

## CANCER AND THE ROLE OF NUTRITIONIST

Krizia Ferrini, PhD student

Department of Experimental Oncology, European  
Institute of Oncology, Milan, Italy  
University of Pavia, Italy

krizia.ferrini@ieo.eu

### Introduction

Cancer is not a single disease but a group of related diseases<sup>1</sup>. Many things in our genes, our lifestyle and the environment around us may increase or decrease our risk of getting cancer<sup>2</sup>.

There is an important resource, the GLOBOCAN 2012, a project which estimates the incidence (Figure1), mortality and prevalence for major types of cancer, at national level, for 184 countries of the world<sup>3</sup>.

There were 14.1 million new cancer cases, 8.2 million cancer deaths and 32.6 million people living with cancer (within 5 years of diagnosis) in 2012 worldwide. 57% (8 million) of new cancer cases, 65% (5.3 million) of the cancer deaths and 48% (15.6 million) of the 5-year prevalent cancer cases occurred in less developed regions.

In terms of mortality, there is less regional variability than for incidence, the rates being 15% higher in more developed than in less developed regions in men, and 8% higher in women.

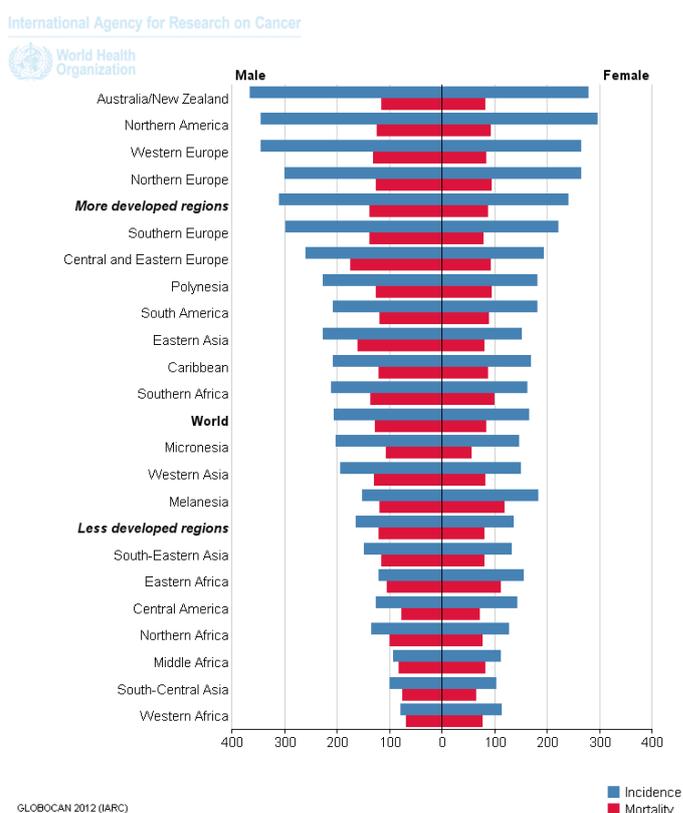
### But how can we prevent cancer? Are there some risk factors?

Actually we know that unhealthy diets and physical inactivity are key risk factors for the

major non communicable diseases such as cancer<sup>4</sup>.

Recognizing the opportunity for reducing deaths and diseases worldwide by improving diets and increasing levels of physical activity, the World Health Assembly adopted the WHO Global Strategy on Diet, Physical Activity and Health, in May 2004<sup>5</sup>.

**Figure 1.** All Cancers (excluding non-melanoma skin cancer) Estimated Incidence, Mortality and Prevalence Worldwide in 2012<sup>3</sup>



This strategy provides recommendations for Member States, WHO, international partners, private sector, civil society and non-governmental organizations on the promotion of healthy diets and regular physical activity for the prevention of non communicable diseases. Heads of State and Government committed in the Political Declaration of the High-level Meeting of the United Nations General Assembly on the Prevention and Control of NCDs<sup>6</sup> to reduce the

exposure of populations to unhealthy diets and physical inactivity. Equally important, the 2013 World Health Assembly endorsed the Global NCD Action Plan 2013-2020, which includes a set of actions for Member States, international partners and the WHO Secretariat to promote healthy diets and physical activity, and to attain 9 voluntary global targets for NCDs including ones on diet and physical activity to be achieved by 2025 (resolution WHA 66.10<sup>7</sup>).

