



E & N News to Use *for cancer patients, survivors and caregivers*

EXERCISE & NUTRITION during/after* **CANCER**

CURRENT PEER-REVIEWED MEDICAL LITERATURE and EXPERT COMMENTARY
from **RELIABLE SOURCES** and **DR. BLEYER**

*Studies on cancer prevention are included if they have special relevance to cancer survivors

October 2009

The 12 months of 2008 *E&N News* are now available as a **year summary** for downloading, either for exercise or nutrition (with each including reports on the combination of exercise and nutrition) at www.defeatcancer.info. Both versions include executive summaries and are indexed and bookmarked.

E&N News is now listed as **one of 7 resources recommended by MD Anderson Cancer Center** in the *Complementary Therapies, General* category and endorsed by the Cancer Patient Education Network of the National Cancer Institute. The MD Anderson Cancer *Complementary/Integrative Medicine Educational Resources* resource (www.mdanderson.org/departments/CIMER) is rated #1.

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▶ **Exercise and Nutrition**

Obesity linked to 124,000 new cancers in Europe [Prevention]

A conservative estimate is that in 2008, at least 124,000 new cancers in Europe may have been related to excess body weight

By Roxanne Nelson, Medscape Medical News

October 1, 2009 (Berlin, Germany) — During the past few decades, the percentage of overweight and obese adults and children has steadily increased, which in turn has elevated the risk for certain cancers. That increase in risk might be substantial, according to the results of a new modeling study presented here at the 15th Congress of the European CanCer Organization and the 34th European Society for Medical Oncology Multidisciplinary Congress. "In 2008, at least 124,000 new cancers in Europe may have been related to excess body weight," said study author **Andrew Renehan, PhD, FRCS, FDS**, a senior lecturer in cancer studies and surgery at the **University of Manchester, United Kingdom**.

These are **very conservative estimates**, and it's quite likely that the numbers are in fact higher.

"I must emphasize that we are trying not to be sensationalist about this," he added. "These are very conservative estimates, and it's quite likely that the numbers are in fact higher."

This number has substantially increased in the past 5 years. In 2002, there were 70,288 new cases of cancer related to excess body weight (Renehan et al. *Int J Cancer*. Published online before print July 30, 2009).

The sex differences also show an increase over the past few years, Dr. Renehan noted. In 2002, it was estimated that new cancers attributed to excess body weight affected 2.5% of men and 4.1% of women. By 2008, these proportions had increased to 3.2% of men and 8.6% of women.

"The proportion of new cancers attributable to a [body mass index] above 25 kg/m² was highest among women in the Czech Republic, Latvia, Slovenia, and Bulgaria," Dr. Renehan said.

The analysis quantifies the burden of incident cancers attributable to excess body mass index in Europe, explained Dr. Renehan. The percentage of obesity-related cancers varied widely between the different countries, but the data were "broadly consistent" across geographic locations.

Percentages of Obesity-Related Cancers

Country	% in Men	% in Women
Denmark	2.4	2.1
United Kingdom	3.4	4.0
Germany	3.3	4.8
Czech Republic	3.5	8.2

Projected Figures Show Continuing Rise in New Cancers

In projecting the figures forward to 2008, the researchers took into account confounders such as rates of smoking and the use of hormone replacement therapy in postmenopausal women. Endometrial cancer (n = 33,421), postmenopausal breast cancer (n = 27,770), and colorectal cancer (n = 23,730) accounted for 65% of all cancers attributable to excess body weight.

After the Women's Health Initiative showed an association between hormone replacement therapy and risk for breast cancer, in 2002, the use of such therapy declined sharply. Hormone replacement therapy helped mask and dilute the effect of obesity on the incidence of breast cancer, Dr. Renehan explained.

But with fewer postmenopausal women using hormone therapy, the effect of excess weight on breast cancer risk is much clearer, he said. With declines in both smoking and the use of hormone replacement therapy, obesity could become the leading cause of cancer among European women.

With breast cancer and weight, there is no cutoff point, explained **Jack Cuzick, PhD**, head of the Department for Epidemiology, Mathematics and Statistics at the **Wolfson Institute of Preventive Medicine in London**, United Kingdom.

"**There is a 1% increase in relative risk for every kilogram of excess weight**," said Dr. Cuzick, who served as moderator for the session. "It's a continuum."

"People in Europe are gaining weight," said Dr. Renehan, "and it is projected to keep rising."

Multiple strategies are needed to circumvent the growing numbers of Europeans who are overweight and obese. There must be policy changes at national and international levels, lifestyle interventions, and new approaches,

including pharmacologic interventions, he said. There is an "urgent need" to better understand the biologic and molecular mechanisms underpinning the link between obesity and different cancers.

