2017

DIET, NUTRITION, PHYSICAL ACTIVITY AND PREMENOPAUSAL BREAST CANCER

		DECREASES RISK	INCREASES RISK
STRONG EVIDENCE	**Convincing**		Adult attained height[1]
	Probable	Vigorous physical activity Body fatness[2] Lactation[3]	Alcoholic drinks[4] Greater birthweight[5]
LIMITED EVIDENCE	**Limited – suggestive**	Non-starchy vegetables (ER– breast cancers only)[6] Dairy products Foods containing carotenoids[7] Diets high in calcium Physical activity[8]	
	Limited – no conclusion	Cereals (grains) and their products; dietary fibre; potatoes; non-starchy vegetables (ER+ breast cancers); fruits; pulses (legumes); soya and soya products; red and processed meat; poultry; fish; eggs; fats and oils; total fat; vegetable fat; fatty acid composition; saturated fatty acids; mono-unsaturated fatty acids; polyunsaturated fatty acids; trans-fatty acids; cholesterol; sugar (sucrose); other sugars; sugary foods and drinks; coffee; tea; carbohydrate; starch; glycaemic index; glycaemic load; protein; vitamin A; riboflavin; vitamin B6; folate; vitamin B12; vitamin C; vitamin D; vitamin E; calcium supplements; iron; selenium; phytoestrogens; isoflavones; dichlorodiphenyldichloroethylene; dichlorodiphenyltrichloroethane; dieldrin; hexachlorobenzene; hexachlorocyclohexane; trans-nonachlor; polychlorinated biphenyls; acrylamide; dietary patterns; culturally defined diets; sedentary behaviour; adult weight gain; energy intake	
STRONG EVIDENCE	**Substantial effect on risk unlikely**		

1   Adult attained height is unlikely to directly influence the risk of cancer. It is a marker for genetic, environmental, hormonal and also nutritional factors affecting growth during the period from preconception to completion of linear growth.
2   Body fatness marked by body mass index (BMI), waist circumference and waist-hip ratio. Also includes evidence on young women aged about 18 to 30 years. Body fatness in young adulthood is marked by BMI.
3   The Panel's conclusion relates to the evidence for overall breast cancer (unspecified). The evidence for premenopausal and postmenopausal breast cancers separately was less conclusive, but consistent with the overall finding.
4   No threshold was identified.
5   Birthweight is a marker both for prenatal growth, reflecting fetal nutrition, and is a predictor of later growth and maturation – e.g., age at menarche – which are also determinants of breast cancer risk.
6   The Panel's conclusion relates to the evidence for overall breast cancer (unspecified). The observed association was in oestrogen-receptor-negative (ER–) breast cancer only.
7   The Panel's conclusion relates to the evidence for overall breast cancer (unspecified). The observed association was stronger for oestrogen-receptor-negative (ER–) breast cancer. Includes both foods that naturally contain carotenoids and foods that have carotenoids added.
8   Physical activity, including occupational, recreational, walking and household activity. There was sufficient evidence for the Panel to make a separate judgement for vigorous physical activity.

2017 — DIET, NUTRITION, PHYSICAL ACTIVITY AND POSTMENOPAUSAL BREAST CANCER

		DECREASES RISK	INCREASES RISK
STRONG EVIDENCE	**Convincing**		Alcoholic drinks[1] Body fatness[2] Adult weight gain Adult attained height[3]
	Probable	Physical activity[4] Body fatness in young adulthood[5] Lactation[6]	
LIMITED EVIDENCE	**Limited – suggestive**	Non-starchy vegetables (ER– breast cancers only)[7] Foods containing carotenoids[8] Diets high in calcium	
	Limited – no conclusion	Cereals (grains) and their products; dietary fibre; potatoes; non-starchy vegetables (ER+ breast cancers); fruits; pulses (legumes); soya and soya products; red and processed meat; poultry; fish; eggs; dairy products; fats and oils; total fat; vegetable fat; fatty acid composition; saturated fatty acids; mono-unsaturated fatty acids; polyunsaturated fatty acids; trans-fatty acids; cholesterol; sugar (sucrose); other sugars; sugary foods and drinks; coffee; tea; carbohydrate; starch; glycaemic index; glycaemic load; protein; vitamin A; riboflavin; vitamin B6; folate; vitamin B12; vitamin C; vitamin D; vitamin E; calcium supplements; iron; selenium; phytoestrogens; isoflavones; dichlorodiphenyldichloroethylene; dichlorodiphenyltrichloroethane; dieldrin; hexachlorobenzene; hexachlorocyclohexane; trans-nonachlor; polychlorinated biphenyls; acrylamide; dietary patterns; culturally defined diets; sedentary behaviour; energy intake	
STRONG EVIDENCE	**Substantial effect on risk unlikely**		

