Online Supplemental Material

Carbohydrates, glycemic index, glycemic load, sugars and breast cancer risk: a systematic review and dose-response meta-analysis of prospective studies

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Supplemental Table 1: Important confounders considered of each study included in the meta-analysis

	Confounders														
Study	**Age**	**HRT use**	**Parity**	**Age at first birth**	**Age at menopause**	**Age at menarche**	**OC use**	**Education**	**BMI or weigh+height**	**Physical activity**	**Smoking**	**Alcohol intake**	**Energy intake**	**Family history**	**History of breast disease**
Farvid et al., 2014, USA	✓	✓	✓	✓	✓	✓	✓		✓		✓	✓	✓	✓	✓
Romieu et al;, 2012, Europe	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		
Tasevska et al, 2012 USA	✓								✓	✓	✓	✓	✓	✓	
Shikany et al., 2011, USA	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
George et al., 2009, USA	✓	✓						✓	✓	✓	✓	✓	✓	✓	
Larsson et al., 2009, Sweden	✓	✓	✓	✓	✓	✓	✓	✓	✓			✓	✓	✓	
Wen et al., 2009, China	✓			✓				✓	✓	✓			✓	✓	✓
Sieri et al 2007, Italy	✓		✓			✓	✓	✓	✓		✓	✓	✓		
Nielsen et al., 2005 Denmark	✓								✓				✓		
Silvera et al., 2005, Canada	✓	✓	✓	✓		✓	✓		✓			✓	✓	✓	✓
Holmes et al., 2004, USA	✓	✓	✓	✓	✓	✓			✓			✓	✓	✓	✓
Higginbotham et al., 2004, USA	✓	✓	✓	✓		✓	✓		✓	✓	✓	✓	✓	✓	✓
Jonas et al., 2003, USA	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
Horn-Ross et al., 2002, USA	✓		✓	✓		✓			✓	✓			✓	✓	

Sieri et al., 2002, Italy	✓		✓					✓		✓				✓		
Kushi et al., 1995, USA	✓									✓				✓		
Barrett-Connor et al. 1993, USA	✓		✓		✓					✓			✓	✓		
Kushi et al, 1992 USA	✓			✓	✓		✓			✓			✓	✓	✓	✓
Knekt et al., 1990 Finland	✓									✓				✓		

Supplemental Table 2. Summary relative risks (RR) and 95% confidence intervals (955 CI) of dose-response meta-analyses of carbohydrates, GI, GL and breast cancer by adjustment for important confounders