Source: 15th Congress of the European CanCer Organization (ECCO 15) and the 34th European Society for Medical Oncology (34th ESMO) Multidisciplinary Congress: Abstract 327. Presented September 24, 2009.

Dr. Bleyer:

- ☑ Europe is beginning to follow the U.S. in facing an epidemic of obesity and now expects increases in cancer incidence similar to what has occurred in the U.S.
- ☑ **DEFEATcancer** particularly notes the "1% increase in relative risk for every kilogram of excess weight" and the observation that breast cancer has no upper limit to the increase
- ☑ The relevance for cancer patients/survivors has been covered many times in these pages: prevention of cancer and prevention of cancer recurrence and progression are closely if not intimately related; the lessons of each are applicable to the other

▶ **Exercise**

Physical activity for the affected limb and arm lymphedema after breast cancer surgery. A prospective, randomized controlled trial with two years follow-up

[A randomized trial in Norway documented the benefit of resistance exercise program in women at risk for lymphedema following surgical evaluation of the armpit for breast cancer](#)

Sagen A, Kåresen R, Risberg MA. Acta Oncol. 2009;48(8):1102-10.

Department of Breast and Endocrine Surgery, Oslo University Hospital, Ullevaal, Norway

Background. The influence of physical activity on the development of arm lymphedema (ALE) after breast cancer surgery with axillary node dissection has been debated. We evaluated the development of ALE in two different rehabilitation programs: a no activity restrictions (NAR) in daily living combined with a moderate resistance exercise program and an activity restrictions (AR) program combined with a usual care program. The risk factors associated with the development of ALE 2 years after surgery were also evaluated.

Material and Methods. Women (n = 204) with a mean age of 55+/-10 years who had axillary node dissection were **randomized into two different rehabilitation programs that lasted for 6 months:** NAR (n = 104) or AR (n = 100). The primary outcomes were the difference in arm volume between the affected and control arms (Voldiff, in ml) and the development of ALE. Baseline (before surgery) and follow-up tests were performed 3 months, 6 months, and 2 years after surgery. Data were analyzed using ANCOVA and regression analysis.

Results. Voldiff did not differ significantly between the two treatment groups. Arm volume increased significantly over time in both the affected and the control arms. The development of ALE from baseline to 2 years increased significantly in both groups (p < 0.001). **The only risk factor for ALE was BMI > 25 kg/m(2).**

Conclusion. Patients that undergo breast cancer surgery with axillary lymph node dissection should be **encouraged to maintain physical activity in their daily lives without restrictions** and without fear of developing ALE.

Dr. Bleyer:

- ☑ In the E&N News to Use for August, **DEFEATcancer** reported the results of a landmark study that demonstrated weight lifting decreased lymphedema and reduced symptoms, opposite of what was expected from prior bias and practice
- ☑ This report further confirms that resistance exercise of the arm at risk does not increase lymphedema for at least two years; it did not demonstrate that lymphedema was lessened with exercise, however, as found in the larger, previously reported study
- ☑ The study also found that overweight women were at greatest risk of development lymphedema (and not just those who were obese) and that this was the only factor in the study that correlated with lymphedema
- ☑ A logical conclusion from both studies is that overweight women need to exercise more than women who are not overweight if they want to reduce their risk or severity of lymphedema

Improving sleep quality for cancer patients: Benefits of a home-based exercise intervention

[This study from Taiwan demonstrates how a simple walking program improved sleep and mental quality of life, and reduced pain, in just 8 weeks](#)

Tang MF, Liou TH, Lin CC. Support Care Cancer. 2009 Oct 16
Taipei Medical University - Wan-Fang Hospital, Taipei, Taiwan.

Purpose: 1) To determine the effect of a home-based walking exercise program on the sleep quality and quality of life of cancer patients, as well as 2) to determine if enhanced sleep quality was associated with improvement in quality of life over time.

Methods: This is a prospective, longitudinal, two-armed, randomized clinical trial. Participants were recruited from oncology outpatient clinics in two university-based medical centers and were **allocated to either usual care** (n = 35) **or a home-based walking exercise intervention for 8 weeks** (n = 36). Measurements included the Taiwanese version of the Pittsburgh Sleep Quality Index, the Medical Outcomes Study Short Form-36, the Taiwanese Version Ratings of the Perceived Exertion Scale, and a walking exercise log. This study was analyzed on an intention-to-treat basis. Effects of the walking exercise program on sleep quality and quality of life were analyzed by the generalized estimating equation method.

