

THE LANCET **Oncology**

Supplementary webappendix

This webappendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

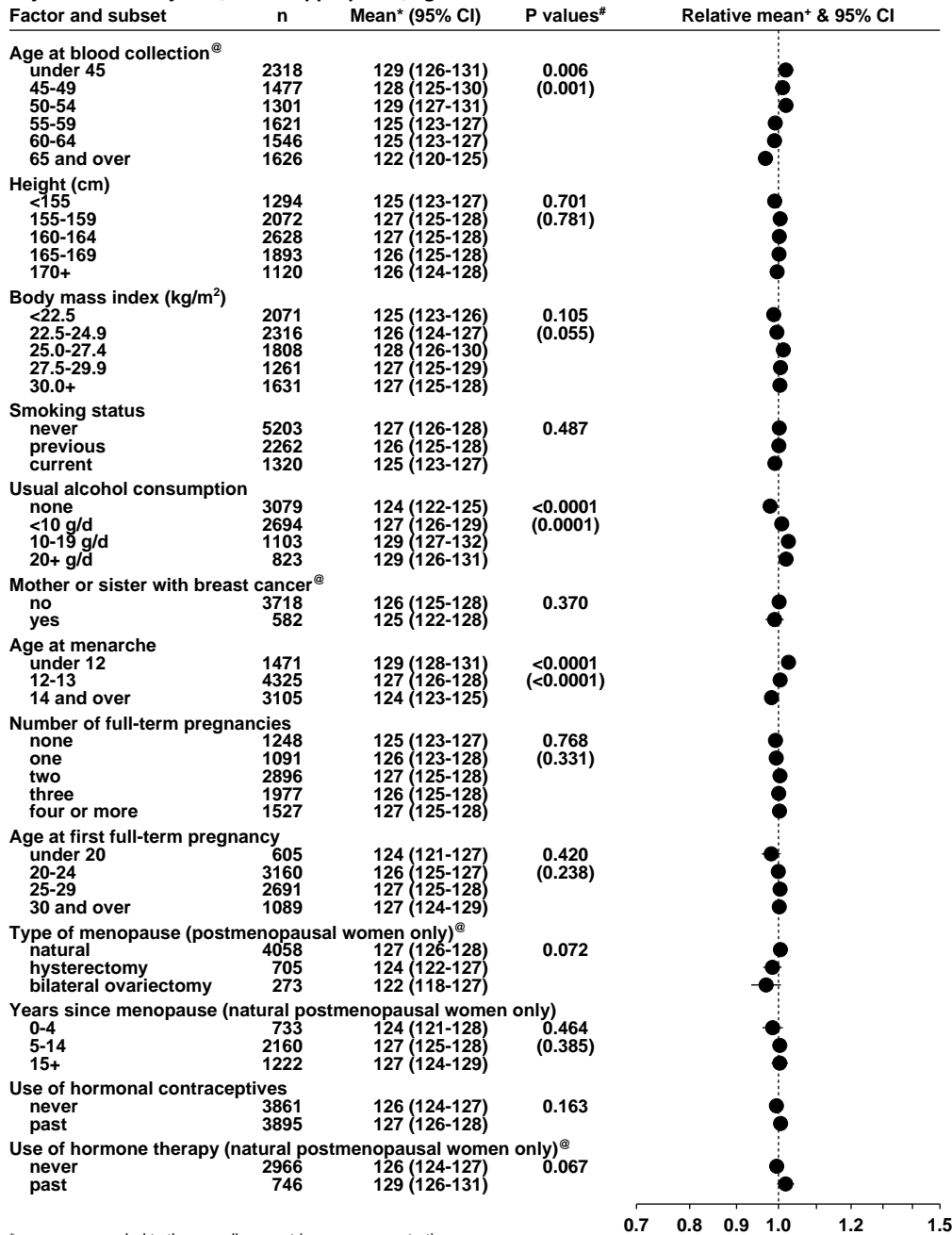
Supplement to: The Endogenous Hormones and Breast Cancer Collaborative Group. Insulin-like growth factor 1 (IGF1), IGF binding protein 3 (IGFBP3), and breast cancer risk: pooled individual data analysis of 17 prospective studies. *Lancet Oncol* 2010; published online May 17. DOI:10.1016/S1470-2045(10)70095-4.

Insulin-like growth factor-I (IGF-I), IGF binding protein-3 (IGFBP-3), and breast cancer risk: reanalysis of seventeen prospective studies

Endogenous Hormones and Breast Cancer Collaborative Group

Supplementary Fig. 1.