1 No threshold was identified.
2 Body fatness, throughout adulthood, marked by body mass index (BMI), waist circumference and waist-hip ratio.
3 Adult attained height is unlikely to directly influence the risk of cancer. It is a marker for genetic, environmental, hormonal and also nutritional factors affecting growth during the period from preconception to completion of linear growth.
4 Physical activity including vigorous, occupational, recreational, walking and household activity.
5 Young women aged about 18 to 30 years. Body fatness in young adulthood is marked by BMI.
6 The Panel's conclusion relates to the evidence for overall breast cancer (unspecified). The evidence for premenopausal and postmenopausal breast cancers separately was less conclusive, but consistent with the overall finding.
7 The Panel's conclusion relates to the evidence for overall breast cancer (unspecified). The observed association was in oestrogen-receptor-negative (ER–) breast cancer only.
8 The Panel's conclusion relates to the evidence for overall breast cancer (unspecified). The observed association was stronger for oestrogen-receptor-negative (ER–) breast cancer. Includes both foods that naturally contain carotenoids and foods that have carotenoids added.

Summary of CUP 2017 meta-analyses and published pooled analyses[1] of breast cancer (unspecified) – non–starchy vegetables

Analysis	Increment/ contrast	RR (95% CI)	I²	No. Studies	No. Cases
CUP Breast Cancer SLR 2017	Per 200 g/day	0.98 (0.93–1.02)	27%	12	24,756
The Pooling Project 2013 [41][2]	Incidence Quintile 5 vs. Quintile 1	0.99 (0.95–1.04)	-	20	34,526
The Pooling Project 2001 [40][3]	Incidence Per 100 g/day	1.00 (0.97–1.02)	-	8	7,377
CUP additional analysis: Pooled analysis of The Pooling Project studies [41] combined with five non-overlapping studies from the CUP [25–27, 34, 43]	Highest vs. lowest	0.97 (0.91–1.02)	31%	25	46,743

[1] Pooled analysis not included in the CUP meta-analysis.
[2] Adjusted for ethnicity, family history of breast cancer, personal history of benign breast disease, alcohol consumption, smoking status, education, physical activity, age at menarche, body mass index, height, oral contraceptive use, menopausal status, energy intake, combination between parity and age of first birth.
[3] Adjusted for age at menarche, interaction between parity and age at birth of first child, oral contraceptive use, history of benign breast disease, menopausal status at follow-up, postmenopausal hormone use, smoking status, education, BMI, BMI–menopausal status interaction, height, alcohol intake and energy intake.

Summary of CUP 2017 meta-analyses and published pooled analysis[1] of breast cancer by hormone receptor type – non-starchy vegetables

Analysis	Increment/ contrast	RR (95% CI)	I²	No. Studies	No. Cases
CUP Breast Cancer SLR 2017	Per 200 g/day ER−PR− ER+PR+ ER+PR−	 0.79 (0.63–0.98) 0.89 (0.79–1.01) 0.96 (0.81–1.13)	 39% 0% 37%	3	 3,950 1,229 1,346
The Pooling Project 2013 [41]²	Incidence Quintile 5 vs. Quintile 1 ER− ER+ PR− PR+ Per 300 g/day ER−	 0.82 (0.74–0.90) 1.04 (0.97–1.11) 0.94 (0.84–1.03) 1.02 (0.96–1.10) 0.88 (0.81–0.95)	 - - - - -	20	34,526

¹ Pooled analysis not included in the CUP meta-analysis.
² Adjusted for ethnicity, family history of breast cancer, personal history of benign breast disease, alcohol consumption, smoking status, education, physical activity, age at menarche, body mass index, height, oral contraceptive use, menopausal status, energy intake, combination between parity and age of first birth.

Summary of CUP 2017 meta-analyses for carotenoid exposures and breast cancer (unspecified).

