表2 肺がんとbody mass indexの関連に関する症例対照研究

References		Study time	Study subjects				Category (body mass index)	Relative risk (95%CI or p)	p for trend	Confounding variables considered
Author	Year		Type and source	Definition	Number of cases	Number of controls				
Kanashiki M, et al.*	2005	1997-2003	Participants in a mass-screening program	Cases: identified in hospital reports or in a cancer registry; Controls: participants of the screening program without history of malignancy and abnormality on screening	230 male cases	690 men	< 20.8 (kg/m^2)	1.9 (1.3-2.9)		Matched (1:3) for year of birth; adjusted for smoking
							20.8-22.8	1.2 (0.7-1.8)		
							22.9-24.9	1.0		
							25.0-	0.9 (0.6-1.4)		
					Five years prior to diagnosis		< 20.8	1.7 (1.0-2.8)		
							20.8-22.8	1.4 (0.8-2.3)		
							22.9-24.9	1.0		
							25.0-	1.1 (0.7-1.9)		
					104 male cases of AD	312 men	< 20.8	1.5 (0.8-2.8)		
							20.8-22.8	0.9 (0.5-1.8)		
							22.9-24.9	1.0		
							25.0-	0.9 (0.5-1.7)		
					133 female cases	399 women	< 20.8	0.8 (0.4-1.4)		
							20.8-22.8	0.5 (0.3-0.9)		
							22.9-24.9	1.0		
							25.0-	0.9 (0.6-1.4)		
					Five years prior to diagnosis		< 20.8	1.2 (0.6-2.4)		
							20.8-22.8	1.0 (0.5-2.0)		
							22.9-24.9	1.0		
							25.0-	1.5 (0.8-2.6)		
					111 female cases of AD	333 women	< 20.8	0.9 (0.5-1.6)		
							20.8-22.8	0.4 (0.2-0.7)		
							22.9-24.9	1.0		
							25.0-	0.9 (0.5-1.6)		

* Kanashiki M, Sairenchi T, Saito Y, Ishikawa H, Satoh H, Sekizawa K. Body mass index and lung cancer: a case-control study of subjects participating in a mass-screening program. Chest 2005; 128: 1490-1496.

表3 肺がんと大豆製品摂取の関連に関するコホート研究

References			Study period	Study population				Food item	Category	Number among cases	Relative risk (95%CI or p)	p for trend	Confounding variables considered	Comments
Author	Year	No.		Number of subjects for analysis	Source of subjects	Event followed	Number of incident cases or deaths							
Hirayama T	1990	1	1966-1982	265,118 men and women	General population	Death	1454 men and 463 women	Miso soup	Non-daily		1.00		Age and sex	Relative risk: figures in parenthesis show 90% CIs.
									Daily		1.06 (0.97-1.15)			
Ozasa K, et al	2001	2	1988-1997	42,940 men	Participants in health check-ups or general population	Death	446 men	Miso soup	< 1 cup/day	146	1.00	p = 0.69	Age, family history of lung cancer, and smoking	
									1-2 cups/day	173	1.06 (0.82-1.36)			
									3+ cups/day	102	1.14 (0.83-1.57)			
								Boiled beans	≤ 1-2/month	187	1.00	p = 0.26		
									1-2/week	66	0.74 (0.56-0.99)			
									3-4/week+	62	0.90 (0.67-1.21)			
								Tofu	≤ 1-2/week	149	1.00	p = 0.14		
									3-4/week	94	0.80 (0.62-1.04)			
									Almost every day	93	0.83 (0.63-1.08)			
				55,308 women			126 women	Miso soup	< 1 cup/day	40	1.00	p = 0.017		
									1-2 cups/day	24	1.47 (0.92-2.33)			
									3+ cups/day	20	1.92 (1.00-3.67)			
								Boiled beans	≤ 1-2/month	47	1.00	p = 0.50		
									1-2/week	23	0.96 (0.58-1.60)			
									3-4/week+	17	0.81 (0.46-1.44)			
								Tofu	≤ 1-2/week	41	1.00	p = 0.43		
									3-4/week	18	0.50 (0.28-0.88)			
									Almost every day	32	0.85 (0.52-1.37)			
Takezaki T, et al	2003	3	1985-1999	5,885 men and women	General population	Incidence	51 men and women	Soybean products	< 3/week	18	1.00	p=0.369	Age, sex, smoking, and occupation	
									3-4/week	18	0.91 (0.47-1.75)			
									5/week+	15	0.73 (0.37-1.45)			
Khan MMH, et al	2004	4	1984-2002	1,524 men	General population (randomly sampled)	Death	41 men	Tofu	Several times/week+ vs. ≤ several		0.6 (0.3-1.3)		Age, health status, health education, screening, and smoking	
				1,634 women			10 women	Tofu	times/month		NA			

