Central adiposity and the risk of invasive breast cancer: results from the Nurses' Health Studies

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Objective

- Examine whether waist circumference (WC), hip circumference (HC), or waist-to-hip ratio (WHR) are associated with incident invasive breast cancer (overall and by tumor subtype), independent of BMI according to menopause status

Background

- Body mass index (BMI) used to measure general adiposity, represents adipose tissue and lean mass
  - Higher BMI associated with ↑ postmenopausal breast cancer risk
  - Higher BMI associated with ↓ premenopausal breast cancer risk
- WC or WHR is often used to measure central adiposity, high levels of visceral adipose tissue (VAT)
  - VAT is considered to be more metabolically active than subcutaneous adipose tissue (SAT)
- In a meta-analysis of prospective studies:
  - Higher WC associated with ↑ postmenopausal breast cancer risk
  - Higher WC suggestively ↑ premenopausal breast cancer risk
  - BMI and WC are highly correlated: the WC x postmenopausal breast cancer association attenuates & WC x premenopausal breast cancer association is stronger and statistically significant with adjustment for BMI
- Research gap: limited sample size for premenopausal; limited assessment of tumor heterogeneity

Methods

- Pooled analysis of 2 prospective cohorts: Nurses' Health Study and Nurses' Health Study II (n=96,746 women)
- Repeated, self-reported assessment of WC, HC and WHR:
  - NHS: 1986, 1996, 2000
  - NHS II: 1993, 2005
- Incident invasive breast cancer self-reported through 2016 (NHS) and 2017 (NHS II), confirmed by medical record
  - 6,129 incident invasive cases (1,131 premenopausal at measurement/ premenopausal at diagnosis [pre/pre], 2,089 pre/post, 2,909 post/post)
- Cox proportional hazard models adjusting for age at menarche, height, parity/age at first birth, family history of breast cancer, benign breast disease diagnosis, alcohol intake, physical activity, smoking, menopausal status (pre/post analyses), postmenopausal hormone use (pre/post, post/post analyses), and age at menopause (pre/post, post/post analyses), with and without BMI, by menopause
- Tumor heterogeneity by hormone receptor and molecular subtypes defined by immunohistochemical markers was assessed using competing risk analyses