	Total no. studies identified in the CUP (publications)[1]	Results of CUP dose-response meta-analyses for breast cancer (unspecified)				
		Increment	RR (95% CI)	I^2	No. Studies	No. Cases
Dietary beta-carotene[2]	24 (16)	Per 5000 µg/day	1.00 (0.98-1.02)	0%	18[2]	3,055
Circulating beta-carotene	13 (19)	Per 50 µg/dL	0.78 (0.66-0.92)	0%	11	3,558
Circulating alpha-carotene	11 (17)	Per 10 µg/dL	0.90 (0.77–1.05)	0%	10	3,506
Circulating total carotenoids	9 (11)	Per 100 µg/dL	0.82 (0.71–0.96)	0%	9	3,407
Circulating lutein	7 (5)	Per 25 µg/dL	0.72 (0.55–0.93)	0%	7	1,296
Circulating beta-cryptoxanthin	11 (14)	Per 15 µg/dL	0.87 (0.68–1.11)	59%	10	3,517
Circulating lycopene	11 (16)	Per 25 µg/dL	0.90 (0.70–1.16)	39%	10	3,506

[1] For references, see CUP Breast SLR 2017.
[2] Summary estimate from pooled analysis [44] – no dose-response analysis conducted for the CUP as all studies were superseded by the pooled analysis.

Summary of results from pooled analyses for breast cancer risk by hormone receptor status (statistically significant or borderline significant findings are presented in bold text) – all carotenoid exposures

Exposure	Study	ER Status	RR (95% CI)	Increment/Contrast
Dietary beta-carotene	Pooling project [44]	ER–	0.84 (0.77–0.93)	Quintile 5 vs. Quintile 1
			0.93 (0.88–0.99)	Per 5000 µg/d
		ER+	1.04 (0.98–1.10)	Quintile 5 vs. Quintile 1
			1.02 (0.99–1.05)	Per 5000 µg/d
Dietary alpha-carotene	Pooling project [44]	ER–	0.87 (0.78–0.97)	Per 5000 µg/d
		ER+	1.04 (0.99–1.09)	Per 5000 µg/d
Dietary beta-cryptoxanthin	Pooling project [44]	ER–	0.90 (0.81–1.00)	Per 5000 µg/d
		ER+	0.96 (0.92–1.00)	Per 5000 µg/d
Dietary lutein/zeaxanthin	Pooling project [44]	ER–	0.87 (0.79–0.95)	Per 5000 µg/d
		ER+	1.00 (0.93–1.08)	Per 5000 µg/d
Dietary lycopene	Pooling project [44]	ER–	0.92 (0.83–1.02)	Per 5000 µg/d
		ER+	0.99 (0.94–1.04)	Per 5000 µg/d
Circulating alpha-carotene	Pooling project [44]	ER–	0.61 (0.40–0.93)	Quintile 5 vs. Quintile 1
		ER+	0.85 (0.65–1.12)	Quintile 5 vs. Quintile 1
Circulating beta-carotene	Pooling project [44]	ER–	0.52 (0.36–0.77)	Quintile 5 vs. Quintile 1
		ER+	0.83 (0.66–1.04)	Quintile 5 vs. Quintile 1
Circulating total carotenoids	Pooling project [44]	ER–	0.81 (0.56–1.16)	Quintile 5 vs. Quintile 1
		ER+	0.86 (0.69–1.07)	Quintile 5 vs. Quintile 1
Circulating beta-cryptoxanthin	Pooling project [44]	ER–	1.03 (0.69–1.53)	Quintile 5 vs. Quintile 1
		ER+	1.09 (0.86–1.39)	Quintile 5 vs. Quintile 1
Circulating lycopene	Pooling project [44]	ER–	0.95 (0.66–1.38)	Quintile 5 vs. Quintile 1
		ER+	0.83 (0.60-1.15)	Quintile 5 vs. Quintile 1

Summary of CUP 2017 meta-analysis, published pooled analysis[1] and meta-analysis of premenopausal breast cancer – dairy products

Analysis	Increment/ contrast	RR (95% CI)	I²	No. Studies	No. Cases
CUP Breast Cancer SLR 2017	Per 200 g/day	0.95 (0.92–0.99)	0%	7	2,862
Published pooled analysis (not included in the CUP analysis)					
The Pooling Project 2002[2] [54][3]	Total dairy fluids, per 100 g/day	0.96 (0.90–1.02)	-	8	7,379
	Total dairy solids, per 100 g/day	0.87 (0.68–1.11)	-		
Published meta-analysis					
Dong et al., 2011 56]	Highest vs. lowest	0.79 (0.63–0.99)	50%	5	~2,137

[1] Pooled analysis not included in the CUP meta-analysis.
[2] The Nurses' Health Study [57] was the only study included in the CUP meta-analysis.
[3] Adjusted for age at menarche, parity, age at birth of first child, oral contraceptive use, history of benign breast disease, family history of breast cancer, menopausal status, BMI, hormone therapy use, smoking status, education, height, alcohol intake, total energy intake.

