

# Regular consumption of lactic acid bacteria and isoflavones reduce breast cancer risk in Japanese women: a population-based case-control study

Masakazu Toi<sup>1)</sup>, Yasuo Ohashi<sup>2)</sup>, The Study Group of Lactic Acid Bacteria and Breast Cancer<sup>3)</sup>

No.1050



1) Department of Surgery, Kyoto University, Kyoto, Japan 2) Department of Biostatistics, University of Tokyo, Tokyo, Japan 3) The Public Health Research Foundation, Tokyo, Japan

## Background & Objective

- Like fermented dairy product such as yogurt, beverages with *Lactobacillus casei* strain Shirota (BLS) are consumed on a regular basis by many Japanese.
- An animal study showed BLS suppressed growth of mammary tumor.
- BLS consumption reduces the risk of bladder cancer (Ohashi et al., (2002)).
- Consumption of soy isoflavones is associated with the risk reduction of breast cancer in Asian population (Wu et al.,(2008)).
- This case-control study evaluated whether past consumption of BLS and soy isoflavones reduces the risk of breast cancer.

## Materials & Methods

### Design

- Case-to-control ratio = 1:2, matched for area of residence and age
- Area of residence: 14 areas in Japan
- Age: matched within two-year age brackets between 40 and 55
- **Population-based case-control study**

### Registration period

- October 2007 to March 2009

### Subjects

- Cases
  1. Patients with primary breast cancer
  2. Stage 0 or 1
  3. Within one year of breast cancer surgery
- Controls
  1. Randomly sampled from the Basic Resident Register and matched with cases for age and area of residence
  2. Non-breast cancer patients

### Sample size

- 355 cases and 710 controls, expected odds ratio = 0.55, type I error = two-sided 5%, 80% power, exposure to BLS = 15%

### Exposure measurement

- Self-administered questionnaire
- Medical history, family history, diet (semi-quantitative food frequency questionnaire for epidemiological study), life-style
- Interview
  - Consumption of BLS- and soy isoflavone-containing food and beverages during three specific periods (**at age 10 to 12, or in the upper grades of elementary school; around age 20; 10 to 15 years**)
  - Conducted by trained interviewers masked to the case/control information

## Beverages with *Lactobacillus casei* strain Shirota (BLS)

Participants were interviewed for their past diet in 1960s, 1970s and 1980s. Yakult is the first live *Lactobacillus casei* strain Shirota (*Lactobacillus casei* strain Shirota) - containing food sold in Japan since 1935. Yakult had been the major live *Lactobacillus*-containing food until other companies started sales of similar products in 1970s. According to the sales record of Yakult Honsha Co. Ltd, 13% of Japanese people consumed Yakult in 1975. Many types of live *Lactobacillus*-containing food are now regularly consumed by Japanese people.



## Soy isoflavones

Isoflavone-rich soy products are popular among Asian people. Japanese favorite soy products include natto (fermented soybean), tofu (bean curd) and miso soup. Japanese consume soy isoflavones more than Western people.



## Demographics

- 368 patients were invited to the study and 321 patients accepted the invitation.
- 8166 invitation letters were sent to control candidates and 884 women accepted.
- 306 cases and 662 controls were included in the analysis.

### Participant demographics

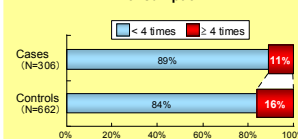
Confounding factor	Unit	Cases (N=306)		Controls (N=662)	
		N	%	N	%
Age*		48	(4.08)	47	(3.72)
Educational background	Other than college/graduate	264	86.27	518	78.25
	College/graduate school or above	42	13.73	144	21.75
Physical activity level*	[Met-h/weekday]	26	(13.28)	27	(12.77)
Benign mammary tumor	None	255	83.33	621	93.81
	Yes	51	16.67	41	6.19
Family breast cancer history	No	277	90.52	634	95.77
	Yes	29	9.48	28	4.23
Menarche* [years]	13	(1.28)	13	(1.30)	
	2	(1.01)	2	(1.09)	
Breast feeding	No	74	24.18	134	20.24
	Yes	232	75.82	528	79.76
Use of female hormone	Currently using	254	83.01	553	83.53
	Not using	52	16.99	109	16.47
Birthweight	>2500g	269	87.91	584	88.22
	<2500g	21	6.86	48	7.25
	Unknown	16	5.23	30	4.53
BMI around 20* [kg/m <sup>2</sup> ]	High†	20	(2.36)	20	(1.18)
	Not smoking/quit	268	87.58	584	88.22
Smoking	Smoking	38	12.42	78	11.78
	1000 kcal/day*	2	(0.63)	2	(0.67)

