The Role of Obesity in Cancer Survival and Recurrence: Workshop Summary

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INTRODUCTION

Recent research suggests that obesity and excess weight can play a prominent role in the incidence and progression of various cancers. Obesity results from an energy imbalance—that is, energy intake that is higher than energy expenditure—could also influence the growth of cancers. In addition, by generating hormones and growth factors, and by fostering inflammation, fat tissue could directly fuel the growth of tumors, thereby affecting cancer incidence, progression, recurrence, and survival rates. Given the current obesity epidemic and an aging population more susceptible to cancer, there is mounting concern about the role that obesity plays in malignancies. There is also interest in exploring possible interventions to break the obesity–cancer link, especially in patients already diagnosed with cancer who are more susceptible to developing new cancers as well as cancer progression and recurrence. Cancer survivors currently number 12 million in the United States and are rapidly increasing in number.

Recognizing the impact that current findings on obesity and cancer could have on future cancer prevention and care, the National Cancer Policy Forum (NCPF) of the Institute of Medicine (IOM) held a 2-day workshop[3] on "The Role of Obesity in Cancer Survival and Recurrence," in Washington, DC, on October 31 and November 1, 2011. At the workshop, experts presented the latest clinical evidence on the obesity–cancer link and the molecular mechanisms that might explain that link. Clinicians, researchers, cancer survivors, and policy makers also discussed potential interventions to counter the effects of obesity on cancer, and research and policy measures needed to stem the rising tide of cancer mortality predicted by an increasingly overweight and older population worldwide. More specifically, the workshop explored:

- The complex web of molecular mechanisms that underlie the obesity–cancer link and whether it is obesity itself, the energy imbalance that leads to obesity, or the molecular pathways that are deregulated due to obesity, that lead to increased risk of cancer initiation or progression;
- Clinical evidence of the obesity link to cancer incidence and outcomes and study design issues that may affect the strength of that evidence and its interpretation, as well as ways to design future studies to acquire the information needed to guide patient care;
- Potential interventions to counter or prevent obesity effects and/or restore energy balance, including lifestyle measures, as well as drug and surgical therapies;
- What to advise cancer patients about weight loss, diet, exercise, and other measures to reduce their risk of cancer progression or recurrence, and the challenges in inducing healthy behaviors; and
- Policy suggestions related to research, education, and dissemination of the findings on obesity and cancer, as well as what the private and public sectors can do to help break the obesity–cancer link.

This document is a summary of the workshop. The views expressed in this summary are those of the speakers and discussants, as attributed to them, and are not the consensus views of workshop participants of the members of the NCPF.

[3] This workshop was organized by an independent planning committee whose role was limited to identification of topics and speakers. This workshop summary was prepared by the rapporteurs as a factual summary of the presentations and discussions that took place at the workshop. Statements, recommendations, and opinions expressed are those of individual presenters and participants, and are not necessarily endorsed or verified by the Forums or the National Academies, and they should not be construed as reflecting any group consensus.

expended when the external temperature drops below 78 degrees Fahrenheit. Disease can affect body temperature as well.

Several researchers have attempted to assess how the various components of energy balance affect cancer risk. A study by Dr. Hursting showed that calorie restriction consistently lowers the risk of cancer mortality across several species, from the mouse to the cow (Hursting et al., 2003). Studies are less consistent on the effects of physical exercise on cancer risk, Dr. Demark-Wahnefried said, although a few studies suggest that when energy intake is kept constant, animals that exercise more have less cancer progression. However, one study found that there is altered activity in several genes when mice are placed on caloric restriction, as compared to relatively few when caloric intake is kept stable, but mice are exercised (Padovani et al., 2009).

Dr. Demark-Wahnefried stressed "the need to disentangle effects of caloric restriction and increased physical activity, as well as obesity. Cancer is complex and energy balance is complex. It's really difficult to make a change in one factor without impacting another." As she noted when people exercise a lot, their appetite tends to increase and leads them to eat more, whereas there is some evidence that moderate amounts of physical activity can actually suppress appetite. "So if you are going to conduct a physical activity intervention, then it is important to measure and control for dietary intake," Dr. Demark-Wahnefried said.