Summary of CUP 2017 meta-analyses and published pooled analysis[1] of premenopausal breast cancer – alcohol (as ethanol)

Analysis	Increment	RR (95% CI)	I²	No. Studies	No. Cases
CUP Breast Cancer SLR 2017	Per 10 g/day	1.05 (1.02–1.08)	0%	10	4,227
The Pooling Project 2016[2] [68][3]	Per 10 g/day	1.03 (0.99–1.08)	-	15	3,730
CUP additional analysis: Pooled analysis of The Pooling Project studies [68] combined with three non-overlapping studies from the CUP [23, 67, 70]	Per 10 g/day	1.03 (0.99–1.07)	19%	18	4,426

[1] Pooled analysis not included in the CUP meta-analysis.
[2] Published after the CUP SLR 2017 search.
[3] Adjusted for age, energy intake, ethnicity, education, BMI, height, physical activity, smoking status, age at menarche, parity and age at birth of first child, oral contraceptive use, family history of breast cancer, personal history of benign breast disease.

Summary of CUP 2017 dose-response meta-analyses of premenopausal breast cancer – alcohol (as ethanol) from beer, wine and spirits

Analysis	Increment	RR (95% CI)	I²	No. Studies	No. Cases
Beer	Per 10 g/day	1.32 (1.06–1.64)	0%	3	818
Wine	Per 10 g/day	1.17 (0.79–1.73)	74%	3	818
Spirits	Per 10 g/day	1.10 (0.92–1.30)	0%	3	818

Summary of CUP 2017 stratified dose-response meta-analyses of postmenopausal breast cancer – alcohol (as ethanol)

Analysis	Increment	RR (95% CI)	I²	No. Studies
GEOGRAPHICAL LOCATION				
Europe	Per 10 g/day	1.08 (1.04–1.12)	41%	9
North America	Per 10 g/day	1.11 (1.07–1.15)	79%	12
HORMONE THERAPY USE				
Current users	Per 10 g/day	1.12 (1.09–1.16)	0%	5
Ever users	Per 10 g/day	1.07 (0.98–1.18)	0%	2
Former users	Per 10 g/day	1.07 (0.82–1.39)	76%	2
Never users	Per 10 g/day	1.04 (1.02–1.07)	0%	6
Former/never users	Per 10 g/day	1.12 (1.00–1.24)	16%	3
HORMONE RECEPTOR STATUS				
ER+PR+	Per 10 g/day	1.06 (1.03–1.09)	61%	6
ER+PR–	Per 10 g/day	1.12 (1.01–1.24)	76%	5
ER–PR–	Per 10 g/day	1.02 (0.98–1.06)	10%	6

Summary of CUP 2017 meta-analyses and published pooled analyses[1] of postmenopausal breast cancer – alcohol (as ethanol)

Analysis	Increment/ contrast	RR (95% CI)	I[2]	No. Studies	No. Cases
CUP Breast SLR 2017	Per 10 g/day	1.09 (1.07–1.12)	71%	22	35,221
The Pooling Project 2016[2,3] [68]	Per 10 g/day	1.09 (1.07–1.11)	-	20	25,411
UK Dietary Cohort Consortium [102][4]	Per 10 g/day	1.09 (1.01–1.18)	-	4	656
National Cancer Institute studies [88][5]	≥7 drinks/week vs. none Nulliparous women, postmenopausal Parous women aged <25 years at first birth Parous women aged ≥25 years at first birth	1.30 (1.11–1.52) 1.22 (1.11–1.35) 1.33 (1.19–1.50)	- - -	4	1,501 4,719 2,856
CUP additional analysis: Pooled analysis of The Pooling Project studies [68] combined with nine non-overlapping studies from the CUP [23, 67, 70, 71, 77, 79, 91, 93, 105]	Per 10 g/day	1.11 (1.06–1.16)	81%	29	33,415

[1] Pooled analysis not included in the CUP meta-analysis.
[2] Published after the CUP 2017 SLR search.
[3] Age, energy intake, ethnicity, education, BMI, height, physical activity, smoking status, age at menarche, hormone therapy use, parity and age at birth of first child, oral contraceptive use, family history of breast cancer, personal history of benign breast disease.
[4] Age, parity, height, weight, hormone therapy use at date of food diary completion, physical activity, total energy intake, folate intake, menopausal status, smoking, education level.
[5] Age, hormone therapy use, BMI, history of benign breast disease, age at menarche, age at natural menopause, ever/never use of oral contraceptive.