Results: **Patients in the exercise group reported significant improvements in sleep quality** (beta = -3.54, p < 0.01) and the mental health dimension of quality of life (beta = 10.48, p < 0.01). **Among patients who exercised, enhanced sleep quality also corresponded with reduced bodily pain** (beta = 0.98, p = 0.04) **and improvements over time in the mental health dimension of quality of life** (beta = -3.87, p < 0.01).

Conclusions: A home-based walking exercise program can be easily incorporated into care for cancer patients who are suffering from sleep disturbances.

Dr. Bleyer:

- ☑ This is first study I have found that specifically addressed sleep in cancer patients, and did so with a simple home-based exercise program
- ☑ That only 71 patients were required in a randomized trial to show beneficial effects indicates that exercise had a potent; any intervention that has a modest effect would have taken far more patients to demonstrate a statistically significant difference
- ☑ Fatigue, a related symptom, and one that cancer patients rank as their most problematic, was probably also improved in the exercise group, but since it was not measured, was probably missed as another benefit
- ☑ DEFEATcancer has used the same method of quality-of-life measurement used in this study: Medical Outcomes Study Short Form SF36

Cost-effectiveness of interventions based on physical exercise in the treatment of various diseases: a systematic literature review

[A review of the medical literature identified cost effectiveness of exercise for cardiac and low back pain patient in multiple studies and evidence of benefit for breast cancer patients in one study](#)

Roine E, Roine RP, Räsänen P, Vuori I, Sintonen H, Saarto T. Int J Technol Assess Health Care. 2009 Oct;25(4):427-54.

Department of Oncology, Helsinki University Central Hospital, Helsinki, Finland

Objectives: The aim of this study was to review studies reporting cost-effectiveness of exercise-based interventions in treatment of various diseases.

Methods: Systematic literature search using several databases. Abstracts initially screened independently by two authors, full-text articles again evaluated by two authors, who decided whether an article should be included. Included were scientifically valid articles describing controlled studies that included an exercise-based intervention in the treatment of an established medical condition, and also reported on the cost-effectiveness of the intervention, or its effect on the utilization of health services. Quality was assessed with an established approach.

Results: A total of 914 articles were identified, of them 151 were obtained for closer review. Sixty-five articles describing sixty-one studies were included. Most (82 percent) were randomized trials. Twenty-eight studies dealt with musculoskeletal disorders, fifteen with cardiology, four with rheumatic diseases, four with pulmonary diseases, three with urinary incontinence, and two with vascular disorders. **There was one study each in the fields of oncology, chronic fatigue, endocrinology, psychiatry, and neurology.** Exercise interventions in musculoskeletal disorders were deemed to be cost-effective in 54 percent, in cardiology in 60 percent, and in rheumatic diseases in

75 percent of the cases. There was some evidence that exercise might be cost-effective in intermittent claudication, **breast cancer patients**, diabetes, and schizophrenia.

Conclusions: The number of studies assessing cost-effectiveness of exercise interventions in various diseases is still limited. The results show large variation but suggest that some exercise interventions can be cost-effective. Most convincing evidence was found for rehabilitation of cardiac and back pain patients; however, even in these cases, the evidence was partly contradictory.

Dr. Bleyer:

- ☑ The importance of this study is that cost-effectiveness, not just benefit *per se* to the patient, was assessed in multiple chronic diseases
- ☑ Of interest is that those diseases that had the most studies (cardiology, musculoskeletal) most clearly demonstrated benefit; this suggests that the diseases that did not (cancer was concluded to have “some benefit”) were limited in doing so because there were too few observations (cancer has only one study in the review)
- ☑ It is therefore quite possible that cancer would also have more evidence for cost-effectiveness of exercise if more studies could have been analyzed
- ☑ Since many, if not most, cancer patients have existing co-morbidities (other chronic conditions like arthritis, heart disease, diabetes, obesity, metabolic syndrome), the sentinel significance of this report is that their other conditions are likely to also benefit from exercise
- ☑ **DEFEATcancer** would add that the combination of exercise and nutrition (**E&N**) would have even greater, more-than-additive, benefit

Objectively measured physical activity and sedentary time of breast cancer survivors, and associations with adiposity: findings from NHANES (2003-2006)

[A report from Australia describes the first study—which happens to be on patients in the U.S.—to describe the objectively-assessed physical activity and sedentary time of breast cancer survivors](#)

Lynch BM, Dunstan DW, Healy GN, Winkler E, Eakin E, Owen N.
Cancer Prevention Research Centre, School of Population Health, The University of Queensland, Brisbane, Australia

Objective: Obesity and physical inactivity are poor prognostic indicators for breast cancer. Studies to date have relied on self-report measures of physical activity, which tend mainly to assess moderate-to-vigorous intensity leisure-time physical activity. We report the cross-sectional associations of objectively assessed physical activity and sedentary time with adiposity in a sample of breast cancer survivors from the United States.