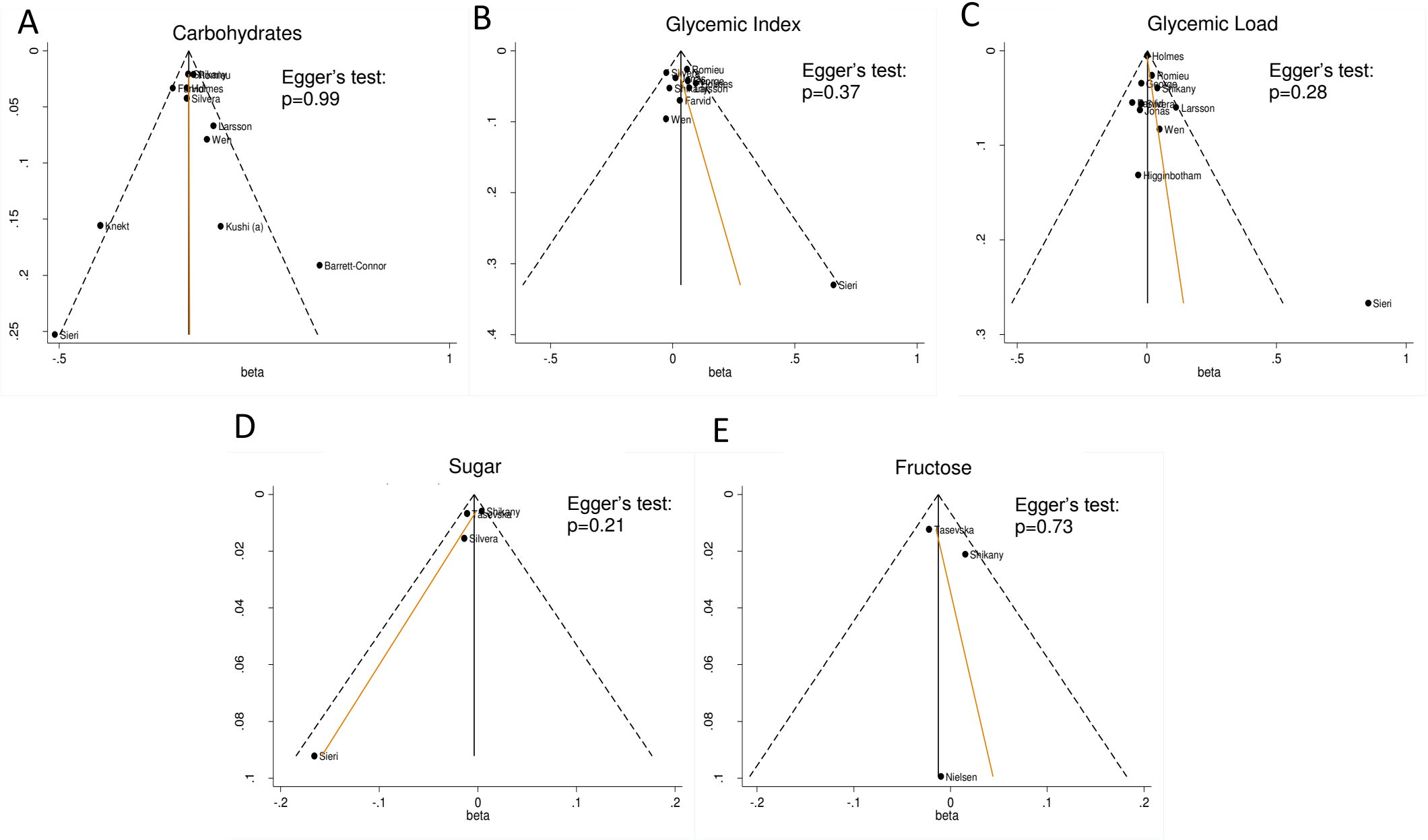
	Carbohydrates (per 50 g/day)					GI (per 10 units/day)					GL (per 50 units/d)				
	Summary RR (95% CI)	n	I^2 (%)	p_{within}[a]	$p_{between}$[b]	Summary RR (95% CI)	n	I^2 (%)	p_{within}[a]	$p_{between}$[b]	Summary RR (95% CI)	n	I^2 (%)	p_{within}[a]	$p_{between}$[b]
All studies	1.00 (0.96-1.05)	11	57.3	.009		1.04 (1.00-1.07)	10	27.2	.194	-	1.01 (0.98-1.04)	11	42.7	.065	
Adjustment for confounders															
HRT use															
Yes	1.00 (0.96-1.04)	7	54.1	.042	.821	1.03 (1.00-1.07)	8	16.4	.301	.821	1.00 (0.99-1.01)	9	0	.543	.269
No	0.89 (0.68-1.16)	4	70.5	.017		1.28 (0.66-2.46)	2	74.9	.046		1.51 (0.69-3.31)	2	87.9	.004	
Parity															
Yes	1.00 (0.95-1.06)	8	58.4	.019	.949	1.03 (0.98-1.08)	7	39.2	.130	.949	1.01 (0.97-1.07)	8	56.7	.024	. 912
No	0.98 (0.85-1.13)	3	65.0	.058		1.06 (1.01-1.10)	3	0	.676		1.01 (0.97-1.05)	3	0	.547	
Age at first birth															
Yes	1.00 (0.97-1.02)	8	7.2	.374	.580	1.03 (1.00-1.06)	8	14.6	.315	.580	1.00 (0.99-1.01)	9	0	.561	.950
No	0.89 (0.49-1.65)	3	86.7	.001		1.31 (0.75-2.29)	2	68.8	.075		1.46 (0.62-3.42)	2	90.6	.001	
Age at menopause															
Yes	1.01 (0.96-1.05)	7	56.0	.034	.715	1.05 (1.01-1.08)	6	0	.602	.715	1.01 (0.98-1.03)	6	19.4	.287	.844
No	0.91 (0.76-1.08)	4	68.2	.024		1.02 (0.93-1.12)	4	56.2	.077		1.03 (0.92-1.16)	5	64.1	.025	
Age at menarche															
Yes	0.99 (0.96-1.03)	8	35.7	.143	.655	1.03 (0.99-1.08)	8	39.0	.119	.655	1.01 (0.97-1.05)	9	51.9	.034	.763
No	1.06 (0.72-1.56)	3	83.3	.003		1.05 (0.97-1.13)	2	0	.393		0.99 (0.93-1.05)	2	0	.429	
OC use															
Yes	0.99 (0.95-1.04)	6	51.1	.069	.807	1.02 (0.98-1.07)	7	35.7	.155	.807	1.02 (0.96-1.08)	8	55.2	.029	.684
No	1.04 (0.89-1.22)	5	69.5	.011		1.07 (1.01-1.13)	3	0	.512		1.00 (0.99-1.01)	3	0	.679	
Education															
Yes	1.02 (0.97-1.07)	5	42.5	.131	.355	1.04 (1.01-1.08)	7	9.1	.360	.355	1.03 (0.98-1.09)	8	52.5	.039	.388
No	0.98 (0.90-1.07)	6	64.8	.014		1.03 (0.95-1.12)	3	58.2	.091		1.00 (0.99-1.01)	3	0	.541	
BMI															
Yes	1.01 (0.97-1.04)	9	44.5	.071	.047	1.04 (1.00-1.07)	10	27.2	.194	-	1.02 (0.97-1.07)	11	47.2	.014	-
No	0.68 (0.52-0.88)	2	0	.557		-	0	-	-		-	0	-	-	
Physical activity															
Yes	1.01 (0.98-1.04)	3	0	.593	.484	1.04 (1.00-1.07)	5	0	.590	.484	1.01 (0.98-1.04)	6	0	.812	.728
No	0.99 (0.91-1.08)	8	66.7	.004		1.05 (0.97-1.13)	5	57.3	.053		1.03 (0.94-1.12)	5	73.2	.005	
Smoking															
Yes	1.00 (0.96-1.05)	4	62.7	.045	.569	1.04 (1.00-1.08)	6	14.7	.320	.569	1.00 (0.95-1.06)	7	55.3	.037	.868
No	1.03 (0.95-1.13)	7	59.7	.021		1.03 (0.96-1.10)	4	49.4	.115		1.01 (0.97-1.06)	4	24.4	.265	
Alcohol intake															
Yes	1.00 (0.96-1.04)	9	55.2	.022	.901	1.04 (1.00-1.08)	9	33.1	.153	.901	1.01 (0.97-1.04)	10	47.5	.047	.735
No	0.89 (0.60-1.33)	2	81.9	.019		0.97 (0.81-1.18)	1	-	-		1.05 (0.89-1.24)	1	-	-	