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表4 肺がんと大豆製品摂取の関連に関する症例対照研究

References			Study time	Study subjects				Food item	Category	Relative risk (95%CI or p)	p for trend	Confounding variables considered	Comments
Author	Year	No.		Type and source	Definition	Number of cases	Number of controls						
Wakai K, et al.	1999	1	1988-1991	Hospital-based (National Okinawa Hospital)	Cases: histologically confirmed; Controls: randomly selected residents	245 male cases	490 men	Tofu	≤ 3-4/week	1.00		Matched for age (± 2 years), sex, and residence; adjusted for education, smoking, and medical history of lung disease	
									Almost every day	0.72 (0.50-1.04)			
								Miso soup	Not daily	1.00	p=0.001		
									1 cup/day	2.31 (1.02-5.22)			
									2 cups/day	3.19 (1.41-7.22)			
									3 cups/day+	3.76 (1.66-8.51)			
								Soybeans	< 1/month	1.00	p=0.049		
									1-2/month	0.69 (0.41-1.18)			
									1-2/week+	0.63 (0.40-0.98)			
						88 female cases	176 women	Tofu	≤ 3-4/week	1.00			
									Almost every day	1.00 (0.54-1.86)			
								Miso soup	Not daily	1.00	p=0.043		
									1 cup/day	3.26 (0.80-13.4)			
									2 cups/day	5.50 (1.40-21.7)			
									3 cups/day+	4.04 (1.03-15.9)			
								Soybeans	< 1/month	1.00	p=0.92		
									1-2/month	1.24 (0.48-3.24)			
									1-2/week+	1.09 (0.49-2.39)			
						115 male cases of SQ	490 men	Tofu	≤ 3-4/week	1.00			
									Almost every day	0.55 (0.34-0.89)			
								Miso soup	Not daily	1.00	p=0.046		
									1 cup/day	2.85 (0.96-8.44)			
									2 cups/day	3.93 (1.31-11.8)			
									3 cups/day+	3.66 (1.22-11.0)			
								Soybeans	< 1/month	1.00	p=0.17		
									1-2/month	0.91 (0.47-1.76)			
									1-2/week+	0.69 (0.40-1.20)			
						19 female cases of SQ	176 women	Tofu	≤ 3-4/week	1.00			
									Almost every day	0.14 (0.02-0.89)			
								Miso soup	≤ 1 cup/day	1.00	p=0.086		
									2 cups/day	4.39 (0.83-23.1)			
									3 cups/day+	4.36 (0.67-28.2)			
								Soybeans	< 1/month	1.00	p=0.92		
									1-2/month	0.98 (0.10-9.67)			
									1-2/week+	0.92 (0.18-4.61)			
						106 male cases of AD	490 men	Tofu	≤ 3-4/week	1.00			
									Almost every day	0.68 (0.42-1.11)			

								Miso soup	Not daily	1.00	p=0.0007	
									1 cup/day	2.26 (0.77-6.67)		
									2 cups/day	2.66 (0.89-7.90)		
									3 cups/day+	4.74 (1.63-13.8)		
								Soybeans	< 1/month	1.00	p=0.49	
									1-2/month	0.97 (0.49-1.90)		
									1-2/week+	0.83 (0.47-1.46)		
						59 female cases of AD	176 women	Tofu	≤ 3-4/week	1.00		
									Almost every day	1.01 (0.54-1.92)		
								Miso soup	Not daily	1.00	p=0.036	
									1 cup/day	3.70 (0.76-18.1)		
									2 cups/day	6.98 (1.45-33.7)		
									3 cups/day+	5.38 (1.06-27.4)		
								Soybeans	< 1/month	1.00	p=0.61	
									1-2/month	1.27 (0.44-3.71)		
									1-2/week+	1.27 (0.55-2.93)		
Takezaki T, et al	2001	2	1988-1997	Hospital-based (Aichi Cancer Center)	Cases: histologically diagnosed; controls: first-visit outpatients without cancer	367 male cases of AD	2964 men	Tofu	< 1/week	1.00	p=0.478	Age, season and year of visit, occupation, prior lung diseases, smoking, and consumption of green vegetables and meat
									1-2/week	1.33 (0.95-1.87)		
									3-4/week	1.27 (0.88-1.84)		
									5/week+	1.24 (0.83-1.85)		
								Miso soup	Almost never	1.00	p=0.346	
									Occasionally	1.93 (0.90-4.14)		
									1/day	1.65 (0.78-3.51)		
									2/day+	1.40 (0.63-3.11)		
						381 male cases of SQ+SM	2964 men	Tofu	< 1/week	1.00	p=0.341	
									1-2/week	1.10 (0.78-1.55)		
									3-4/week	1.09 (0.76-1.57)		
									5/week+	1.23 (0.84-1.81)		
								Miso soup	Almost never	1.00	p=0.112	
									Occasionally	2.24 (0.98-5.11)		
									1/day	2.40 (1.07-5.38)		
									2/day+	2.50 (1.08-5.79)		
						240 female cases of AD	1189 women	Tofu	< 1/week	1.00	p=0.021	
									1-2/week	0.89 (0.55-1.43)		
									3-4/week	0.93 (0.56-1.52)		
									5/week+	0.52 (0.30-0.91)		
								Miso soup	Almost never	1.00	p=0.690	
									Occasionally	0.79 (0.36-1.72)		
									1/day	0.90 (0.42-1.93)		
									2/day+	0.69 (0.30-1.59)		
						57 female cases of SQ+SM	1189 women	Tofu	< 1/week	1.00	p=0.519	

								1-2/week	3.68 (0.99-13.6)		
								3-4/week	2.86 (0.73-11.2)		
								5/week+	3.00 (0.72-12.6)		
							Miso soup	Almost never	1.00	p=0.556	
								Occasionally	0.51 (0.12-2.07)		
								1/day	0.45 (0.11-1.77)		
								2/day+	0.51 (0.11-2.42)		
Huang XE, et al.	2004	3	1988-1998	Hospital-based (Aichi Cancer Center)	Cases: identified in the hospital cancer registry; controls: first-visit outpatients without cancer	1,296 cases without family history of lung cancer	48,443 first-visit non-cancer patients without family history of lung cancer	Tofu	< 3/week	1.00	Age and sex
									3/week+	1.03 (0.86-1.23)	
							Miso soup	< 1/day	1.00		
								1/day+	1.15 (1.02-1.30)		
						102 cases with family history of lung cancer	2,263 first-visit non-cancer patients with family history of lung cancer	Tofu	< 3/week	1.00	
									3/week+	1.24 (0.65-2.38)	
							Miso soup	< 1/day	1.00		
								1/day+	1.28 (0.82-2.00)		