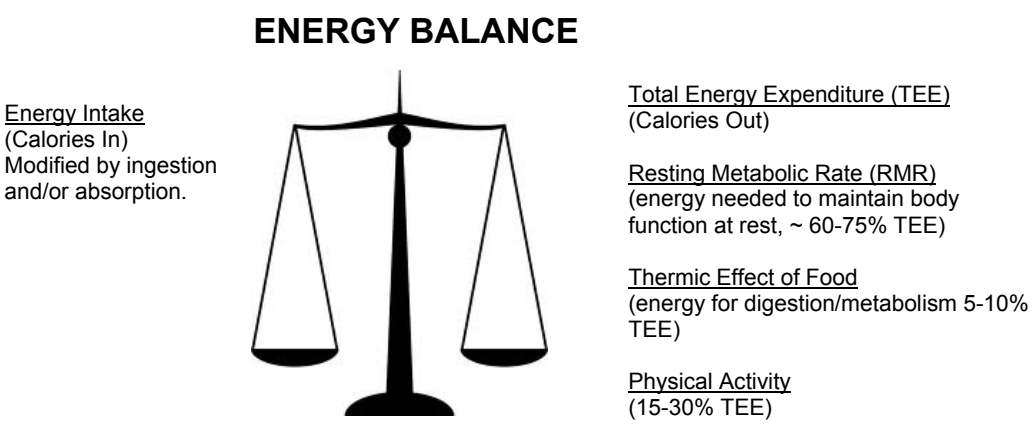

FIGURE 1 Energy balance. Weight maintenance occurs when energy input equals energy expenditure, with gains and losses occurring when there is an imbalance. A gain of one pound occurs when approximately 3,500 calories are consumed in excess of energy needs. For most individuals, resting metabolic rate comprises the major component of energy expenditure, accounting for 60-75 percent of energy needs (Institute of Medicine, 2005; Pi-Sunyer, 2000). Resting metabolic rate is largely governed by lean tissue, which has a higher metabolic rate than adipose tissue. Neoplastic tissue also may a higher metabolic rate, though a study of 200 cancer patients compared to 200 healthy controls found that metabolic rate was highly variable among cancer patients (50-175 percent of predicted values) and greatly influenced by tumor stage and site (Knox et al., 1983). Speculation also exists that RMR may be influenced by various cytokines, though more research is necessary (Pi-Sunyer, 2000). The Thermic Effect of Food, also known as Specific Dynamic Action, is the energy needed for digestion and metabolism of food—transient energy needs that go above and beyond normal metabolism. The Thermic Effect of Food accounts for only 5-10 percent of energy needs and is dependent upon the magnitude of dietary intake, and also may be influenced by the consumption of specific foods or food-related substances. For example, tea, capsaicin, and caffeine may increase metabolism even further (Bell and Goodrick, 2002), though more studies are needed to determine if these transient increases are clinically meaningful. Physical activity comprises the third component of energy expenditure and for individuals living in the developed world, usually accounts for 15-30 percent of energy needs. The energy expended for physical activity is the most modifiable component of energy expenditure. Furthermore, given the potential of exercise (especially resistance training) to increase lean body mass, physical activity also may act indirectly to increase RMR.

SOURCE: Demark-Wahnefried (October 31, 2011). Reprinted with permission from Wendy Demark-Wahnfried.

The increasing incidence of breast cancer in developing countries is thought to reflect the increase in obesity in these nations, added Dr. Ballard-Barbash. Dr. Nathan Berger, a professor of medicine and director for the Center for Science, Health, and Society at the Case Western Reserve University School of Medicine, added that "the convergence of obesity and aging is the perfect storm or tsunami in terms of increasing the overall incidence of cancer."

But obesity does not appear to have a blanket effect on all types of cancers, nor to affect cancer risk the same in men and women. One study found that obesity increases the risk of dying from all cancers by about 52 percent in men, but nearly doubled the risk of dying from any type of cancer in women (Calle et al., 2003). For some cancers, such as liver cancer, obesity was linked to about a five-fold increased risk of cancer mortality in both sexes. In contrast, the association between obesity and colon cancer mortality is not equally strong in women and men, perhaps because body mass index (BMI) is a better measure of abdominal fat in men than women, or because of hormonal factors that are protective, Dr. Gapstur pointed out (Box 2).

BOX 2
How Obesity Is Measured

There are several assessments of overweight and obesity; the most common is body mass index (BMI). BMI is weight (kg)/height squared (m2). It is frequently used in studies because it is a single measure that can be determined easily, Dr. Susan Gapstur pointed out, and is comparable among studies. Below are the World Health Organization criteria for overweight and obesity:

- Underweight = BMI < 18.5 kg/m^2
- Normal weight = BMI 18.5-24.9 kg/m^2
- Overweight = BMI 25.0-29.9 kg/m^2
- Obese = BMI 30+ kg/m^2

An individual's body fat distribution can also be assessed with anthropometric methods such as measurements of waist and hip circumference or the ratio of the two, or techniques such as air displacement or bioelectrical impedance to determine percentage of body fat. BMI correlates well with percentage of body fat in the average population, according to Dr. Gapstur.

Obesity-related breast cancer risk also varies by menopausal status. Increasing BMI levels are linked to a lower incidence of breast cancer in premenopausal women, but a greater incidence of breast cancer in postmenopausal women, Dr. Gapstur said, for reasons that are not yet clearly defined. Obesity's influence on prostate cancer risk also varies. Although obesity is associated with a lower incidence of prostate cancer, studies suggest that obesity is linked to a greater risk of being diagnosed with a more aggressive form of prostate cancer, and studies have consistently shown that obesity substantially increases the risk of dying from prostate cancer. "These data suggest that one shoe doesn't fit all, and it may be very important to separate the different disease types," she said.

Growing evidence also indicates that obesity during childhood can increase the risk of childhood cancers, such as leukemia, and young-onset brain tumors, Dr. Ballard-Barbash noted.