Summary of CUP 2017 dose-response meta-analyses of postmenopausal breast cancer – alcohol (as ethanol) from beer, wine and spirits

Analysis	Increment	RR (95% CI)	I²	No. Studies	No. Cases
Beer	Per 10 g/day	1.06 (0.94–1.21)	66%	7	7,798
Wine	Per 10 g/day	1.12 (1.08–1.17)	0%	6	3,913
Spirits	Per 10 g/day	1.05 (0.93–1.17)	73%	7	7,798

Summary of CUP 2017 meta-analysis and published meta-analysis of premenopausal breast cancer – total physical activity

Analysis	Contrast	RR (95% CI)	I²	No. Studies	No. Cases
CUP Breast SLR 2017	Highest vs. lowest	0.93 (0.79–1.08)	0%	4	1,834
Wu et al., 2013 [119]	Highest vs. lowest	0.77 (0.69–0.86)	15%	6	2,258

Summary of CUP 2017 meta-analyses of premenopausal breast cancer – other physical activity exposures

Analysis	Increment/ contrast	RR (95% CI)	I²	No. Studies	No. Cases
Occupational	Highest vs. lowest	0.82 (0.59–1.15)	76%	6	4,494
Recreational	Per 10 MET-hr/week	0.96 (0.90–1.03)	69%	3	2,331
	Highest vs. lowest	0.93 (0.74–1.16)	59%	10	>3,901

*Note: Vigorous activity is covered separately in **Section 7.7** of this report.*

Summary of CUP 2017 meta-analysis and published meta-analysis of postmenopausal breast cancer – total physical activity

Analysis	Contrast	RR (95% CI)	I²	No. Studies	No. Cases
CUP Breast SLR 2017	Highest vs. lowest	0.87 (0.79–0.96)	16%	8	11,798
Wu et al., 2013 [119]	Highest vs. lowest	0.87 (0.87–0.92)	15%	17	32,623

Summary of CUP 2017 meta-analyses of postmenopausal breast cancer – other physical activity exposures

Analysis	Increment/contrast	RR (95% CI)	I²	No. Studies	No. Cases
Occupational	Highest vs. lowest	0.89 (0.83–0.96)	0%	8	22,352
Recreational	Per 10 MET-hr/week	0.98 (0.97–0.99)	0%	5	18,486
	Highest vs. lowest	0.87 (0.81–0.94)	37%	17	>24,253
Walking	Highest vs. lowest	0.94 (0.86–1.04)	0%	4	7,300

*Note: Vigorous activity is covered separately in **Section 7.7** on pages 45–48 of this report.*

Summary of CUP 2017 stratified dose-response meta-analyses of premenopausal breast cancer – BMI

Analysis	Increment	RR (95% CI)	I²	No. Studies
GEOGRAPHICAL LOCATION				
Europe	Per 5 kg/m²	0.89 (0.86–0.92)	11%	17
North America	Per 5 kg/m²	0.97 (0.91–1.03)	40%	11
Asia	Per 5 kg/m²	1.16 (0.99–1.37)	0%	9
HORMONE RECEPTOR STATUS				
ER+	Per 5 kg/m²	1.02 (0.90–1.15)	68%	7
ER–	Per 5 kg/m²	1.01 (0.94–1.08)	0%	7

Summary of CUP 2017 meta-analysis, and published pooled analyses[1] and meta-analyses of premenopausal breast cancer – BMI