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分担研究報告書

生活習慣改善による乳がん予防法の開発と評価

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研究要旨

わが国における乳がんと食事要因(脂肪、大豆摂取、BMI)に関する分析疫学研究のレビューを行った。乳がんと脂肪、大豆摂取に関する研究は未だ研究が少なく、現段階でのまとまった評価は困難である。乳がんと BMI に関する研究は閉経後肥満女性に乳がんリスクが高いという海外での結果と概ね一致していたが、コホート研究数は3と日本女性におけるリスクの大きさを評価するには少ない。

野菜にメラトニンが含まれることが報告されており、がん予防のメカニズムに関与するかも知れない。メラトニンを多く含むことが知られている野菜を多く摂取することにより、実際、尿中のメラトニン代謝物が増加するのかを調べるため、介入研究をおこなった。一般女性97名を対象に、2ヶ月間メラトニン含有野菜を摂取する群とこれらの摂取を避けてもらうコントロール群に無作為割付した。介入実施期間を終了し、尿中メラトニン代謝物の測定、食事記録からの各種栄養・食品摂取量の推定を行っている。

I. 日本人における食事要因と乳がんリスクに関する研究レビュー

A. 研究目的

食習慣、栄養が乳がんリスクに影響をおよぼすという仮説はあるものの実際どのような栄養因子が関与るかは未だ明らかでない。既に野菜、果物摂取と乳がんリスクについて過去に日本で実施された分析疫学研究のレビューをおこなったが、今回、古くから乳がんとの関連性が注目されてきた脂肪摂取、また日本における伝統的食品で近年になりがん予防効果が期待されている大豆摂取について同様にレビューを行った。また、食事関連要因として体型も項目に加えた。閉経後の肥満が、乳がんリスクを増加させることはほぼ確定的な知見となっているが、日本人におけるデータが必要である。

B. 研究方法

日本における乳がんのコホート研究、ケース・コントロール研究を Medline にて検索し、乳がんと脂肪、大豆製品、body mass index (BMI)との関連性が相対危険度/オッズ比として記載された研究を対象とした。脂肪摂取が定量的に推定されている研究は少なく、肉類、魚類の摂取と乳がんリスクについて評価を行った研究も対象に加えた。

(倫理面での配慮)

この研究方法は、既に論文に報告された結果に基づいており、倫理面での問題はない。

C. 研究結果

1. 脂肪および肉類摂取と乳がん(表1、表2)

コホート研究2、ケース・コントロール研究3と少ない。脂肪摂取を定量的に評価したのは、コホート研究、

ケース・コントロール研究各1つである。コホート研究では魚に多く含まれる long-chain n-3 脂肪酸の摂取が高いほどリスクの低下が認められた。Hirayama らの研究では肉類の摂取が少ない女性にリスクの低下が認められたが、Wakai らの研究では全脂肪、long-chain n-3 脂肪酸をのぞく各脂肪タイプとは有意な関連性は認められなかった。ケース・コントロール研究も魚類摂取とリスクとの負の関連性が見られるが脂肪摂取との関連性は認められなかった。

2. 大豆製品摂取と乳がん(表3、表4)

コホート研究3、ケース・コントロール研究4が発表されているが同施設で行われたケース・コントロール研究が含まれている。コホート研究では2つに有意なあるいは有意に近い負の関連性が認められた。ケース・コントロール研究は2施設での研究のうち1つは、脂肪換算した大豆摂取量はケースとコントロールに差はなかった。一方では豆腐摂取において負の関連性が報告されている。

3. BMI と乳がんに関する研究(表5、表6)

コホート研究で3つと少ないもののケース・コントロール研究は比較的多い。但し同施設での研究も含む。2つのコホート研究において BMI の高い女性に有意なリスク上昇が見られた。ベースライン時に閉経後女性において特に高いリスクが認められた。ケース・コントロール研究では、概して閉経後女性には BMI と乳がんリスクに正の関連性が認められるが閉経前女性において関連性は一致していない。

D. 考察、結論

脂肪、大豆摂取と乳がんの関連性は、コホート研究、ケース・コントロール研究とも未だ研究が少なく、現段階でのまとまった評価は困難であり、さらなる研究の必要性が強調される。

BMIと乳がんの関連性は閉経後の乳がんにおいて正の関連性を示した研究が多いが、ケース・コントロール研究は寧ろ結果が一致しておらず、コホート研究での知見が重要と考えられる。

II. 野菜摂取とメラトニンに関する研究

A. 研究目的

がん予防のために野菜を多く摂取するよう奨励されている。しかし一体、野菜に含まれるどの物質が、がん予防に寄与するものかは明らかにされていない。カロチノイド、ビタミン類などがその候補として取り上げられ研究中である。一方、最近の研究で、ほ乳類のみに産生されると思われていたメラトニンが植物にも含まれていることがわかった。メラトニンは実験研究ではがん予防の可能性も示唆されており、野菜からのメラトニン摂取が、がん予防につながるのかもしれない。既に横断研究のデザインで野菜摂取と体内中のメラトニンに正の関連性を認めた。メラトニンを多く含むことが知られている野菜を多く摂取することにより、実際、尿中のメラトニン代謝物が増加するのかを調べるため介入研究をおこなった。

B. 研究方法

対象者は55歳以下の女性97名である。メラトニンを多く含む野菜、かいわれ、とうもろこし、春菊、ゴーヤ、しいたけ、しめじを現物支給し、2ヶ月間毎日350g 以上を目指し積極的に摂ってもらう介入群と、期間中これら指定の野菜摂取はなるべく避けてもらうコントロール群に対象者を無作為割付した。野菜以外にあわ、ひえ、ケールなどメラトニン含有量の多い食品は両群とも介入期間中は摂取を控えてもらった。