Geometric mean IGFBP-3 (nmol/L) among controls by selected factors, adjusted for study and, where appropriate, age at blood collection



* means are scaled to the overall geometric mean concentration

[#] P values for tests of heterogeneity and, where applicable and in parenthesis, linear trend

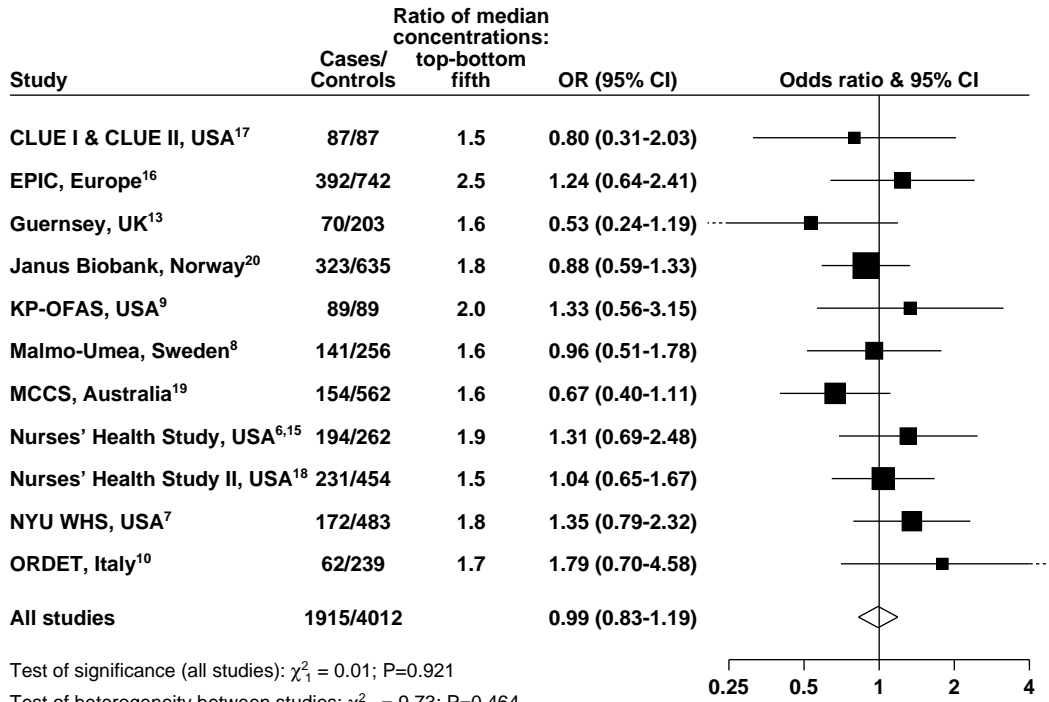
⁺ values are depicted as a proportion of the overall geometric mean concentration (dotted line)

[®] P<0.05 for test of interaction with study

Webfigure 1. Geometric mean IGFBP-3 concentrations (nmol/l with 95% confidence intervals) among controls by selected factors. Adjusted for study and age at blood collection, as appropriate.

Supplementary Fig. 2a.

Association of breast cancer risk with IGFBP-3 concentration among premenopausal women, by study

