

COLLEGIUM RAMAZZINI STATEMENT
CANCER PREVENTION, SCREENING AND EARLY DIAGNOSIS,
THE NEGLECTED SIDE OF CANCER CONTROL
A Call for Action

Cancer is a leading cause of morbidity, mortality, and premature death worldwide.¹ While cancer was previously a problem principally of the industrially developed countries, it increasingly is a problem in the developing ones. Today, half of the world's newly diagnosed cancers and over 70% of all cancer deaths occur in middle and low-income countries². This persistent and growing burden of cancer in the world's populations warrants heightened public health attention.

Prevention, early detection, and therapy have all proven effective in controlling certain types of cancer and in reducing the burden of premature death and advanced disease.³ In many countries, however, these well established approaches to cancer control have not been applied to their full potential and in many countries are not applied at all. Furthermore, great disparities still exist in cancer control in relation to gender, race, ethnicity, and socio-economic status.

To confront the growing global epidemic of cancer, the *Collegium Ramazzini* calls for the adoption in all countries of the world of vigorous, proactive, and comprehensive programs for cancer prevention, screening and early diagnosis.

The Collegium Ramazzini is an international scientific society that examines critical issues in occupational and environmental medicine with a view towards action to prevent disease and promote health. The Collegium derives its name from Bernardino Ramazzini, the father of occupational medicine, a professor of medicine of the Universities of Modena and Padua in the late 1600s and the early 1700s. The Collegium is comprised of 180 physicians and scientists from 35 countries, each of whom is elected to membership. The Collegium is independent of commercial interests.

The present statement was drafted by an ad hoc Working Group: John C. Bailar, Fellow Collegium Ramazzini and Chair, Cancer Committee - Massimo Crespi, Fellow Collegium Ramazzini and Chair of the Working Group - Maria Stella de Sabata, UICC - Anders Englund, Fellow Collegium Ramazzini - Philip Landrigan, President Collegium Ramazzini - Steven B. Markowitz, Fellow Collegium Ramazzini - James Melius, Fellow Collegium Ramazzini - Rengaswamy Sankaranarayanan, IARC - Robert A. Smith, American Cancer Society and Co-Chair of the Working Group - Morando Soffritti, Secretary General Collegium Ramazzini. The statement has been fully approved by the Collegium Ramazzini.

Background

In the past, the *Collegium Ramazzini* has called for the prevention of cancer through *primary prevention* of workplace exposures to carcinogens, most commonly through elimination of exposures to carcinogenic materials. *Primary prevention* has been and remains the most effective and often the most cost-effective means of cancer control. Those calls for primary prevention have been based in the clear recognition that the prime responsibility of employers and health authorities is to ensure that workers are protected from exposure to agents that can cause cancer and that are harmful to health.

Previous calls by the *Collegium Ramazzini* and specific actions for the primary prevention of cancer have greatly reduced exposures to proven occupational carcinogens such as asbestos, benzene, benzidine, vinyl chloride ionizing radiation and 1,3-butadiene.⁴⁻⁷ Control of such exposures has already led to the prevention of tens of thousands of cancer cases. Now the *Collegium* extends its call, urging health care providers, employers, and national health agencies and institutions in all countries to adopt proven, well-documented, successful approaches to primary and secondary cancer prevention.

With respect to cancer prevention, perhaps the highest international priority is the prevention of exposure to carcinogens in the workplace and the environment, first of all of tobacco use. Some cancer prevention is also achieved by the detection and treatment of lesions known to be precursors of invasive cancer, as in the case of cervical and colorectal cancer. The potential for secondary prevention and early detection interventions lies on a continuum that is influenced by the strength of the scientific evidence, costs, infrastructure, and the burden of disease. However, the knowledge exists today to reduce avoidable morbidity, mortality and economic losses from several of high prevalence cancers through the application of proven prevention or early detection strategies (Table 1).