割付前には生活習慣に関する調査、3日間食事記録、介入終了前の3日間の食事記録を依頼した。介入群は支給された野菜の実際の消費状況を報告し、コントロール群は指定野菜を摂取した場合、その摂取量を記録することとした。対象者からは介入前、介入開始後約1ヶ月後、介入後、自宅で摂取した早朝尿を持参してもらい、介入前後の早朝尿におけるメラトニン代謝物量変化を介入群とコントロール群で比較するものである。期間中就寝時刻の記録を行うが、尿採取日の前日は午前0時までに就寝するように依頼した。

(倫理面での配慮) 対象者からのインフォームド・コンセントが得られている。岐阜大学医学部倫理審

査委員会の許可を得ている。

C. 研究結果

介入期間を終え、現在、尿中メラトニン代謝物の測定、食事記録からの各種栄養素、食品摂取量の推定をおこなっている。

D. 考察

メラトニン含有量が測定されている植物は数少なく、野菜からあるいは全体の食事からのメラトニン摂取量は推定困難である。これまで測定された野菜から特にメラトニンの多い野菜を選択したが、野菜の両グループでのメラトニン摂取量の差は小さいかもしれない。

E. 結論

来年度に残りの測定、解析まとめを行う。

F. 健康危険情報

なし

G. 研究発表

1. 論文発表

1) Nagata C, et al. Association of vegetable intake with urinary 6-sulfatoxymelatonin level. Cancer Epidemiol Biomarkers Prev 2005;14,1333-5.

2. 学会発表

なし

H. 知的財産権の出願・登録状況

なし

表1 Cohort studies on cancer of breast and fats and meats

References Author	Year	Study period	Study population Number of subjects for analysis	Source of subjects	Event followed	Number of incident cases or deaths	Category	Number among cases	Relative risk (95%CI or p)	p for trend	Confounding variables considered	Comments
Hirayama	1990	1966-82	142,857	Six-prefecture cohort	Mortality	241	Meats				Adjusted for: Age	
							Daily		1.00			
							Occasional		0.55 (0.39-0.78)			
							Rare		0.59 (0.40-0.87)			
							None		0.42 (0.23-0.78)			
							Fish					
							Daily		1.00			
							Occasional		1.03 (0.82-1.30)			
							Rare		0.87 (0.52-1.45)			
							None		0.70 (0.19-2.61)			
Wakai et al.	2005	1988-1997	26,291	JACC study	Incidence	129	Total fat				Adjusted for: Age, study area, educational level, family history oh breast cancer, age at menarche, age at manopause, age at first birth, parity,use of exogenous female hormones, alcohol consumption, smoking, consumption of green leafy vegetables, daily walking, height, body mass index, and total energy intake.	
							Q1< 18.44	31	1.00			
							Q2 18.44-21.53	41	1.29 (0.80-2.08)			
							Q3 21.54-24.54	31	0.95 (0.57-1.59)			
							Q4 ≧ 24.55	26	0.80 (0.46-1.38)	0.32		
							Saturated fatty acids					
							Q1< 5.25	34	1.00			
							Q2 5.25-6.36	42	1.13 (0.72-1.79)			
							Q3 6.37-7.44	26	0.68 (0.40-1.14)			
							Q4 ≧ 7.45	27	0.68 (0.40-1.15)	0.066		
							Monounsaturated fatty					
							Q1< 5.50	34	1.00			
							Q2 5.50-6.48	34	0.96 (0.59-1.55)			
							Q3 6.49-7.54	39	1.10 (0.68-1.77)			
							Q4 ≧ 7.55	22	0.62 (0.36-1.09)	0.19		
							Polyunsaturated fatty acids					
							Q1< 4.39	32	1.00			
							Q2 4.39-5.21	35	1.13 (0.69-1.86)			
							Q3 5.22-6.02	31	1.01 (0.60-1.71)			
							Q4 ≧ 6.03	31	1.10 (0.63-1.90)	0.83		
							Long-chain n-3 fatty acids					
							Q1< 0.29	42	1.00			
							Q2 0.29-0.42	29	0.68 (0.42-1.10)			
							Q3 0.43-0.60	36	0.83 (0.52-1.30)			
							Q4 ≧ 0.61	22	0.50 (0.30-0.85)	0.024		

表2 Case-control studies on cancer of breast and fats or meats

References author	year	Study time	Study subjects Type and source	Definition	Number of cases	Number of controls	Category	Relative risk (95%CI or p)	p for trend	Confounding variables	Comments
Hirohata et al.	1985	Not given	Hospital-based (National Kyushu Cancer Center, Kyusyu Univ, Fukuoka Univ, Kurume Univ, National Fukuoka Central Hospital)	Cases: histologically confirmed cases; Controls: hospital control without history of cancer and benign breast disease, neibourhood control	212	424	Animal protein			Matched (1:2) for : Age (±5 yrs); Adjusted for: age,weight, menopause, and parity.	
							Q1	1.00			
							Q2	0.99 (0.60-1.64)			
							Q3	1.68 (1.03-2.76)			
							Q4	1.12 (0.65-1.93)			
							Total fat				
							Q1	1.00			
							Q2	1.33 (0.81-2.19)			
							Q3	1.08 (0.65-1.79)			
							Q4	1.01 (0.60-1.71)			
							Animal fat				
							Q1	1.00			
							Q2	1.53 (0.93-2.50)			
							Q3	1.88 (1.13-3.13)			
							Q4	1.28 (0.75-2.18)			
							Vegetable fat				
							Q1	1.00			
							Q2	1.01 (0.62-1.65)			
							Q3	0.82 (0.50-1.34)			
							Q4	0.75 (0.45-1.24)			
Kato et al.	1992	1990-1991	Hospital-based (10 large hospitals in 8 perfectures)	Cases: histologically confirmed cases; Controls: hospital controls without hormone-related cancers	908	908	Meats			Matched (1:1) for : Age(±3 yrs) and hospital	
							<=1-2/wk	1.00			
							3-4/wk	1.03 (0.84-1.27)			
							Daily	0.89 (0.65-1.22)	0.587		
							Fish				
							<=1-2/wk	1.00			
							3-4/wk	0.85 (0.69-1.06)			
							Daily	0.81 (0.62-1.06)	0.09		