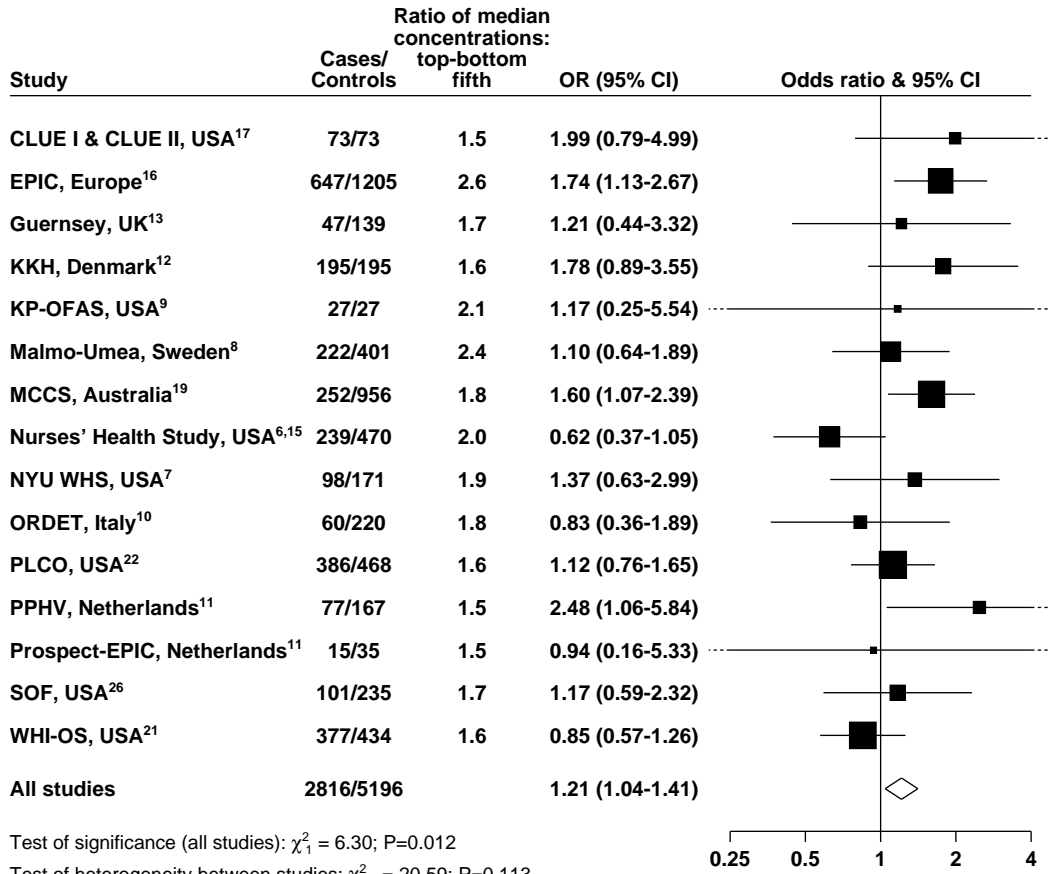


The odds ratio is the estimate of the linear trend for IGFBP-3 concentration obtained using a variable that was scored 0, 0.25, 0.5, 0.75, and 1, corresponding to the fifths of concentration.

Webfigure 2a. Odds ratios (ORs) for breast cancer associated with an increase in IGFBP-3 concentration among women who were premenopausal at blood collection. The OR is the estimate of the linear trend for IGFBP-3 obtained by replacing the categorical variables representing the fifths of concentration among controls by a continuous variable scored as 0, 0.25, 0.5, 0.75 and 1. The black squares indicate the ORs and the horizontal lines show the 95% confidence intervals. The area of each square is proportional to the amount of statistical information (inverse of the variance of the logarithm of the OR). The diamond indicates the OR and 95% CI for all studies combined. Estimates are from conditional logistic regression on case-control sets matched within each study.

Supplementary Fig. 2b.

