

Eating seeds could 'reduce risk of dying from breast cancer by 40 per cent'

By Claire Bates

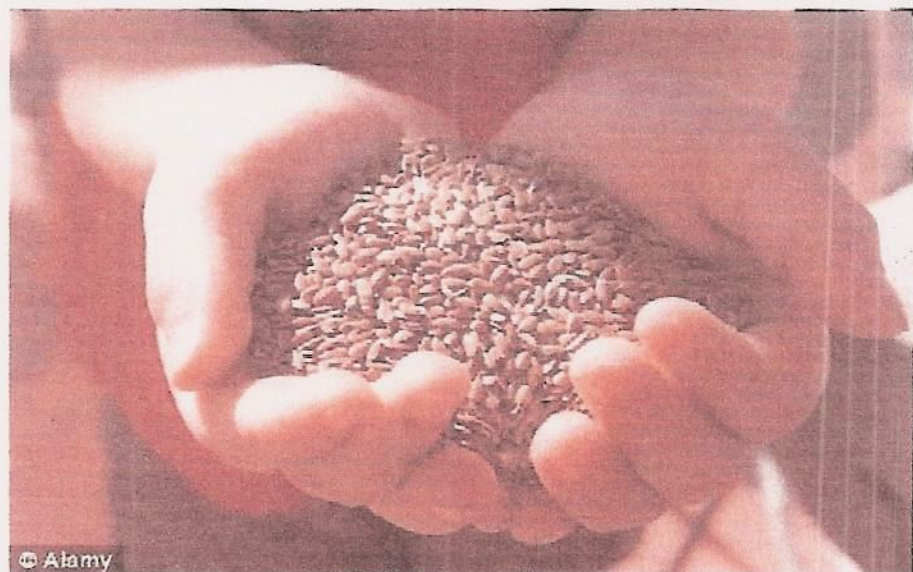
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Eating flaxseeds can help cut the risk of dying from breast cancer later in life by 40 per cent, scientists claim.

Foods including seeds, wheat and vegetables contain special plant compounds called phytoestrogens, the most important of which are lignans.

Scientists found these compounds kill off cancer cells and prevent secondary tumours by stopping the growth of new blood vessels.



Food for thought: Flax seeds are rich in lignans which turn into enterolactone in the bowel. Scientists found they had a protective effect against breast cancer

Flaxseeds were found to be particularly high in lignans. They can be sprinkled on cereals or salads, added to cakes or mixed in with yoghurt.

Once in the body, these phytoestrogens attach to oestrogen, the female sex hormone, and are thought to help protect against cancer.

German researchers analysed blood samples of over 1,000 women diagnosed with premenopausal breast cancer over a three year period.

They analysed levels of enterolactone, which is what phytoestrogens become when they enter the bowel.

Results showed that women with the highest levels of enterolactone levels had their mortality rate reduced by two fifths compared to women with the lowest levels of the same substance.

They also showed that having a high level of enterolactone also afforded similar levels of protection against the spread of cancer and the formation of secondary tumours.



A radiologist assesses a mammogram: The scientists looked at post-menopausal women

The study authors, whose findings are published in the *Journal of Clinical Oncology*, claim that phytoestrogens helped curtail cancer both because of its hormonal properties, as well as by killing off cancer cells and preventing the growth of new blood vessels.

It also gives a clue as to why Asian women are less frequently affected by breast cancer.

Their soy-rich diet contains large amounts of another type of phytoestrogens called isoflavones.

Study author Professor Jenny Chang-Claude, from the German Cancer Research Centre in Heidelberg said: 'We now have first clear evidence showing that lignans lower not only the risk of developing postmenopausal breast cancer, but also the mortality risk.'

'The result was significant only for the group of tumors that have no receptor for the estrogen hormone (ER-negative tumors).'

'This gives reason to suspect that enterolactone protects from cancer not only by its hormone-like effect.'