By the early 1980s, there was a good deal of evidence that diet might be important in cancer causation by analogy with animal studies and from some epidemiology studies<sup>8-11</sup>.

All of these data are collected in the World Cancer Report<sup>12</sup> that provides a professional, multidisciplinary assessment of all aspects of the geographical distribution, biology, etiology, prevention, and control of cancer, predicated on research.

There is a growing body of evidence for lifestyle interventions that aim to enhance weight management and to promote physical activity as having the potential to counter some of the adverse effects of cancer treatments, disease progression and other outcome<sup>12</sup>.

There have been a number of reviews and meta-analyses that have addressed issues of cancer prevention, but the most comprehensive possibly being the 2007 report by the World Cancer Research Fund, 'Food, Nutrition, Physical Activity and the Prevention of Cancer: a Global Perspective'<sup>13</sup>.

### **Body fatness, Obesity and Evidence**

To date, WCRF research from the Continuous Update Project and Second Expert Report has shown that excess body fatness is linked to an

increased risk of developing eight cancers. Body fatness [marked by body mass index (BMI)], is a key factor influencing health and well being throughout life<sup>14</sup>. To date, WCRF research has shown that excess body fatness is linked to an increased risk of developing eight cancers<sup>15</sup>.

Body fatness influences the levels of a number of hormones and growth factors. Insulin and leptin are all elevated in obese people, and can promote the growth of cancer cells. In addition, insulin resistance is increased, in particular by abdominal fatness, and the pancreas compensates by increasing insulin production. This hyperinsulinemia increases the risk of cancers of the colon and endometrium, and possibly of the pancreas and kidney<sup>16</sup>.

Such chronic inflammation can promote cancer development. Also, obesity is associated with a low-grade chronic inflammatory state<sup>17</sup>.

Obese adipose tissue is characterized with macrophage infiltration and these macrophages are an important source of inflammation in this tissue<sup>18</sup>.

The adipocyte (fat cell) produces pro-inflammatory factors, and obese individuals have elevated concentrations of circulating tumor necrosis factor (TNF)-alpha interleukin (IL)-6, and C-reactive protein, compared with lean people, as well as of leptin, which also functions as an inflammatory cytokine<sup>19</sup>.

Various organizations, such as the American Cancer Society (ACS), the World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) and most recently the American College of Sports Medicine (ACSM) have issued guidelines for diet and/or physical activity that target cancer survivor<sup>12</sup>; these reports serve as

resources for health care providers, patient advocates, and other stakeholders to improve the health and well-being of this rapidly expanding and high risk population.

These guidelines emanate from a large body of epidemiologic findings that have consistently found associations between overweight and obesity and the primary risk of cancer, as well as cancer-related mortality – data which are expanding at a rapid pace as the world's population becomes increasingly overweight.

Alteration in the eating habit from traditional to westernized diets appears to correlate with the increased risk of many common cancers in both developed and developing countries<sup>20</sup>.

It is believed that increased food consumption can influence the expression of genes involved in important cellular functions, such as DNA repair, cell proliferation and differentiation, and apoptosis, by altering the levels of metabolic hormones and growth factors, and can lead to accumulation of damage and mutations and ultimately malignant transformation<sup>21</sup>.

Therefore, it can be assumed that by controlling our diet we might also control cancer risk. Energy deprivation prolongs life span, while excess calories are associated with obesity, human cancer, and shortened life span. At the cellular level, normal proliferating cells activate metabolic pathways and couple them with cell mass accumulation and DNA synthesis for cell reproduction<sup>22</sup>.