Methods: One hundred and eleven women from the National Health and Nutrition Examination Survey (NHANES) 2003-2004 and 2005-2006 reported a history of breast cancer. **Participants wore an accelerometer for 7 days**, and activity levels were summarized as moderate-to-vigorous intensity (accelerometer counts/min $\geq 1,952$), light intensity (counts/min 100-1,951), and sedentary time (counts/min < 100). Anthropometric measures were taken by study staff at examination centers.

Results: **Participants spent the majority of their day in sedentary time (66%) or in light intensity activities (33%).** Log moderate-to-vigorous intensity physical activity was negatively associated with adiposity (waist circumference beta = -9.805 [95% CI: -15.836, -3.775]; BMI beta = -3.576 [95% CI: -6.687, -0.464]). Light intensity physical activity was negatively associated with adiposity; however, the fully adjusted models did not retain statistical significance. Similarly, sedentary time was positively associated with adiposity, but the fully adjusted models were not statistically significant.

Conclusions: This is the first study to describe the objectively assessed physical activity and sedentary time of breast cancer survivors. Increasing moderate-to-vigorous and light intensity physical activity, and decreasing sedentary time, may assist with weight management and improve other metabolic health outcomes for breast cancer survivors.

Dr. Bleyer:

- ☑ If 33% of the average day was spent on sedentary activities and 66% was spent on sedentary activities, that leaves 1% of day, on the average, spent on moderate-to-vigorous activity
 - ☑ Yet, the only statistically-significant correlation with obesity was the 1% of the day spent on moderate-to-vigorous activity; this underscores the power of exercise in preventing or treating obesity (and adiposity)
 - ☑ It also suggests that humans over-report (overstate, exaggerate) the amount of time spent on moderate-to-vigorous activity ... a not surprising observation and one that support increased use of accelerometers and pedometers, as advocated by **DEFEATcancer**
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► **Nutrition**

Occurrence of urolithins, gut microbiota ellagic acid metabolites and proliferation markers expression response in the human prostate gland upon consumption of walnuts and pomegranate juice

[A study in Spain in men with prostate cancer and in rats detected small amounts of the putative active anti-cancer substances in pomegranate juice and walnuts after their oral consumption prior to prostate surgery](#)

González-Sarrías A, et al (12 co-authors). Mol Nutr Food Res. 2009 Nov 2. [Epub ahead of print]
Research Group on Quality, Safety and Bioactivity of Plant Foods, Department of Food Science and Technology, CEBAS-CSIC, Murcia, Spain

Objectives: Epidemiology supports the important role of nutrition in prostate cancer (PCa) prevention. Pomegranate juice (PJ) exerts protective effects against PCa, mainly attributed to PJ ellagitannins (ETs). Our aim was to assess whether ETs or their metabolites ellagic acid and urolithins reach the human prostate upon consumption of ET-rich foods and to evaluate the effect on the expression of three proliferation biomarkers.

Methods: **Sixty-three patients** with BPH or PCa were **divided into controls and consumers of walnuts (35 g walnuts/day) or pomegranate (200 mL PJ/day) for 3 days before surgery.**

Results: Independently of the ETs source, the main metabolite detected was urolithin A glucuronide, 3,8-dihydroxy-6H-dibenzo[b,d]pyran-6-one glucuronide, (up to 2 ng/g) together with the traces of urolithin B glucuronide, 3-hydroxy-6H-dibenzo[b,d]pyran-6-one glucuronide, and dimethyl ellagic acid. The small number of prostates containing metabolites was likely caused by clearance of the compounds during the fasting. This was corroborated in a parallel rat study and thus the presence of higher quantities of metabolites at earlier time points cannot be discarded. No apparent changes in the expression of CDKN1A, MKi-67 or c-Myc were found after consumption of the walnuts or PJ.

Conclusions: Our results suggest that urolithin glucuronides and dimethyl ellagic acid may be the molecules responsible for the beneficial effects of PJ against PCa.