Family history of breast cancer						.									
Yes	0.99 (0.96-1.02)	7	9.4	.357	.869	1.02 (0.99-1.06)	8	4.9	.392	.360	1.00 (0.99-1.01)	9	0	.563	.541
No	0.94 (0.68-1.29)	4	81.4	.001		1.31 (0.75-2.29)	2	69.5	.070		1.48 (0.66-3.35)	2	89.7	.002	
History of breast disease															
Yes	0.98 (0.94-1.02)	5	57.3	.009	.461	1.02 (0.97-1.06)	5	19.3	.292	.238	1.00 (0.99-1.01)	5	0	.779	.461
No	1.01 (0.93-1.10)	6	72.4	.003		1.05 (1.01-1.10)	5	21.6	.277		1.04 (0.97-1.12)	6	64.4	.015	

CI, confidence interval; ER, oestrogen receptor; GI, glycemic index; GL, glycemic load; n, number of studies; PR, progesterone receptor; RR, relative risk

[a] $p_{within,}$ p for heterogeneity within each subgroup

[b] $p_{between}$, p for heterogeneity between subgroups with meta-regression



Supplemental Figure 1: Funnel plot of studies included in the dose response meta-analyses of (A) carbohydrate intake, (B) glycemic index, (C) glycemic load, (D) sugar intake, (E) fructose intake and risk of breast cancer