Analysis	Increment/contrast	RR (95% CI)	I²	No. Studies	No. Cases
CUP Breast Cancer SLR 2017	Per 5 kg/m² Incidence Mortality	 0.93 (0.90–0.97) 1.00 (0.73–1.38)	 55% 75%	 37 36	 16,371 545
Published pooled analyses (not included in the CUP analysis)					
Breast Cancer Association Consortium Studies (BCAC) [172][2]	>30 vs. <25kg/m² Incidence, invasive breast cancer ER+ ER–	 0.81 (0.69-0.95) 1.10 (0.92-1.30)	 - -	 12	 10,900 3,895
The Metabolic Syndrome and Cancer Project (Me-Can) [170][3]	>31.7 vs. <20kg/m² Incidence Mortality	 0.70 (0.57–0.85) 1.22 (0.64–2.31)	 - -	 6	 3,043
Asia-Pacific Cohort Studies Collaboration (APCSC) [169][4]	Mortality 30–60 vs. 18.5–24.9kg/m² Per 5 kg/m²	 0.93 (0.42–2.09) 1.13 (0.97–1.33)	 - -	 35	 324 Breast cancer (unspecified)
Published meta-analyses[5,6]					
Munsell, 2014 [190]	Incidence 25–29.9 vs. <25kg/m² ≥30 vs. <25kg/m²	 0.99 (0.92–1.07) 0.72 (0.55–0.94)	 47% 77%	 6	 4,469
Xia, 2014 [189]	Incidence Per 5 kg/m²	 0.99 (0.98–1.00)	 -	 12	 4,699
Cheraghi, 2012 [186]	Incidence Overweight vs. normal Obese vs. normal	 1.01 (0.77–1.31) 0.91 (0.71–1.18)	 72% 34%	 4	 564
Suzuki, 2009 [185]	Per 5 kg/m² ER+PR+	 0.90 (0.82–0.99)	 -	 4	 1,720

[1] Pooled analyses not included in the CUP meta-analysis.
[2] Adjusted for age, study, age at menarche, nulliparity, age at birth of first child.
[3] Adjusted for year of birth, age at measurement, smoking, stratified for cohort.
[4] Adjusted for attained age, smoking status, stratified by study.
[5] All cohort studies identified were included in the CUP 2017 analyses, apart from Barlow, 2006 [191], which was identified in Cheraghi, 2012 [186], as this study from the Breast Cancer Surveillance Consortium estimated the risk of developing breast cancer within a year of mammography screening.
[6] Pierobon, 2013 [187] and Amadou, 2013 [188] are not included in the table as they included cohort and case-control studies.

Summary of CUP 2017 stratified dose-response meta-analyses of postmenopausal breast cancer – BMI

Analysis	Increment	RR (95% CI)	I²	No. Studies
GEOGRAPHICAL LOCATION				
Europe	Per 5 kg/m²	1.10 (1.06–1.15)	75%	19
North America	Per 5 kg/m²	1.10 (1.08–1.12)	30%	25
Asia	Per 5 kg/m²	1.37 (1.24–1.50)	27%	11
HORMONE RECEPTOR STATUS				
ER+	Per 5 kg/m²	1.17 (1.09–1.25)	91%	14
ER–	Per 5 kg/m²	1.00 (0.95–1.06)	7%	13
PR+	Per 5 kg/m²	1.47 (1.36–1.60)	0%	5
PR–	Per 5 kg/m²	1.05 (0.93–1.18)	0%	5
ER+PR+	Per 5 kg/m²	1.29 (1.19–1.40)	78%	9
ER+PR–	Per 5 kg/m²	0.94 (0.87–1.01)	0%	6
ER–PR–	Per 5 kg/m²	0.96 (0.87–1.06)	33%	9
HORMONE THERAPY USE				
Current	Per 5 kg/m²	0.98 (0.90–1.06)	69%	5
Ever	Per 5 kg/m²	1.01 (0.96–1.06)	0%	13
Never	Per 5 kg/m²	1.16 (1.10–1.23)	72%	15
Never/former	Per 5 kg/m²	1.20 (1.15–1.25)	0%	4

Summary of CUP 2017 meta-analysis, and published pooled analyses[1] and meta-analyses of postmenopausal breast cancer – BMI