References author	year	Study time	Study subjects Type and source	Definition	Number of cases	Number of controls	Category	Relative risk (95%CI or p)	p for trend	Confounding variables	Comments
Hirose et al	2003	1988-2000	Hospital-based (Aichi Cancer Center)	Cases: histologically confirmed cases; Controls: cancer-free	2,385	19,013	Cooked/raw fish			Adjusted for: age, visit year, family history, age at menarche, parity and age at first birth.	
					1,332 premenopausal	11,943 premenopausal	<1-3 times/mo	1.00			
							1-2 times/wk	0.89 (0.76-1.03)			
							3-4 times/wk	0.92 (0.78-1.10)			
							>=5 times/wk	0.95 80.70-1.28)	0.52		
							Dried/salted fish				
							Almost never	1.00			
							1-3 times/mo	0.99 (0.83-1.19)			
							1-2 times /wk	1.17 (0.97-1.40)			
							3-times/wk	1.15 (0.89-1.49)	0.03		
					1,039 postmenopausal	6,932 postmenopausal	Cooked/raw fish			Adjusted for: age, visit year, family history, age at menarche, age at menopause, parity and age at first	
							<1-3 times/mo	1.00			
							1-2 times/wk	0.98 (0.81-1.18)			
							3-4 times/wk	0.86 (0.70-1.05)			
							>=5 times/wk	0.75 (0.60-1.01)	0.01		
							Dried/salted fish				
							Almost never	1.00			
							1-3 times/mo	0.96 (0.79-1.17)			
							1-2 times /wk	0.89 (0.73-1.08)			
							3-times/wk	0.78 (0.60-1.01)	0.04		

表3 Cohort studies on cancer of breast and soy

References Author	Year	Study period	Study population Number of subjects for	Source of subjects	Event followed	Number of incident cases or	Category	Number among cases	Relative risk (95%CI or p)	p for trend	Confounding variables considered	Comments
Hirayama	1990	1966-82	142,857	Six-prefecture cohort	Mortality	241	Miso soup				Adjusted for: Age	
							Non-daily		1.00			
							Daily		0.55 (0.68-1.06)			
Key et al.	1999	1969-1993		Atomic-bomb survivors	Incidence	427	Tofu				Adjusted for: Age,calender period, city and age at time of bombing and radia.	
							≦1/wk	139	1.00			
							2-4/wk	199	0.99 (0.80-1.24)			
							≧5wk	52	1.07 (0.78-1.47)	0.71		
							Miso soup					
							≦1/wk		1.00			
							2-4/wk		1.03 (0.81-1.31)			
							≧5wk	0.31	0.87 (0.68-1.12)	0.31		
Yamamoto et al.	2003	1990-1999	21,852	JPHC study	Incidence	179	Miso soup				Adjusted for: age, area, age at menarche, no.of pregnancies, age at 1st pregnancy, active and passive smoking, alcohol consumption, phisical activity,education level, and meat, fish, vegetable, and fruit consumption.	
							<1 cup/day	51	1.00			
							1 cup/day	39	1.1 (0.67-1.7)			
							2 cups/day	58	0.74 (0.46-1.2)			
							>=3 cups/day	31	0.60 (0.34-1.1)	0.042		
							Soy foods					
							<2 times/wk	38	1.00			
							3-4 times/wk	60	0.83 (0.52-1.3)			
							Almost daily	81	0.81 (0.49-1.3)	0.44		
							Isoflavones					
							Q1	44	1.00			
							Q2	50	0.76 (0.47-1.2)			
							Q3	52	0.90 (0.56-1.5)			
							Q4	33	0.46 (0.25-0.84)	0.043		
						Premenopausal	Isoflavones					
							Q1	21	1.00			
							Q2	29	1.0 (0.50-2.0)			
							Q3	29	1.6 (0.79-3.1)			
							Q4	10	0.66 (0.25-1.7)	0.97		
						Postmenopausal	Isoflavones					
							Q1	22	1.00			
							Q2	21	0.58 (0.29-1.1)			
							Q3	23	0.50 (0.25-1.0)			
							Q4	21	0.32 (0.14-0.71)	0.006		

