior to 2006. It remains to be seen what impact OICR studies will have on cancer control but the effort is clearly in that direction. As long as collaborations ensure that bench findings are translated directly to the bedside in a well organized fashion and that clinical results are fed directly back to the lab, we can be optimistic about the

TABLE 2 **RESEARCH FUNDING ALLOCATION IN 2006** (New Grants)

Agency	Total ($)	Basic (%)	Treatment	Prevention	Diagnosis	Supportive	Health Service	Palliative	Not Cancer
CRS	$5,371,623	98.9%	1.1%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
CIHR	$27,330,860	75.9%	4.6%	6.2%	8.3%	1.6%	1.6%	0.7%	1.1%
PROSTATE	$980,000	75.0%	6.3%	0.0%	18.8%	0.0%	0.0%	0.0%	0.0%
OICR	$13,729,296	64.9%	25.0%	0.0%	10.1%	0.0%	0.0%	0.0%	0.0%
NCIC	$23,738,000	58.5%	28.8%	9.8%	0.7%	0.2%	1.2%	0.8%	0.0%
CBCRA	$4,909,000	44.6%	8.2%	17.1%	3.1%	26.2%	0.0%	0.9%	0.0%
TOTALS	$76,058,779	68.07%	15.85%	6.40%	5.46%	2.34%	0.92%	0.56%	0.39%
NCIC									
TFF	$6,661,000	96.1%	3.9%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
CCS	$17,077,000	43.9%	38.5%	13.6%	1.0%	0.3%	1.6%	1.1%	0.0%

CRS Cancer Research Society
CIHR Canadian Institutes of Health Research
PROSTATE Prostate Cancer Research Foundation of Canada
OICR Ontario Institute for Cancer Research
NCIC National Cancer Institute of Canada
CBCRA Canadian Breast Cancer Research Alliance
TFF Terry Fox Foundation
CCS Canadian Cancer Society

TABLE 3 **RESEARCH FUNDING ALLOCATION**

TYPE OF RESEARCH	NCIC		CIHR	
	2003-4	2005-6	2003-4	2005-6
Basic	65%	44%	73%	76%
Diagnosis	3%	1%	3%	8%
Treatment	16%	39%	7%	5%
Supportive care	3%	<1%	2%	2%
Palliative care	2%	1%	1%	1%
Prevention	10%	14%	14%	6%

returns for the effort.

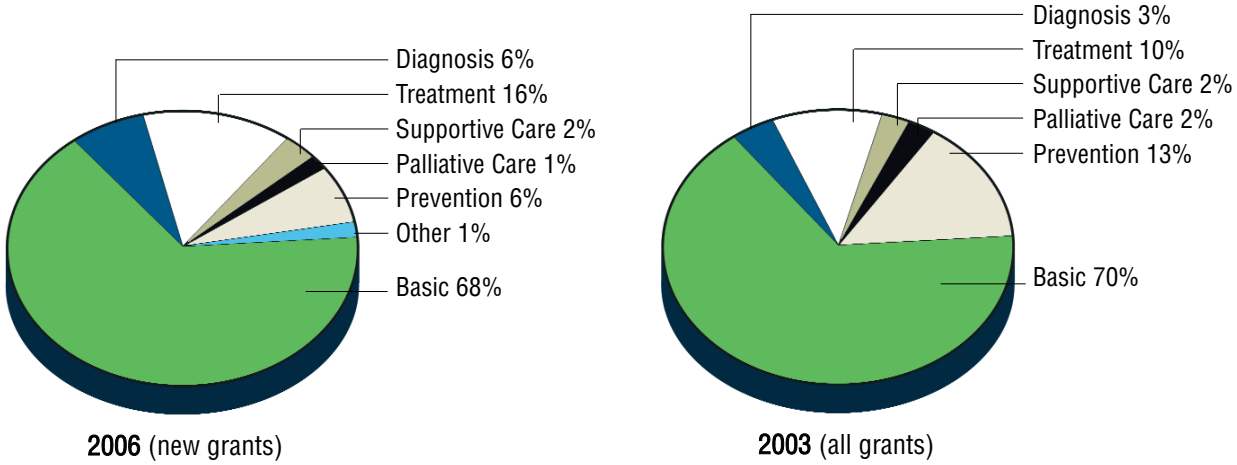
The Canadian Cancer Research Alliance (CCRA) has recently published the results of a study of cancer grant distribution in the year.[1] The CCRA study differs from our study in two respects. Firstly, CCRA included more of the cancer research agencies extant in Canada than we did. Secondly, their final results are different from ours: they indicate that only 45 per cent went for "biology "research, compared to the 68 per cent which we report herein for essentially the same category, namely "basic" research.