Table 1. Potential Impact of Prevention, Early Detection, and Therapy on the Control of Cancer, by Site			
Site	Prevention	Early Detection	Therapy (Local vs. Advanced Stage)
Lung	++++	+ (+)	++ / +
Esophagus	+	+	+ / +
Stomach	+	++	++ / +
Colon & Rectum	+++	+++	+++ / +
Breast	-	+++	++++ / ++
Uterine Cervix	+++	+++	+++ / +
Testicle	---	+	++++ / +++
Skin (non-melanoma)	++++	++++	++++
Lymphoma/Leukemia	---	----	++ / ++
Prostate	----	++	++++ / ++
Ovary	----	+	++++ / ++
Pancreas	---	+	+ / +
Bladder	+++	++	+++ / +
Oral cavity	++++	+++	+++ / ++
++++ Optimal +++ Good ++ Fair + Low ---- Little or no benefit --- Scarce - Inadequate data			

Cancer screening programs have been shown to reduce avoidable morbidity and mortality, most notably from colorectal, breast, and cervical cancers (Table 2). The future holds promise that additional cancers become targets for successful early detection programs.

Table 2. Evidence Supporting the Value of Screening for the Early Detection of Cancer			
Cancer Site	Test	Study	Mortality Reduction
Breast*	Mammography (24 months)	Swedish Two County Trial, women ages 40-74 invited to screening	31%
	Mammography (18-24 months)	Evaluation of Service Screening, 9 Swedish counties, women ages 40-69 who actually participated in screening	45%
Cervix**	Pap test	Population Trends in the U.S. and Europe	Dramatic declines in cervical cancer incidence, and 20-60% mortality reductions
Colon & Rectum	FOBT (annual)	Minnesota Colon Cancer Control Study, men and women aged 50-80	33%
	FOBT (biannual)	Denmark Study of Colorectal Cancer Screening with FOBT, men and women aged 40-75	18%
Lung	Chest X-ray Spiral CT	Uncontrolled screening trials demonstrate that lung and prostate cancer can be detected at early stages. These screening modalities are undergoing evaluation of mortality reduction at this time in prospective randomized controlled trials in the U.S. and Europe.	
Prostate	PSA		
Ovarian	CA-125, Ultrasound	Evaluation of screening for cancer of the ovary is being tested in prospective randomized controlled trials in the U.S. and Europe. New, experimental screening strategies based on molecular markers continue to show promise.	
Oral cavity	Oral visual inspection	Trivandrum oral cancer screening trial, subjects aged 35 years and above invited to three rounds of screening at three year interval	34% reduction among users of tobacco or alcohol or both
* Mammography Screening in women ages 40-49 is not universally accepted because of costs and enduring controversy related to the balance of benefits and harms.			
** Vaccination against HPV in young women holds the potentiality to further expand primary prevention and screening			
FBOT = Fecal occult blood test; CT = Computed tomography, PSA = Prostate specific antigen			

Although continued research will be needed to define new strategies and further refine existing approaches, there is sufficient knowledge and experience today for employers, government agencies, and other relevant authorities to initiate or expand programs to reduce the avoidable burden of cancer without need to wait for further research. Fulfilling the potential that exists today to control cancer, principally by tobacco control and implementation of secondary prevention strategies directed at several cancers, is an urgent international priority.

Practical and ethical considerations for cancer detection programs

The decision to implement cancer prevention and early detection initiatives should be based on the criteria established by the World Health Organization 40 years ago for cancer screening.⁸ Even when there is sound evidence supporting the efficacy of a cancer prevention or early detection strategy, local considerations and circumstances, as well as the magnitude of the disease problem, still are relevant considerations and will not be uniform in all settings. The key decision criteria are described below:

1. A prerequisite is to understand the epidemiology of cancer(s) in the target population. Cancer profiles in different regions of the world and within some population subgroups may differ substantially, and therefore it is important to focus resources on those cancers that represent a significant disease burden in a particular population, and for which prevention and detection strategies are possible and effective diagnostic and treatment resources are available.
2. The population that is the target of prevention and screening programs must be defined. The definition may be very broad, i.e., all adults within a certain age range or all adults with prolonged exposure to an environmental agent (i.e., tobacco smoke), or very narrow, i.e., an industrial population exposed to a toxic agent in a specific manufacturing plant. Everyone for whom screening is medically relevant and of proven efficacy should have access to regular testing. The screening services must be provided on a voluntary basis and by free and well-informed consent. Privacy issues must be respected, as well as confidentiality of medical information.
3. Successful early detection programs require population adherence and clear guidelines for early detection, early diagnosis and surveillance. Family doctors and other health professionals play a crucial role in promoting awareness on the benefits of screening and, in collaboration with health agencies, ensure actions to increase such benefits by adherence with screening intervals, high quality in the testing process, prompt follow-up of abnormal results, and prompt diagnosis and treatment.
4. Communication between health services and the target population in the case of an organized screening program, or between the family doctor and the individual in the case of opportunistic screening, must address the importance of early detection, and what will or may occur as a result of screening, including the possibility of harm associated with false negative or false positive screening test results, or harm associated with diagnosis and treatment. Counseling of persons with suspicious or positive results should be included in each program.

The implementation of screening for some cancers also provides the opportunity to promote awareness of actions and/or healthy behaviors that may contribute to primary prevention of these same cancers.

5. While the cost of early detection programs initially is high, they usually are cost-effective from a societal standpoint, and can be quite cost-effective within an individual worksite or industry. Thus, continuous evaluation and cost-effectiveness analysis have the potential to document that early detection programs are highly productive strategies in reducing treatment costs and the burden of suffering, identify opportunities for improvement and possibly costs-savings, and therefore allow a better use of limited resources.
6. A critical element in advancing cancer prevention and early detection is the importance of working with and through each country's health infrastructure. Broad support from both the health authorities and health professionals in the field is essential but will be expressed in different ways that depend on available resources, local law and custom, and many other elements. A comprehensive approach to health promotion can raise and continually reinforce awareness among health care professionals and the public that cancer can be controlled through prevention *and* early detection, transferring the simple but effective message *cancer is a preventable disease*.

Conclusion

Cancer prevention, screening and early detection programs that follow the above mentioned principles can be effective, and in many settings, inexpensive in relation to the short and long term costs of advanced cancer and adaptable to the situation in each country, manufacturing plant or other organization that sponsors the screening. There is great potential to reduce avoidable cancer related morbidity and mortality throughout the world through the application of existing knowledge. Our call to action is based on our fundamental belief that the community and the workplace should be viewed as an overlapping continuum of opportunity for broader implementation of effective cancer control strategies.

References

1. Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. *CA Cancer J Clin.* 2005;55:74-108.
2. Kanavos P. The rising burden of cancer in the developing world. *Ann Oncol.* 2006;17 Suppl 8:viii15-viii23.
3. Curry SJ, Byers T, Hewitt M, (eds). *Fulfilling the Potential of Cancer Prevention and Early Detection.* Washington, D.C.: National Academy Press; 2003.
4. Call for an international ban on asbestos. *Collegium Ramazzini. Am J Ind Med.* 1999;36:227-229.
5. Soffritti M, Belpoggi F, Minardi F, Maltoni C. Ramazzini. Foundation cancer program: history and major projects, life-span carcinogenicity bioassay design, chemicals studied, and results. *Ann N Y Acad Sci.* 2002;982:26-45.
6. Soffritti M, Landrigan PJ. Statement of the Collegium Ramazzini. *Am J Ind Med.* 2004;46:88.
7. Landrigan PJ, Soffritti M. Collegium Ramazzini call for an international ban on asbestos. *Am J Ind Med.* 2005;47:471-474.
8. Wilson JMG, Junger G. *Principles and practice of screening for disease.* Geneva, Switzerland: World Health Organization; 1968.