'Indeed, studies of cells and animals had already provided evidence suggesting that the substance also has an influence on cancer growth irrespective of oestrogen.'

'Thus, it promotes cell death and inhibits sprouting of new blood vessels.'

She added that they would discourage people from taking food supplements to boost lignan levels as they do not fully understand the impact they have on hormones.

'By eating a diet that is rich in wholemeal products, seeds and vegetables, which is considered to be health-promoting anyway, everybody can take in enough lignans,' she said.

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Serum Enterolactone and Prognosis of Postmenopausal Breast Cancer

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Abstract

Purpose Lignans—plant-derived compounds with estrogen-dependent and -independent anticarcinogenic properties—have been associated with postmenopausal breast cancer risk, but data are limited regarding their effect on survival. Dietary lignans are metabolized to enterolignans, which are subsequently absorbed and become bioavailable.

Patients and methods We assessed the prognosis of 1,140 postmenopausal patients with breast cancer age 50 to 74 years who were diagnosed between 2002 and 2005. Vital status through the end of 2009 was ascertained via local population registries, and deaths were verified by death certificates. Information on recurrences and secondary tumors was verified by clinical records and attending physicians. Associations of postdiagnostic serum enterolactone (a biomarker for dietary lignans) with overall survival and distant disease-free survival were assessed by using Cox proportional hazards models stratified by age at diagnosis and adjusted for prognostic factors.

Results Median enterolactone levels for deceased patients and those still alive were 17.0 and 21.4 nmol/L, respectively. During a median of 6.1 years of follow-up after diagnosis, 162 deaths were confirmed. Higher serum enterolactone levels were associated with significantly reduced hazard ratios (HRs) for death (HR per 10 nmol/L increment, 0.94; $P = .04$; HR for the highest quartile, 0.58; 95% CI, 0.34 to 0.99). For distant disease, HR was 0.94 per 10 nmol/L increment ($P = .08$) and 0.62 (95% CI, 0.35 to 1.09) for the highest quartile. The highest quartile of serum enterolactone was associated with a significantly reduced risk of death only for estrogen receptor–negative tumors (HR, 0.27; 95% CI, 0.08 to 0.87) but not for estrogen receptor–positive tumors (HR, 0.91; 95% CI, 0.45 to 1.84; P for heterogeneity = .09).

Conclusion Postmenopausal patients with breast cancer who have high serum enterolactone levels may have better survival.

Footnotes

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Flaxseed and Breast Cancer: What Should We Tell Our Patients?

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In the United States alone, there are approximately 2.6 million survivors of breast cancer.¹ This population is highly motivated to initiate lifestyle changes in diet and exercise to improve their prognosis.²

Dietary lignans have been identified as potentially protective against breast cancer via estrogen-dependent and independent anticarcinogenic activity.³ Lignans are bioactive, non-nutrient, noncaloric phenolic plant compounds that are found in large amounts in flaxseeds and sesame seeds and in small amounts in whole grains, legumes, and certain fruits and vegetables (Table 1).³ For example, one half cup of whole wheat meal is estimated to provide approximately 325 µg lignans, whereas one half cup of flaxseed provides approximately 275,000 µg lignans. In humans, lignans are metabolized by the gut microflora into enterolignans; enterolactone is the main metabolite.⁴ Therefore, enterolactone concentrations in serum, plasma, and urine have been used as biomarkers of dietary lignans.