表4 Case-control studies on cancer of breast and soy

References author	year	Study time	Study subjects Type and source	Definition	Number of cases	Number of controls	Category	Relative risk (95%CI or p)	p for trend	Confounding variables	Comments
Hirohata et al.	1985	Not given	Hospital-based (National Kyushu Cancer Center, Kyusyu Univ, Fukuoka Univ, Kurume Univ, National Fukuoka Central Hospital)	Cases: histologically confirmed cases; Controls: hospital control without history of cancer and benign breast disease, neighbor control	212	424	Fat from soy Cases Controls Hospital Neighborhood	Mean 26g/wk 22g/wk 26g/wk		Matched (1:2) for : Age (±5 yrs); Adjusted for: age,weight, menopause, and parity.	
Hirose et al.	1995	1988-1992	Hospital-based (Aichi Cancer Center)	Cases: histologically confirmed cases; Controls: First-visit outpatients without history of cancer	1,186 607 premenopausal	23,163 15,084 premenopausal	Miso soup Occasional, Daily	 1.00 1.16 (0.98-1.37)		Adjusted for: Age and first-visit year	
							Bean curd <=3/mo 1-2/wk >=3/wk	 1.00 0.93 (0.72-1.19) 0.78 (0.60-1.00)			
					445 postmenopausal	6,215 postmenopausal	Miso soup Occasional, Daily	 1.00 0.96 (0.78-1.17)			
							Bean curd <=3/mo 1-2/wk >=3/wk	 1.00 0.89 (0.64-1.24) 0.96 (0.70-1.31)			
Hirose et al	2003	1988-2000	Hospital-based (Aichi Cancer Center)	Cases: histologically confirmed cases; Controls: cancer-free	2,385 1,332 premenopausal	19,013 11,943 premenopausal	Soybean curd <1-3 times/mo 1-2 times/wk 3-4 times/wk >=5 times/wk	 1.00 0.98 (0.82-1.17) 0.86 (0.71-1.04) 0.84 (0.67-1.04)	 0.02	Adjusted for: age, visit year, family history, age at menarche, parity and age at first birth.	
							Miso soup Almost never Occasionally 1 time/day >=2 times/day	 1.00 0.98 (0.72-1.35) 1.08 (0.79-1.48) 1.14 (0.79-1.65)	 0.11		

References author	year	Study time	Study subjects Type and source	Definition	Number of cases	Number of controls	Category	Relative risk (95%CI or p)	p for trend	Confounding variables	Comments
					1,039 postmenopausal	6,932 postmenopausal				Adjusted for: age, visit year, family history, age at menarche, age at menopause, parity and age at first birth, and BMI.	
							Soybean curd				
							<1-3 times/mo	1.00			
							1-2 times/wk	0.89 (0.72-1.12)			
							3-4 times/wk	0.89 (0.70-1.11)			
							>=5 times/wk	0.83 (0.65-1.05)	0.15		
							Miso soup				
							Almost never	1.00			
							Occasionally	1.01 (0.72-1.43)			
							1 time/day	1.07 (0.76-1.50)			
							>=2 times/day	0.89 (0.61-1.30)	0.64		
Hirose et al	2005	2001-2002	Hospital-based (Aichi Cancer Center)	Cases: histologically confirmed cases; Controls: cancer-free	167 79 premenopausal	854 414 premenopausal					
							Soybean				
							Low	1.00			
							Middle	0.60 (0.30-1.18)			
							High	0.53 (0.27-1.04)	0.06		
							Isoflavone				
							Low	1.00			
							Middle	0.62 (0.32-1.20)			
							High	0.44 (0.22-0.89)	0.02		
							Tofu				
							Low	1.00			
							Middle	0.44 (0.22-0.90)			
							High	0.49 (0.25-0.95)	0.03		
							Miso				
							Low	1.00			
							Middle	1.14 (0.59-2.19)			
							High	0.58 (0.28-1.20)	0.15		
							Atsuage				
							Low	1.00			
							Middle	0.67 (0.34-1.34)			
							High	0.70 (0.35-1.38)	0.31		
							Aburage				
							Low	1.00			
							Middle	1.67 (0.82-3.40)			
							High	1.07 (0.51-2.26)	0.97		
							Natto				
							Low	1.00			
							Middle	0.89 (0.46-1.74)			
							High	0.84 (0.43-1.64)	0.56		

References author	Study time year	Study subjects Type and source	Definition	Number of cases	Number of controls	Category	Relative risk (95%CI or p)	p for trend	Confounding variables	Comments
						Koyadofu				
						Low	1.00			
						Middle	0.68 (0.27-1.73)			
						High	1.38 (0.69-2.79)	0.52		
				88 postmenopausal	440 postmenopausal	Soybean				
						Low	1.00			
						Middle	0.87 (0.47-1.61)			
						High	0.70 (0.37-1.33)	0.28		
						Isoflavone				
						Low	1.00			
						Middle	0.76 (0.41-1.40)			
						High	0.58 (0.30-1.10)	0.09		
						Tofu				
						Low	1.00			
						Middle	1.34 (0.73-2.44)			
						High	0.71 (0.36-1.39)	0.34		
						Miso				
						Low	1.00			
						Middle	0.52 (0.27-0.98)			
						High	0.64 (0.34-1.17)	0.11		
						Atsuage				
						Low	1.00			
						Middle	1.95 (0.98-3.86)			
						High	2.28 (1.15-4.51)	0.02		
						Aburage				
						Low	1.00			
						Middle	1.75 (0.89-3.43)			
						High	1.62 (0.83-3.14)	0.17		
						Natto				
						Low	1.00			
						Middle	1.00 (0.54-1.87)			
						High	0.79 (0.41-1.51)	0.47		
						Koyadofu				
						Low	1.00			
						Middle	0.81 (0.40-1.64)			
						High	0.99 (0.50-1.97)	0.84		