Normal cells sense nutrient cues and evolves mechanisms to diminish macromolecular synthesis and ATP consumption while enhancing ATP production pathways when deprived of nutrients. Autophagy evolved to sustain starved

cells through self-eating to recycle cell components for energy production. The by-products of metabolism, specifically ROS, can damage cells and promote oncogenic DNA mutations; thus, metabolism can trigger tumorigenesis<sup>23</sup>.

Mutations of oncogenes and tumor suppressors, in turn, drive cell growth and proliferation coupled with import of adequate bioenergetics substrates<sup>24</sup>.

Therefore mutant metabolic enzymes can drive tumor genesis and cancer genes regulate metabolism such that cellular machineries driving cell growth and proliferation are tightly coupled with the cell's ability to assimilate nutrients and energy<sup>21</sup>.

The therapeutic windows for targeting cancer cell metabolism reside in differences between normal and mutant oncogenic enzymes and addiction of cancer cells to nutrient to support deregulated cell growth programs enforced by cancer genes. Hence, the complex regulatory networks involving cancer genes and metabolic pathways need to be defined for specific cancer types so that targeting of cancer cell metabolism could be strategically guided by somatic genetic changes in cancers<sup>21</sup>.

### **Nutrition Prevention and Cancer Care**

Nutrition in cancer care embodies prevention of disease, treatment, cure, or supportive palliation<sup>25</sup>.

Proactive nutritional care can prevent or reduce the complications typically associated with the treatment of cancer. Malnutrition and accompanying weight loss can be part of an

individual's presentation or can be caused or aggravated by treatments for the disease. Screening and nutrition assessment should be interdisciplinary; the healthcare team (e.g., physicians, nurses, registered dietitians, social workers, psychologists) should all be involved in nutritional management throughout the continuum of cancer care<sup>26</sup>.

Optimal nutritional status is an important goal in the management of individuals diagnosed with cancer. Although nutrition therapy recommendations may vary throughout the continuum of care, maintenance of adequate intake is important<sup>27</sup>.

Whether patients are undergoing active therapy<sup>28</sup>, recovering from cancer therapy, or in remission and striving to avoid cancer recurrence, the benefit of optimal caloric and nutrient intake is well documented<sup>29</sup>.

Nutritional status can be adversely affected by the disease process, including the symptoms and side effects of cancer and its treatment (e.g., chemotherapy, surgery, immunotherapy, and radiation therapy)<sup>26</sup>.

The goals of nutrition therapy are to accomplish the following<sup>30-32</sup>:

- Prevent or reverse nutrient deficiencies.
- Preserve lean body mass.
- Help patients better tolerate treatments.
- Minimize nutrition-related side effects and complications.
- Protect immune function, decreasing the risk of infection.
- Aid in recovery and healing.
- Maximize quality of life.
- Lessen side effects.
- Improve well-being.

The nutrition professional works with patients, families and/or caregivers, physicians, and other members of the oncology multidisciplinary team to help maintain optimal nutritional status throughout the continuum of care (prevention, treatment, survivorship, palliative care, and hospice). The practical strategies<sup>33</sup>, models of nutrition programs and tools for developing a successful nutrition program depend on developing an Early Intervention Model and a "Culture of Nutrition". Oncology treatment occurs over a lengthy period of time and creates symptoms that can change day to day. Each staff member interacts with patients in his or her own professional role, and may garner information that impacts nutritional status<sup>34</sup>.

Clinical Nutritionist provides for<sup>35-37</sup>:

- Coordination of treatment diet with complex medical histories.
- Management of tube feeding and total parenteral nutrition.
- Nutrition to promote wound healing.
- Nutritional strategies for the altered or shortened gut.
- Guidance on use of pancreatic enzymes and nutritional supplements.
- Modified diets for patients with nutrient malabsorption.
- Evaluation of complementary and alternative nutrition strategies.
- Information on nutrition and cancer prevention and survivorship nutrition.
- Management of the late effects from treatment.
- Behavior modification to assist patients in changing unhealthy lifestyles.