Analysis	Increment	RR (95% CI)	I²	No. Studies	No. Cases
CUP Breast Cancer SLR 2017	Per 5 kg/m² Incidence Mortality	1.12 (1.09–1.15) 1.20 (1.13–1.27)	74% 49%	56 38	80,404 4,131
Published pooled analyses (not included in the CUP analysis)					
Breast Cancer Association Consortium Studies (BCAC) [172][2]	≥30 vs. ≤25 kg/m² Incidence invasive breast cancer ER+ ER−	BMI did not significantly modify the association	-	12	
The Metabolic Syndrome and Cancer Project (Me-Can) [170][3]	≥31.7 vs. ≤20 kg/m² Incidence Mortality	0.87 (0.71–1.07) 0.92 (0.66–1.27)	- -	6	1,106 219
Asia-Pacific Cohort Studies Collaboration (APCSC)[169][4]	Mortality 30–60 vs. 18.5–24.9 kg/m² Per 5 kg/m²	1.63 (1.13–2.35) 1.19 (1.03–1.38)	- -	35	324 Breast cancer (unspecified)
Published meta-analyses[5,6]					
Munsell, 2014 [190]	Incidence 25–29.9 vs. <25kg/m² >30 vs. <25 kg/m²	1.13 (1.09–1.18) 1.20 (1.11–1.31)	6% 64%	12	16,180
Xia, 2014 [189][7]	Incidence 25 vs. 21.75 kg/m² ≥30 vs. 21.75 kg/m² 35 vs. 21.75 kg/m²	1.02 (0.98–1.06) 1.12 (1.01–1.24) 1.26 (1.07–1.50)	- - -	25 estimates from 20 prospective studies and 1 pooled analysis of cohorts	22,809
Cheraghi, 2012 [186][8]	Incidence Overweight vs. normal	1.12 (1.06–1.18)	56%	8	9,878

[1] Pooled analyses not included in the CUP meta-analysis.
[2] Adjusted for age, study, age at menarche, nulliparity, age at first birth.
[3] Adjusted for year of birth, age at measurement, smoking, stratified for cohort.
[4] Adjusted for attained age, smoking status, stratified by study.
[5] All cohorts and RCTs identified were included in the CUP 2017 analyses unless otherwise specified.
[6] Pierobon, 2013 [187], Esposito, 2013 [230] and Suzuki, 2009 [185] are not included in the table as they included cohort and case-control studies.
[7] Four studies (Cecchini, 2012, P-1; Cecchini, 2012, STAR; Opdahl, 2011; Li, 2006) [139, 176, 216] included in Xia, 2014 [189] had insufficient BMI categories and one study (Canchola, 2012) [150] reported results only by hormone receptor subtype; these studies were not included in the non-linear analysis of the CUP 2017 analyses (36 studies, 13 studies not in Xia, 2014 [189]).
[8] Two studies included in Cheraghi, 2012 [186] were not included in the CUP 2017 analyses. Barlow, 2006 (Breast Cancer Surveillance Consortium) [191] estimated the risk of developing breast cancer within a year of mammography screening and no relevant data could be found in Lee, 2006 [231].

Summary of CUP 2017 meta-analysis and published pooled analysis[1] of postmenopausal breast cancer – waist circumference

Analysis	Increment	RR (95% CI)	I²	No. Studies	No. Cases
CUP Breast SLR 2017	Per 10 cm BMI unadjusted	1.11 (1.09–1.13)	0%	11	14,033
	BMI adjusted	1.06 (1.01–1.12)	72%	5	12,022
ANZDCC [227] [2]	Per 1 SD	1.06 (1.01–1.12)	-	10	1,323

[1] Pooled analysis not included in the CUP meta-analysis.
[2] Adjusted for smoking status, education, cohort, age as timescale in model.

Summary of CUP 2017 stratified dose-response meta-analyses of postmenopausal breast cancer – waist–hip ratio

Analysis	Increment	RR (95% CI)	I²	No. Studies
GEOGRAPHICAL LOCATION				
Europe				
BMI adjusted	Per 0.1 unit	0.93 (0.82–1.06)	0%	2
BMI unadjusted	Per 0.1 unit	1.05 (0.87–1.28)	69%	5
North America				
BMI adjusted	Per 0.1 unit	1.08 (1.02–1.15)	11%	7
BMI unadjusted	Per 0.1 unit	1.11 (1.08–1.14)	0%	11
ANTHROPOMETRIC ASSESSMENT METHOD				
Self-reported				
BMI adjusted	Per 0.1 unit	1.09 (1.02–1.17)	36%	6
BMI unadjusted	Per 0.1 unit	1.12 (1.06–1.19)	43%	10
Measured				
BMI adjusted	Per 0.1 unit	1.02 (0.85–1.23)	31%	4
BMI unadjusted	Per 0.1 unit	1.09 (0.98–1.21)	69%	8

Summary of CUP 2017 meta-analysis and published pooled analysis[1] of postmenopausal breast cancer – waist–hip ratio

Analysis	Increment	RR (95% CI)	I²	No. Studies	No. Cases
CUP Breast SLR 2017	Per 0.1 unit	1.10 (1.05–1.16)	60%	18	15,643
ANZDCC [227][2]	Per 1 SD	1.06 (0.95–1.07)	-	10	1,323

[1] Pooled analysis not included in the CUP meta-analysis.
[2] Adjusted for smoking status, education, cohort, age as timescale in model.