It is unlikely that the difference in years studied, 2006 in the present study verus 2005 in the CCRA analysis, explains the difference reported in distribution of research funding. Research funding allocations would not have changed so drastically in one year. It is also unlikely the more inclusive coverage of agencies by the CCRA explains the difference in distribution of research funding. The additional agencies included by CCRA compared to the present survey were relatively small (in the aggregate accounting for only 10 per cent more research dollars) and their pattern of funding largely followed the same pattern as the larger agencies, namely an emphasis on biology or basic research.

The reason for the discrepancy is more likely explained by the different classifications of research categories that were used in the two analyses. Our classification stipulates that research classified as prevention, diagnosis, and treatment must either involve humans or material taken directly from humans. As explained earlier, the CCO classification allows certain types of basic laboratory research to be categorized as clinical research.

Close perusal of Table 6 in the CCRA publication reveals that fully 19 per cent of the money judged by CCRA to be directed to diagnosis and treatment was for the sub-categories of discovery and development (codes 4.1, 4.2, 5.1, and 5.3). Most, if not all, of this research would have been conducted in animals and cultured cells, not in humans or using human tissue or blood products. Such studies we would classify as basic research. Our experience has consistently been that studies classified in these sub-categories are frequently only very loosely related to problems relevant to humans,

FIGURE 1 **COMPARISON OF RESEARCH FUNDING ALLOCATION 2006 vs. 2007**



in which case they rarely lead to timely advances in cancer control. Hence, the 19 per cent allocated to these categories by CCRA, when added to the 46 per cent they allocated for "biology" research yields 65 per cent essentially the same as the 68 per cent we report herein for "basic" research.

Basic research is important and should not be neglected. It has yielded fascinating biological insights which will ultimately translate into practical applications. Already an abundance of new and effective (and very expensive) cancer drugs is entering the clinic. Important new knowledge is evolving regarding genetic variations of either tumor susceptibility to drugs or individuals' ability to metabolize cancer drugs. Especially important from the viewpoint of cancer prevention, is the possibility that individuals' susceptibility to carcinogenic influences is genetically determined. However, these results have yet to have a material impact on cancer incidence and mortality. One must look at what has been their influence on the cancer epidemic, to date it continues unabated.

Canadian laboratory researchers rightfully enjoy an international reputation for excellence. We must continue to support them. But we also need a large cadre of new researchers to study cancer prevention.

To be more specific, studies should be greatly increased to find better ways to prevent cancer in otherwise healthy individuals (primary prevention), to improve screening for early cancer (secondary prevention), and ways to prevent cancer from recurring in cancer survivors (tertiary prevention).

Studies could focus on the following:

Prevention

(1) The relationship between mood and risky behaviors, incidence, treatment success, post-treatment disability, recurrence rates, and survival.
(2) Enhanced methods for detecting and reducing risky behaviors in "normal" individuals or in cancer survivors.
(3) Improving adoption by doctors and patients of proven methods for preventing cancer.

Treatment

(6) Strategies to reduce waiting times.
(7) Identification of patients most likely to respond to new cancer drugs.
(8) Pharmacogenetic reasons for failure to respond to cancer drugs.

Supportive Care

(9) Enhancing the role of nurses in supportive care.
(10) Ways to reduce increased utilization of health care systems by cancer survivors.

Conclusions

Cancer research priorities are too important to be left to the sole discretion of the researchers. In the 2004 Report Card we suggested that Canada needed an all-party parliamentary committee to ensure alignment of research priorities with societal priorities. The newly-formed Canadian Partnership Against Cancer (CPAC) Research Action Group, combined with the change in strategy of the NCIC/CCS, may help achieve this goal. But there still needs to be ongoing public scrutiny of cancer research objectives and results.

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Reference

1. Cancer Research Investment in Canada, 2005, Canadian Cancer Research Alliance, September 2007, p 25.