\* Summary statistics for continuous data shown in mean (SD)

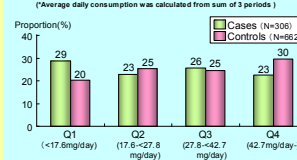
## Results

**Association between BLS and soy isoflavone consumption in elementary school/around age 20/10 to 15 years ago and breast cancer:** conditional logistic regression analysis with adjustment for age (bicategorical, 40s and 50s) and several other factors taking into account matching for area of residence

### Average weekly BLS Consumption



### Average daily soy isoflavone Consumption\*



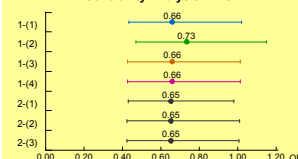
### Conditional Logistic Regression: BLS

	OR	95%CI	p
< 4 times	Reference.		0.0564
≥ 4 times	0.657	0.426 1.011	

### Conditional Logistic Regression: Soy isoflavones

	OR	95%CI	p (trend)
Q1	Reference.		0.0006
Q2	0.633	0.418 0.958	
Q3	0.616	0.407 0.933	
Q4	0.454	0.296 0.695	

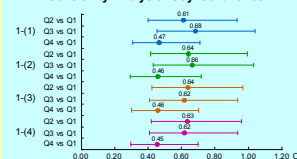
### Sensitivity Analysis: BLS



\*Models for sensitivity analysis

1. Conditional Logistic Regression
- 1- (1) Matched with area and age
- 1- (2) Matched with area and age and adjustment factors
- 1- (3) Matched with area and adjustment factors (including age)

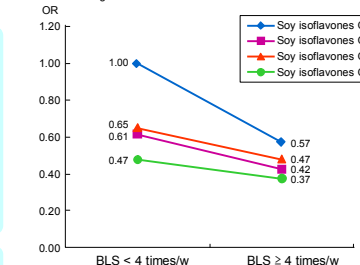
### Sensitivity Analysis: Soy Isoflavones



1. (4) Matched with area and adjustment factors (including age,40s,50s)
2. Unconditional Logistic Regression
- 2- (1) No adjustment factors
- 2- (2) Adjustment factors including area and age
- 2- (3) Adjustment factors including area and age,40s,50s

### BLS-soy isoflavone interaction

• A test of interaction term showed no statistical significance but a tendency that consumption of both BLS and soy isoflavones might reduce OR.



## Conclusions

- BLS and soy isoflavone consumption was different between women with breast cancer and women without breast cancer.
- Women without breast cancer had consumed more BLS and soy isoflavones compared with women with breast cancer.
- As shown in the previous studies, family breast cancer history and benign mammary tumor were identified as risk factors in this study.
- Regular consumption of BLS and soy isoflavones in young age may reduce the breast cancer risk in middle-aged Japanese women.

## Conflict of Interest

This study was funded by Comprehensive Support Project for Oncology Research (CSPOR) of Public Health Research Foundation. The research fund was provided to CSPOR by Yakult Honsha Co., Ltd. Yakult Honsha took no part in this study other than providing product information. All decisions concerning the planning, implementation and publication of this study were made by the executive committee of this study.

## References

1. Ohashi et al. Habitual Intake of Lactic Acid Bacteria and Risk Reduction of Bladder cancer. *Urol Int* 2002; 68: 273-280.
2. Wu et al. Epidemiology of soy exposures and breast cancer risk. *Br J Cancer* 2008; 98: 9-14.