表5 Cohort studies on cancer of breast and BMI

References		Study period	Study population				Category	Number among cases	Relative risk (95%CI or p)	p for trend	Confounding variables considered	Comments
Author	Year		Number of subjects for analysis	Source of subjects	Event followed	Number of incident cases or deaths						
Goodman et al.	1997	1979-1987	22,200	Atomic bomb survivors Tumor registry at the RERF	Incidence	161	<20	36	1.00		Adjusted for: City, age, age at the time of the bomings, and radiation dose to the breast.	
							20.00-22.51	37	0.81 (0.51-1.29)			
							22.52-24.66	37	1.13 (0.71-1.80)			
							≧24.67	39	1.21 (0.77-1.19)	0.23		
Key et al.	1999	1969-1993	34,759	Atomic bomb survivors Tumor registry at the RERF	Incidence	427	<20	95	1.00		Adjusted for:Age, calender period,city and age at time of bombing radiation dose.	
							20-22.4	118	1.05 (0.80-1.38)			
							22.5-24.9	93	1.07 (0.80-1.43)			
							≧25	86	1.37 (1.02-1.84)	0.05		
Kuriyama et al.	2005	1984-1992	15,054	3 municipalities in Miyagi	Incidence	115	18.5-24.9	73	1.00		Adjusted for:Age, smoking status, alcohol drinking status, consumption of meat, fish, fruits, and bean-paste soup, type of health insurance, menopausal status, parity, age at menarche, and age at end of first pregnancy.	
							25.0-27.4	23	1.20 (0.75-1.93)			
							27.5-29.9	12	1.55 (0.84-2.87)			
							≧30	7	1.90 (0.87-4.15)	0.04		
						33 pre	18.5-24.9	25	1.00		Adjusted for:Age, smoking status, alcohol drinking status, consumption of meat, fish, fruits, and bean-paste soup, type of health insurance, parity, age at menarche, and age at end of first pregnancy.	
							25.0-27.4	5	0.85 (0.32-2.24)			
							27.5-29.9	3	0.84 (0.24-2.88)	0.70		
							≧30					
						65 post	18.5-24.9	37	1.00		Adjusted for:Age, smoking status, alcohol drinking status, consumption of meat, fish, fruits, and bean-paste soup, type of health insurance, parity, age at menarche, and age at end of first pregnancy.	
							25.0-27.4	16	1.70 (094-3.07)			
							27.5-29.9	7	1.82 (0.80-4.12)			
							≧30	5	2.67 (1.03-6.92)	0.01		

表6 Case-control studies on cancer of breast and BMI

References author	Study time year	Study subjects Type and source	Definition	Number of cases	Number of controls	Category	Relative risk (95%CI or p)	p for trend	Confounding variables considered	Comments
Kyogoku et al.	1990 1975-1978	Hospital-based (5hospitals in Fukuoka)	Cases: histologically confirmed cases; Controls: hospital controls without cancers and benign breast disease and neighbours	121 postmenopausal	363 postmenopausal	Q1	1.00		Matched (1:3) for : Age(±5 yrs) and hospital Adjusted for: age at first birth, age at menopause, and family history of breast cancer.	
						Q2	1.4 (0.7-3.1)			
						Q3	0.9 (0.4-1.8)			
						Q4	1.1 (0.5-2.4)	0.37		
Kato et al.	1992 1990-1991	Hospital-based (10 large hospitals in 8 perfectures)	Cases: histologically confirmed cases; Controls: hospital controls without hormone-related cancers	459 premenopausal	459	<=20.2	1.00		Matched (1:1) for : Age(±3 yrs) and hospital	
						20.3-21.9	1.27 (0.89-1.82)			
						22.0-24.0	0.99 (0.70-1.40)			
						24.1+	1.77 (1.16-2.71)	0.087		
				446 postmenopausal	446	<=20.2	1.00			
						20.3-21.9	0.82 (0.55-1.21)			
						22.0-24.0	1.16 (0.79-1.71)			
						24.1+	1.63 (1.11-2.40)	0.002		
Wakai et al.	1994 1990-1991	Hospital-based (Cancer Institute Tokyo)	Cases: histologically confirmed cases; Controls: patiens without breast cancer	300	900	Weight			Matched (1:1) for : Age Adjusted for: Menopausal status, weight, height, lactation and no.of births.	
						-49	1.00			
						50-59	1.18 (0.86-1.62)			
						60-69	1.32 (0.84-2.08)			
						70-	3.06 (1.47-6.37)	<0.05		
				168 premenopausal	472 premenopausal	Weight				
						-49	1.00			
						50-59	1.77 (1.12-2.80)			
						60-69	1.59 (0.82-3.05)			
						70-	2.76 (0.96-7.89)	<0.05		
				127 postmenopausal	390 postmenopausal	Weight				
						-49	1.00			
						50-59	0.77 (0.47-1.26)			
						60-69	1.09 (0.54-2.21)			
						70-	4.82 ('1.53-15.2)	NS		

References author	year	Study time	Study subjects Type and source	Definition	Number of cases	Number of controls	Category	Relative risk (95%CI or p)	p for trend	Confounding variables considered	Comments
Hirose et al.	1995	1988-1992	Hospital-based (Aichi Cancer Center)	Cases: histologically confirmed cases; Controls: First-visit outpatients without history of cancer	1,186	23,163				Adjusted for: Age and first-visit year	
					607 premenopausal	15,084 premenopausal	<=20.0	1.00			
							20.1-26.4	1.05 (0.84-1.32)			
							26.5+	1.44 (0.96-2.18)			
					445 postmenopausal	6,215 postmenopausal	<=20.0	1.00			
							20.1-26.4	1.77 (0.91-1.51)			
							26.5+	3.60 (2.36-5.48)			
Hu	1997	1989-1993	Hospital-based (Gihoku General Hospital)	Cases: histologically confirmed cases; Controls: participamts in breast cancer screening	87 premenopausal	202 premenopausal	-22.9	1.00		Matched for : Age and residential area	
							21-22,9	0.87 (0.44-1.71)			
							23+	0.45 (0.27-0.92)		Adjusted for: BMI, age at menarche, age at first birth, no.of births, and duration of breast-feeding	
							p for trend	0.037			
					67 postmenopausal	159 postmenopausal	-21.4	1.00			
							21.5-23.9	1.03 (0.43-2.44)			
							24+	1.98 (0.86-4.55)	0.495		
Ueji et al.	1998	1990-1997	Tsukuba Univ Hospital,Tsukuba Medical Center Hospital Community controls	Cases: histologically confirmed cases; Controls: no history of breast cancer	65 premenopausal	96 premenopausal	-21.4	1.00		Matched for : Age and residence	
							21.5-23.9	1.20 (0.53-2.71)			
							24.0-	0.45 (0.16-1.26)	0.164	Adjusted for: Family history of breast cancer, education, menopausal status, age at menarche, parity, and age at primiparity.	
					54 postmenopausal	89 postmenopausal	-21.4	1.00		Matched for : Age and residence	
							21.5-23.9	1.62 (0.66-3.99)			
							24.0-	1.57 (0.61-3.99)	0.217	Adjusted for: Family history of breast cancer, education, menopausal status, age at menarche, age at menopause, parity, and age at primiparity.	