Summary of CUP 2017 stratified dose-response meta-analyses of postmenopausal breast cancer – adult weight gain

Analysis	Increment	RR (95% CI)	I^2	No. Studies
GEOGRAPHICAL LOCATION				
Europe	Per 5 kg	1.06 (1.03–1.10)	0%	3
North America	Per 5 kg	1.06 (1.05–1.07)	19%	9
Asia	Per 5 kg	1.26 (1.14–1.39)	0%	2
HORMONE RECEPTOR STATUS				
ER+PR+	Per 5 kg	1.13 (1.04–1.22)	91%	5
ER+PR–	Per 5 kg	1.00 (0.95–1.04)	0%	3
ER–PR–	Per 5 kg	1.02 (0.98–1.06)	4%	5
HORMONE THERAPY USE				
Current	Per 5 kg	1.00 (0.98–1.03)	19%	3
Ever	Per 5 kg	1.08 (1.00–1.16)	44%	3
Never	Per 5 kg	1.06 (1.03–1.09)	0%	4
Never/former	Per 5 kg	1.09 (1.07–1.12)	37%	3

Summary of CUP 2017 meta-analysis and published meta-analysis[1] of postmenopausal breast cancer – adult weight gain

Analysis	Increment/ Contrast	RR (95% CI)	I²	No. Studies	No. Cases
CUP Breast SLR 2017	Per 5 kg	1.06 (1.05–1.08)	38%	15	16,600
Keum 2015 [245]	No or low hormone therapy users: Per 5 kg Highest vs. lowest	1.11 (1.08–1.13) 1.75 (1.54–2.00)	22% 0%	7	4,750
	No use of hormone therapy: Per 5 kg Highest vs. lowest	1.11 (1.08–1.13) 1.83 (1.58–2.13)	39% 0%	5	
	Hormone therapy users: Per 5 kg Highest vs. lowest	1.01 (0.99–1.02) 1.14 (1.00–1.30)	0% 0%	4	

[1] Vrieling, 2010 [246] not included in the table as it included mainly case-control studies.
Note: All cohort studies were included in the CUP 2017 analyses.

Summary of CUP 2017 stratified dose-response meta-analyses of premenopausal breast cancer – adult attained height

Analysis	Increment	RR (95% CI)	I^2	No. Studies
GEOGRAPHICAL LOCATION				
Europe	Per 5 cm	1.04 (0.99–1.09)	27%	17
North America	Per 5 cm	1.08 (1.03–1.12)	0%	6
Asia	Per 5 cm	1.20 (1.04–1.37)	26%	3

Summary of CUP 2017 stratified dose-response meta-analyses of postmenopausal breast cancer – adult attained height

Analysis	Increment	RR (95% CI)	I²	No. Studies
GEOGRAPHICAL LOCATION				
Europe	Per 5 cm	1.10 (1.08–1.12)	5%	18
North America	Per 5 cm	1.06 (1.04–1.08)	0%	11
Asia	Per 5 cm	1.13 (0.93–1.38)	68%	3

Summary of CUP 2017 meta-analysis, published pooled analysis[1] and meta-analyses of breast cancer (unspecified) – lactation

Analysis	Increment/ Contrast	RR (95% CI)	I²	No. Studies	No. Cases
CUP Breast SLR 2017	Per 5-month duration	0.98 (0.97–0.99)	0%	13	11,610
Published meta-analyses					
Islami, 2015 [275]	Ever vs. never ER–PR– Triple negative ER+PR+ ER+ and/or PR+	 0.84 (0.72–0.97) 0.73 (0.62–0.87) 1.00 (0.90–1.10) 0.97 (0.88–1.07)	 50% 0% 54% 78%	 7 3 4 7	>1,777
Zhou, 2015 [274]	Highest vs. lowest	1.00 (0.91–1.08)	0%	3	3,849

¹ Pooled analysis not included in the CUP meta-analysis.
Note: All cohort studies from Islami 2015 [275], and Zhou 2015 [274], were included in the CUP 2017 analyses.