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Q/ Does high dietary soy intake affect a woman's risk of primary or recurrent breast cancer?

EVIDENCE-BASED ANSWER

A/ **No,** it doesn't affect the risk of primary breast cancer, but it does (favorably) affect the risk of cancer recurrence.

Compared with diets low in soy, high dietary intake of soy protein or soy isoflavones isn't associated with any alteration in the risk of developing primary breast cancer (strength of recommendation [SOR]: **B**, systematic review of prospective cohort studies). In patients with breast cancer, however, consuming a diet high in soy is associated with a 25% decrease in cancer recurrence and a 15% decrease in mortality (SOR: **B**, prospective cohort studies).

Evidence summary

A large systematic review evaluated the relationship between dietary soy intake and risk of a primary breast cancer diagnosis. It included 7 prospective cohort studies, which comprised the best quality evidence available (numerous other reviewed studies were of lower quality). The review found no significant association between dietary soy intake and primary breast cancer (**TABLE**[1-6]).

Investigators either surveyed women for intake of soy isoflavones or soy foods or products (tofu, soybeans, lentils, miso) or measured urinary or plasma levels of soy isoflavones. They adjusted for age, alcohol use, smoking status, body mass index, caloric intake, and hormone replacement therapy, then followed subjects for 7 to 23 years, comparing the risk of breast cancer for the lowest and highest levels of soy intake.

Six of the prospective cohort studies found no association between soy intake and breast cancer risk; one study, comprising 4% of the total population, found a lower risk with higher soy intake (effect size=0.44; 95% confidence interval [CI], 0.26-0.73; an effect size of 0.2 is considered small, 0.6 medium, and 1.2 large). The authors didn't do a meta-analysis of the prospective cohort studies.

Other cohort studies yield similar findings

Four other large systematic reviews evaluating soy intake and breast cancer risk incorporated a total of 6 individual prospective cohort studies that weren't included in the previously described review (again, these studies comprised the best quality evidence within the reviews). The 6 studies found no association between soy intake and breast cancer risk.

In 2 of the studies, investigators surveyed postmenopausal women and followed them for 4 to 8 years.[2] Investigators in another study adjusted for age, family and gynecologic history, hormone and medication use, exercise, and other factors.[3] In 2 other studies, investigators evaluated population subsets that consumed the most vs the fewest servings per week or kilograms per year of soy foods.[4] The sixth study compared low with high intake of soy foods and miso.[5]

Soy intake after breast cancer diagnosis reduces recurrence risk in most studies

Most prospective cohort studies evaluating

TABLE

Associated risk of primary or recurrent breast cancer relative to soy intake[1-6]

Outcome	Type of study	Population	Comparison groups (highest vs lowest dietary intake of soy)	Result (95% confidence interval)
Primary breast cancer incidence	Systematic review with 7 prospective cohort studies[1]	Western and Asian women (N=~170,000)	Highest vs lowest dietary intake of soy isoflavone, soy foods/products, or measured isoflavone levels	No overall difference in risk
	2 prospective cohort studies[2]	American and Dutch postmenopausal women (N=50,500)	Highest vs lowest soy isoflavone intake and soy supplementation vs no supplement	No overall difference in risk in either study
	1 prospective cohort study[3]	Japanese women (N=30,454)	Highest vs lowest tertile, soy food intake	No overall difference in risk
	2 prospective cohort studies[4]	Chinese women (N=1800)	Highest vs lowest soy food intake	No overall difference in risk
	1 prospective cohort study[5]	American and Japanese women (N=178,000)	Highest vs lowest soy food intake (tofu and miso)	No overall difference in risk
Breast cancer recurrence and breast cancer-related mortality	Meta-analysis of 5 prospective cohort studies[6]	Chinese and American women with prior diagnosis of breast cancer (N=11,206)	**Soy protein intake** >13 g/d vs <2 g/d **Soy isoflavones** >17 mg/d vs <7.6 mg/d	**Overall** Highest vs lowest dietary soy intake (pooled) Recurrence: HR=0.79 (0.72–0.87); mortality: HR=0.85 (0.77–0.93) **Estrogen receptor positive** Highest vs lowest soy intake Recurrence: HR=0.81 (0.63–1.04); mortality: HR=0.72 (0.61–0.84)* **Estrogen receptor negative** Highest vs lowest Recurrence: HR=0.64 (0.44–0.94);* mortality: HR=0.75 (0.64–0.88)*

HR, hazard ratio.

* Statistically significant.

the association between dietary soy intake after breast cancer diagnosis found an overall 21% decrease in recurrence with high soy intake and a 15% reduction in mortality (**TABLE**[1-6]).

Investigators in a meta-analysis of 5 studies that followed women for 4 to 7 years after first breast cancer diagnosis found that higher soy intake was associated with lower mortality but not less recurrence in women who were estrogen receptor positive. Both recurrence and mortality were decreased in estrogen receptor negative women.[6]

The study also found lower recurrence

and mortality in premenopausal women with higher soy intake (recurrence hazard ratio [HR]=0.91; 95% CI, 0.72-1.14; mortality HR=0.78; 95% CI, 0.69-0.88). In postmenopausal women, higher intake was likewise associated with improvement of both outcomes (recurrence HR=0.67; 95% CI, 0.56-0.80; mortality HR=0.81; 95% CI, 0.73-0.91).

An earlier meta-analysis of 4 prospective cohort studies, 2 of which were not included above, also found reduced risk of breast cancer recurrence in groups with high vs low soy isoflavone intake (HR=0.84; 95% CI, 0.70-0.99).[7] Women taking tamoxifen showed no difference in mortality or recurrence risk associated with soy intake.

An additional small prospective cohort study (n=256) found similar reductions in recurrence and mortality associated with higher consumption of soy protein.[8] JFP

References

1. Chen M, Rao Y, Zheng Y, et al. Association between soy isoflavone intake and breast cancer risk for pre- and post-menopausal women: a meta-analysis of epidemiological studies. *PLoS One*. 2014;9:e89288.
2. Fritz H, Seely D, Flower G, et al. Soy, red clover, and isoflavones and breast cancer: a systematic review. *PLoS One*. 2013;8:e81968.
3. Nagata C, Mizoue T, Tanaka K, et al. Soy intake and breast cancer risk: an evaluation based on a systematic review of epidemiologic evidence among the Japanese population. *Jpn J Clin Oncol*. 2014;44:282–295.
4. Liu XO, Huang YB, Gao Y, et al. Association between dietary factors and breast cancer risk among Chinese females: systematic review and meta-analysis. *Asian Pac J Cancer Prev*. 2014;15:1291–1298.
5. Qin LQ, Xu JY, Wang PY, et al. Soyfood intake in the prevention of breast cancer risk in women: a meta-analysis of observational epidemiological studies. *J Nutr Sci Vitaminol* (Tokyo). 2006;52:428–436.
6. Chi F, Wu R, Zeng YC, et al. Post-diagnosis soy food intake and breast cancer survival: a meta-analysis of cohort studies. *Asian Pac J Cancer Prev*. 2013;14:2407–2412.
7. Dong JY, Qin LQ. Soy isoflavones consumption and risk of breast cancer incidence or recurrence: a meta-analysis of prospective studies. *Breast Cancer Res Treat*. 2011;125:315-323.
8. Kang HB, Zhang YF, Yang JD, et al. Study on soy isoflavone consumption and risk of breast cancer and survival. *Asian Pac J Cancer Prev*. 2012;13:995–998.