Dr. Bleyer:

- ☑ The conclusion is a “stretch” since there minor to trace amounts of the metabolites the authors propose to be the active ingredients of pomegranate juice were found in the prostates of patients who drank 6-7 ounces of the juice every day for three days prior to surgery
- ☑ Moreover, the amounts that were detected were not associated with a decrease in biologic factors in the prostate that have been implicated in prostate cancer progression
- ☑ Although there was a control group of men who did not eat/drink the walnuts and pomegranate juice, it appears that this was not a randomized study; the results are therefore more subject to bias and confounding factors, even if the results are interpreted as positive
- ☑ The result imply to **DEFEATcancer** that it is unlikely that pomegranate juice alone can prevent prostate cancer or cancer progression; rather **DEFEATcancer** expect that a major change in nutrition, especially with exercise, is necessary for a clinically significant effect

The cytotoxic effect of Bowman-Birk isoinhibitors, IBB1 and IBBD2, from soybean (Glycine max) on HT29 human colorectal cancer cells is related to their intrinsic ability to inhibit serine proteases [Laboratory Study]

[A study in Spain in colon cancer cells suggests that if soybeans have anti-cancer properties, the responsible biochemicals may be serine protease inhibitors, a class of compounds that includes several cancer chemotherapy agents](#)

Clemente A, Moreno FJ, Marín-Manzano MD, Jiménez E, Domoney C. Mol Nutr Food Res. 2009 Nov 2. [Epub ahead of print]

Department of Physiology and Biochemistry of Nutrition, Estación Experimental del Zaidín, Granada, Spain.

Objectives: Bowman-Birk inhibitors (BBI) from soybean and related proteins are naturally occurring protease inhibitors with potential health-promoting properties within the gastrointestinal tract. In this work, we have investigated the effects of soybean BBI proteins on HT29 colon adenocarcinoma cells, compared with non-malignant colonic fibroblast CCD-18Co cells.

Methods: Two major soybean isoinhibitors, IBB1 and IBBD2, showing considerable amino acid sequence divergence within their inhibitory domains, were purified in order to examine their functional properties, including

their individual effects on the proliferation of HT29 colon cancer cells. IBB1 inhibited both trypsin and chymotrypsin whereas IBBD2 inhibited trypsin only.

Results: Despite showing significant differences in their enzyme inhibitory properties, the median inhibitory concentration values determined for IBB1 and IBBD2 on HT29 cell growth were not significantly different (39.9±2.3 and 48.3±3.5 μM, respectively). The cell cycle distribution pattern of HT29 colon cancer cells was affected by BBI treatment in a dose-dependent manner, with cells becoming blocked in the G0-G1 phase. Chemically inactive soybean BBI had a weak but non-significant effect on the proliferation of HT29 cells.

Conclusions: The anti-proliferative properties of BBI isoinhibitors from soybean reveal that both trypsin- and chymotrypsin-like proteases involved in carcinogenesis should be considered as potential targets of BBI-like proteins.

Dr. Bleyer:

- ☑ This report has potential relevance for cancer patients whose chemotherapy includes the serine protease inhibitors like cisplatin (Platinol®), paraplalin (Carboplatin®), docetaxel (Taxotare®), and paclitaxel (Taxol®) since if the investigators are correct, nutritional sources of such inhibitors may help control their cancer
- ☑ **DEFEATcancer** would not expect soybeans alone to provide a sufficient amount of such inhibitors, however

Nutrition during and after cancer therapy

[A well known cancer nutrition expert summarizes how oncology nurses can help cancer patients and survivors improve their nutrition](#)

Barrera S, Demark-Wahnefried W. Oncology (Williston Park). 2009 Feb;23(2 Suppl):15-21.
The University of Texas M.D. Anderson Cancer Center Houston, Texas, USA.

Diet and nutritional factors play a large role in influencing both the quality and quantity of life after the diagnosis of cancer. The oncology nurse is well-positioned to: 1) help ensure that nutritional needs are met for patients who are newly diagnosed, undergoing active treatment, or have advanced disease; 2) facilitate referral of patients with more intensive nutritional needs to registered dietitians; and 3) promote the importance of weight management and a healthful plant-based diet, low in saturated fat and simple sugars, and high in fruits and vegetables and unrefined whole grains, to patients likely to join the ranks of an ever-expanding population of cancer survivors--who now constitute roughly 4% of the US population and number more than 11 million.

Dr. Bleyer:

- ☑ Although this commentary is directed at oncology nurses, the message of a plant-based diet high in fruits, vegetables and whole grains, and low in fats and simple sugars should be noted by all
 - ☑ **DEFEATcancer** recognizes that Dr. Demark-Wahnefried has moved from Duke University to the M.D. Anderson Cancer Center, where **E&N News to Use** is posted online every month
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