## Conclusion

The WCRF Report<sup>13</sup> sets out public health goals and personal Recommendations for Cancer Prevention. These goals and recommendations were made by an expert panel of 21 world-renowned scientists, who reviewed the findings and made judgments based on the available body of evidence. The report is the largest study of its kind and its conclusions are as definitive as the available evidence allows.

There is a pressing need to direct more attention to this issue, in particular during the development of interventions to improve long-term health outcomes for the growing number of breast cancer survivors.

Maintaining regular physical activity and a healthy diet and grasping the implications for cancer survivors are important to enhancing health and well-being over the long-term. The best starting point is an understanding of what the scientific evidence tells us; the risk of morbidity and mortality from causes other than cancer should be considered when making dietary or exercise recommendations for cancer survivors; diet regimens that emphasize vegetables, fruit, whole grain, fiber and low fat dairy foods and that are low in saturated fat are advised as a prudent strategy to promote health and prevent disease.

## References

1. Robert A. Weinberg. *The Biology of Cancer*, Second Edition. 2013
2. Denlinger CS, Ligibel JA, Are M, et al. Survivorship: nutrition and weight management, version 2.2014. *J Natl Compr Canc Netw* 2014 Oct;12(10):1396-406.
3. Bray F, Ren JS, Masuyer E, Ferlay J. Global estimates of cancer prevalence for 27 sites in the adult population in 2008. *Int J Cancer*. 2013 Mar 1;132(5):1133-45
4. Waxman A. Why a global strategy on diet, physical activity and health? *World Rev Nutr Diet*. 2005;95:162-6.
5. Bauman A, Craig CL. The place of physical activity in the WHO Global Strategy on Diet and Physical Activity. *Int J Behav Nutr Phys Act*. 2005 Aug 24;2:10
6. Mendis S, Chestnov O. Policy reform to realize the commitments of the Political Declaration on noncommunicable diseases. *Br Med Bull*. 2013;105:7-27
7. Sixty-sixth World Health Assembly Provisional Agenda item 13.3, A66/10 Rev.1, 16 May 2013. Draft Comprehensive Mental Health Action Plan 2013 - 2020
8. Committee on Diet Nutrition and Cancer. *Diet, nutrition and cancer* Washington, D.C.: National Academy Press, 1982
9. Barrdahl M, Canzian F, Joshi AD, et al Post-GWAS gene-environment interplay in breast cancer: results from the Breast and Prostate Cancer Cohort Consortium and a meta-analysis on 79 000 women. *Hum Mol Genet*. 2014 Oct 1;23(19):5260-70