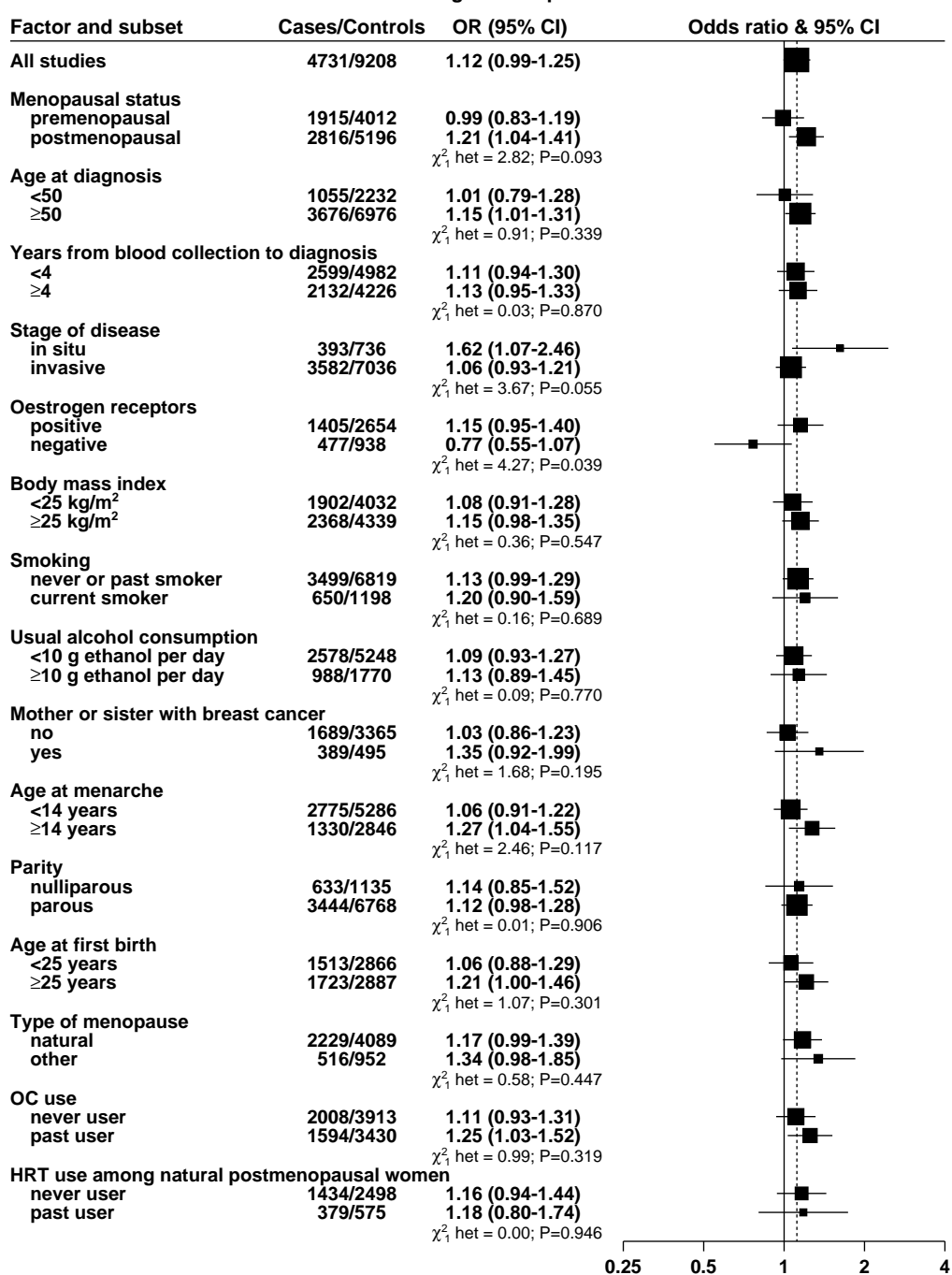
Association of breast cancer risk with IGFBP-3 concentration among postmenopausal women, by study



Webfigure 2b. Odds ratios (ORs) for breast cancer associated with an increase in IGFBP-3 concentration among women who were postmenopausal at blood collection. The OR is the estimate of the linear trend for IGFBP-3 obtained by replacing the categorical variables representing the fifths of concentration among controls by a continuous variable scored as 0, 0.25, 0.5, 0.75 and 1. The black squares indicate the ORs and the horizontal lines show the 95% confidence intervals. The area of each square is proportional to the amount of statistical information (inverse of the variance of the logarithm of the OR). The diamond indicates the OR and 95% CI for all studies combined. Estimates are from conditional logistic regression on case-control sets matched within each study.

Supplementary Fig. 3.

Odds ratios associated with IGFBP-3 according to menopausal status and other factors



Webfigure 3. Odds ratios (ORs) for breast cancer associated with IGFBP-3 concentration, according to menopausal status at blood collection and other factors. The OR is the estimate of the linear trend obtained by replacing the categorical variables representing the fifths of IGFBP-3 concentration among controls by a continuous variable scored as 0, 0.25, 0.5, 0.75 and 1. Black squares indicate the OR and the horizontal lines show the 95% confidence intervals. The area of each square is proportional to the amount of statistical information (inverse of the variance of the logarithm of the OR). The vertical dotted line indicates the OR for all studies. Tests for heterogeneity are for the difference in the association of IGFBP-3 with breast cancer risk between subgroups. Estimates are from conditional logistic regression on case-control sets matched within each study.

Webtable 1: Relationships of IGF-I with breast cancer risk among all women, according to plasma concentrations of IGFBP-3

Thirds of IGFBP-3	Thirds of IGF-I					
	Low		Medium		High	
	Cases/controls	RR (95% CI)	Cases/controls	RR (95% CI)	Cases/controls	RR (95% CI)
Low	825/1730	1.00 (ref)	518/988	1.12 (0.97-1.28)	223/427	1.15 (0.95-1.40)
Medium	408/847	0.99 (0.86-1.15)	592/1194	1.06 (0.93-1.21)	572/1018	1.22 (1.06-1.40)
High	239/505	0.91 (0.75-1.11)	464/896	1.05 (0.90-1.22)	886/1591	1.18 (1.04-1.34)
Test of interaction: $\chi^2_4=1.15$, P=0.887						