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Table 1.
Major Food Sources of
Lignans*

The article by Buck et al⁵ that accompanies this editorial investigates the association of enterolactone with breast cancer outcomes. Specifically, the authors found that among 1,140 patients with breast cancer who were postmenopausal, serum enterolactone concentrations in the highest quartile were associated with an approximate 40% reduced risk of overall mortality (hazard ratio, 0.58; 95% CI, 0.34 to 0.99) and distant disease (hazard ratio, 0.62; 95% CI, 0.35 to 1.09). Although this is the first such study in survivors of breast cancer, these findings are supported by a recent meta-analysis that indicates that enterolactone biomarkers are associated with a statistically significant 28% reduced risk of incident breast cancer.⁶

The use of serum enterolactone as an exposure measure offers many advantages in comparison with assessment of dietary intake. Use of a biomarker eliminates the considerable error and bias in dietary self-reporting.⁷⁻¹⁰ In addition, this biomarker bypasses numerous problems that are associated with establishing the lignan content of foods, which can vary substantially within a food according to variety, crop season, location, and processing methods.⁴ Finally, the reliability coefficient for serum enterolactone is 0.55,⁴ which suggests that this measure provides a reasonably robust estimate of usual exposure.

Given this objective evidence that a biomarker of lignan intake improves breast cancer outcomes, should we declare success and recommend that our patients with breast cancer supplement their diet with flaxseed? When considering the study by Buck et al,⁵ it is instructive (and sobering) to recall the demise of the carotenoid hypothesis regarding β-carotene and chemoprevention of lung cancers. In the 1980s, there was considerable epidemiologic evidence that higher dietary intake of fruits and vegetables and blood levels of β-carotene (a marker of fruit and vegetable intake¹¹) were associated with a lower risk of epithelial cancers.^{12,13} These epidemiologic studies were bolstered by laboratory research that identified several plausible biologic mechanisms by which β-carotene could act to reduce tumor incidence.^{12,14} In response, two large trials were launched to test the effect of β-

carotene supplements on lung cancer incidence in high-risk populations (eg, smokers). Unexpectedly, both trials found that β -carotene supplementation increased the incidence of lung cancers as well as cardiovascular and all-cause mortality.^{15,16} A subsequent review of randomized trials of antioxidant supplements, including 25 trials of β -carotene, concluded that use of this supplement increased overall mortality by 7% (relative risk, 1.07; 95% CI, 1.02 to 1.11).¹⁷ These findings reversed the trend toward widespread use of β -carotene supplements and fortification of common foods with this compound and likely resulted in many lives saved.

A striking observation in both of these trials^{15,16} was that higher baseline serum β -carotene concentrations were strongly associated with a reduced risk of lung cancer, although supplementation with β -carotene in this same population increased the risk of lung cancer.¹⁸ A number of interpretations of these apparently paradoxical findings have been put forward. For example, it is possible that the physiological effects of relatively low blood concentrations of compounds (such as β -carotene or enterolactone) obtained from a mixed diet do not predict the effect of high-dose supplementation, particularly in an at-risk population. Another possible explanation is that serum β -carotene concentrations are serving as a biomarker of a healthy lifestyle, even after adjustment for covariates such as education, body mass index, and physical activity. Given that the major dietary sources of lignans are fiber from whole grains, legumes, fruits, and vegetables, a healthy lifestyle biomarker interpretation of the Buck et al study findings is plausible.

Finally, there is a considerable amount to be learned about the degree to which serum enterolactone concentrations reflect dietary intake of lignans. The bioavailability of lignans from various food sources is not well understood, the colonic environment affects the conversion of dietary lignans to enterolactone, other factors (eg, smoking, alcohol intake) affect serum concentrations, and the potential effect of endogenous and exogenous hormones on lignan metabolism and excretion has not been fully established.⁴ Therefore, serum enterolactone concentrations are an imperfect measure of dietary intake because they reflect (in unknown proportions) dietary intake of lignans, other dietary and environmental exposures, and host characteristics.

In the face of the unknowns regarding dietary lignans and breast cancer risk, clinicians find themselves once again recommending the unexciting balanced diet that includes plenty of whole grains, fruits, and vegetables. Nonetheless, until a trial of lignan intake/supplementation and disease end points quantifies the risks and benefits of such an intervention, the prudent clinician should be wary of recommending high doses of any dietary compound solely on the basis of laboratory and observational epidemiologic studies.

First, do no harm.

AUTHOR'S DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

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Footnotes

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