10. Sonn GA, Aronson W, Litwin MS. Impact of diet on prostate cancer: a review. *Prostate Cancer Prostatic Dis.* 2005;8(4):304-10
11. Stewart BW, Wild CP. *World Cancer Report 2014* (IARC Non Serial Publication), February 1, 2014
12. Pekmezi DW1, Demark-Wahnefried W. Updated evidence in support of diet and exercise interventions in cancer survivors. *Acta Oncol.* 2011 Feb;50(2):167-78
13. Friedenreich CM, Neilson HK, Lynch BM. State of the epidemiological evidence on physical activity and cancer prevention. *Eur J Cancer.* 2010 Sep;46:2593-604.
14. Fontana L. Effects of long-term calorie restriction and endurance exercise on glucose tolerance, insulin action, and adipokine production. *Age (Dordr).* 2010 Mar;32(1):97-108
15. Renehan AG, Roberts DL, Dive C. Obesity and cancer: Pathophysiological and biological mechanisms. *Arch Physiol Biochem.* 2008 Feb;114(1):71-83
16. Perera PS, Thompson RL, Wiseman MJ. Recent Evidence for Colorectal Cancer Prevention Through Healthy Food, Nutrition, and Physical Activity: Implications for Recommendations. *Curr Nutr Rep* 2012;1:44-54
17. Canello R, Clément K. Is obesity an inflammatory illness? Role of low-grade inflammation and macrophage infiltration in human white adipose tissue. *BJOG.* 2006 Oct;113(10):1141-7
18. Louie SM, Roberts LS, Nomura DK. Mechanisms linking obesity and cancer, *Biochim Biophys Acta.* 2013 Oct;1831(10):1499-508.
19. Ramos-Nino ME. The Role of Chronic Inflammation in Obesity-Associated Cancers *ISRN Oncology* 2013: 697521, 25p
20. Swinburn BA, Caterson I, Seidell JC, James WPT, Diet, nutrition and the prevention of excess weight gain and obesity, *Public Health Nutrition: 7(1A), 123–146.*
21. Dang CV. Links between metabolism and cancer. *Genes Dev.* 2012 May 1;26(9):877-90.
22. Speakman JR, Mitchell RE, Caloric restriction. *Mol Aspects Med.* 2011 Jun;32(3):159-221
23. Harris TE, Lawrence JC Jr. TOR Signaling. *Sci STKE.* 2003 Dec 9;2003(212):re15.
24. Dang CV, Hamaker M, Sun P, Le A, Gao P. Therapeutic targeting of cancer cell metabolism. *J Mol Med (Berl).* Mar 2011; 89(3): 205–212
25. Shils ME: Principles of nutritional therapy. *Cancer* 1979; 43 (5 Suppl): 2093-102
26. Eldridge B, Rock CL, McCallum PD. Nutrition and the patient with cancer. In: Coulston AM, Rock CL, Monsen ER, eds.: *Nutrition in the Prevention and Treatment of Disease.* San Diego, Calif: Academic Press, 2001, 397-412
27. Leandro-Merhi VA, de Aquino JL, Sales Chagas JF. Nutrition status and risk factors associated with length of hospital stay for surgical patients. *JPEN J Parenter Enteral Nutr* 2011;35:241–248.
28. Eldridge B, Hamilton K. Management of Nutrition Impact Symptoms in Cancer and Education Handouts. American Dietetic Association 2004
29. McCallum PD, Polisena CG, eds.: *The Clinical Guide to Oncology Nutrition.* Chicago, Ill: The American Dietetic Association, 2000

30. Sarhill N, Mahmoud FA, Christie R, et al.: Assessment of nutritional status and fluid deficits in advanced cancer. *Am J Hosp Palliat Care* 2003;20(6):465-73
  31. Bloch AS. Nutrition Management of the Cancer Patient. Rockville, Md. Aspen Publishers, 1990.
  32. Rivlin RS, Shils ME, Sherlock P: Nutrition and cancer. *Am J Med* 75 (5): 843-54, 1983.
  33. National Cancer Institute. Eating Hints: Before, during and after cancer treatment. January 2011
  34. Robien K, Bechard L, Elliott L, Fox N, et al. American Dietetic Association: Revised Standards of Practice and Standards of Professional Performance for Registered Dietitians (Generalist, Specialty, and Advanced) in Oncology Nutrition Care. *J American Dietetic Assn.* 2010;110 (2):310-317.
  35. American Dietetic Association/Commission on Dietetic Registration. Code of ethics for the profession of dietetics and process for consideration of ethics issues. *J Am Diet Assoc.*2009; 109:1461-1467
  36. American Dietetic Association. Evidence Analysis Library/Oncology Toolkit: Oncology Evidence-Based Nutrition Practice Guideline. Chicago, IL: American Dietetic Association, 2010
  37. American Dietetic Association. International Dietetics & Nutrition Terminology (IDNT) Reference Manual: Standardized Language for the Nutrition Care Process, 3rd edition. Chicago, IL: American Dietetic Association, 2011
-