References author	year	Study time	Study subjects Type and source	Definition	Number of cases	Number of controls	Category	Relative risk (95%CI or p)	p for trend	Confounding variables considered	Comments
Tung et al.	1999	1990-1995	Hospital-based (Osaka Medical Center for Cancer and Cardiovascular disease)	Cases: histologically confirmed cases; Controls: patiens without diagnosis of cancer	190 premenopausal	119 premenopausal	20	1.00		Adjusted for: Age at diagnosis	
							20.1-23.0	1.12 (0.57-2.14)			
							23.1-25.0	0.58 (0.28-1.19)			
							25.1	0.98 (0.46-2.06)	0.486		
					186 postmenopausal	282 postmenopausal	20	1.00			
							20.1-23.0	1.43 (0.80-2.56)			
							23.1-25.0	1.22 (0.68-2.16)			
							25.1	1.90 (1.10-3.24)	0.037		
Hirose et al.	1999	1988-1995	Hospital-based (Aichi Cancer Center)	Cases: histologically confirmed cases; Controls: cancer-free	1,465	25,488	<20.0	1.00		Adjusted for: Age, marital status, age at menarche, menstrual regularity, age at first birth, and parity	
							20-24.9	1.21 (1.05-1.40)			
							>=25	1.49 (1.24-1.78)			
Hirose et al.	1999	1989-1995	Hospital-based (Aichi Cancer Center)	Cases: histologically confirmed cases; Controls: cancer-free	1,359	24,207	<18.75	1.00		Adjusted for: Age, age at menarche, number of births, age at first birth, and family history	
							18.75-19,89	0.85 (0.71-1.03)			
							19.90-20.87	0.94 (0.79-1.12)			
							20.88-22.26	0.91 (0.76-1.08)			
							>22.26	0.76 (0.63-0.91)	0.02		
					651 premenopausal	13,873 premenopausal	<18.75	1.00			
							18.75-19,89	0.80 (0.63-1.02)			
							19.90-20.87	1.01 (0.80-1.27)			
							20.88-22.26	0.96 (0.76-1.22)			
							>22.26	0.81 (0.62-1.06)	0.49		
					435 postmenopausal	7,195 postmenopausal	<18.75	1.00			
							18.75-19,89	0.96 (0.70-1.33)			
							19.90-20.87	0.83 (0.60-1.15)			
							20.88-22.26	0.93 (0.68-1.26)			
							>22.26	0.72 (0.53-0.98)	0.04		

References author	year	Study time	Study subjects Type and source	Definition	Number of cases	Number of controls	Category	Relative risk (95%CI or p)	p for trend	Confounding variables considered	Comments
Yoo et al.	2001	1988-1992	Hospital-based (Aichi Cancer Center Hospital)	Cases: histologically confirmed cases; Controls: cancer-free	1,154	21,714	<=20.0	1.0		Adjusted for: Age, occupation, family history of breast cancer among first-degree relatives, age at menarche, age at first pregnancy,no.of full-term pregnancies, duration of breast feeding, BMI, and drinking habits.	
							20.1-21.9	1.33 (1.08-1.63)			
							22<=	1.57 81.30-1.89)			
					Premenopausal	Premenopausal	Per 1kg/m2	1.01 (0.98-1.04)			
					Postmeopausal	Postmeopausal	Per 1kg/m2	1.07 (1.04-1.10)			
Hirose et al.	2001	1988-1997	Hospital-based (Aichi Cancer Center)	Cases: histologically confirmed cases; Controls: cancer-free	1,584	15,331					
					861 pre, without family history	9622 pre, without family history	<20.0	1.00		Adjusted for: Age, age at menarche, menstrual regularity in the 20s, age at first birth, and parity	
							20-22.9	1.24 (1.0-1.5)			
							23-24.9	1.08 (0.85-1.4)			
							>=25	1.18 (0.91-1.5)	0.41		
					65 pre, with family history	413 pre, with family history	<20.0	1.00			
							20-22.9	0.82 (0.40-1.7)			
							23-24.9	0.68 (0.28-1.7)			
							>=25	0.78 (0.29-2.2)	0.52		
					605 post, without family history	4991post, without family history	<20.0	1.00		Adjusted for: Age, age at menarche, menstrual regularity in the 20s, age at first birth, and parity	
							20-22.9	1.27 (0.96-1.7)			
							23-24.9	1.75 (1.3-2.4)			
							>=25	2.17 (1.6-2.9)	<0.001		
					44 post, without family history	213post, without family history	<20.0	1.00			
							20-22.9	1.53 (0.47-5.0)			
							23-24.9	1.63 (0.48-5.6)			
							>=25	2.07 (0.60-7.1)	0.26		