Results

**Table 1.** Characteristics at baseline by quintiles of WHR

	NHS (1986)			NHS II (1993)		
	Q1 (n=8281)	Q3 (n=9424)	Q5 (n=9517)	Q1 (n=11527)	Q3 (n=8393)	Q5 (n=9868)
WC, cm	66.0 (2.6)	76.7 (1.5)	96.3 (8.2)	65.7 (2.7)	76.7 (1.4)	98.6 (10.2)
HC, cm	91.9 (5.4)	99.1 (5.7)	113.1 (11.1)	91.4 (5.0)	98.9 (5.7)	114.6 (13.3)
WHR	0.72 (0.05)	0.78 (0.05)	0.86 (0.08)	0.72 (0.04)	0.78 (0.04)	0.87 (0.10)
BMI, kg/m^2	20.7 (2.0)	23.6 (2.2)	30.6 (4.8)	20.6 (1.9)	23.5 (2.4)	31.3 (6.0)
Age, y	50.9 (7.0)	53.6 (7.0)	55.0 (6.8)	38.1 (4.6)	38.8 (4.6)	39.6 (4.6)
Parity	2.9 (1.4)	3.2 (1.5)	3.3 (1.6)	2.1 (0.9)	2.2 (0.9)	2.2 (1.0)
Alcohol intake, g/day	6.6 (10.5)	7.0 (11.5)	5.1 (11.0)	3.5 (6.1)	3.4 (6.4)	2.5 (6.1)
Physical activity, MET-h/wk	19.0 (24.6)	14.7 (20.1)	10.6 (16.2)	27.7 (33.5)	20.6 (24.8)	16.0 (22.2)
History of BBD, %	40	36	28	43	40	35
Postmenopausal, %	68	68	70	4	5	6
HT use, %	34	31	21	90	90	85
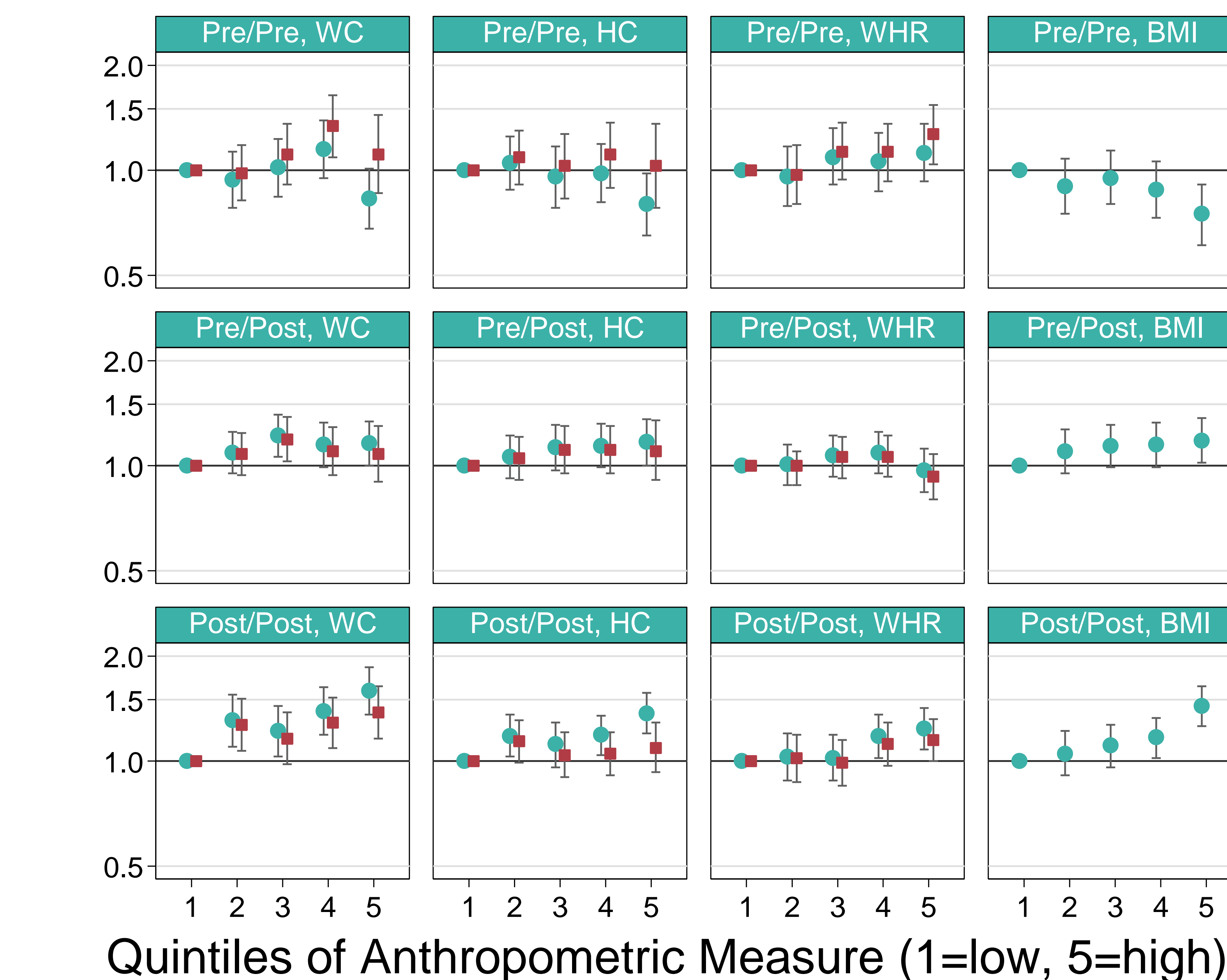
Figure 1. Hazard ratio (HR) and 95% confidence intervals (CI) of invasive breast cancer by quintiles of anthropometric measures

Table 2. Correlations between anthropometric measures approximately 10 years apart

	WC, cm		HC, cm		WHR	
Mean (SD)	1st 79.0 (10.9)	2nd 79.0 (10.9)	1st 100.9 (10.0)	2nd 100.9 (10.0)	1st 0.78 (0.07)	2nd 0.78 (0.07)
HC, cm	0.76	0.75				
WHR	0.73	0.76	0.18	0.21		
BMI, kg/m^2	0.79	0.71	0.81	0.77	0.39	0.32
Height	0.15	0.13	0.23	0.21	-0.01	-0.01
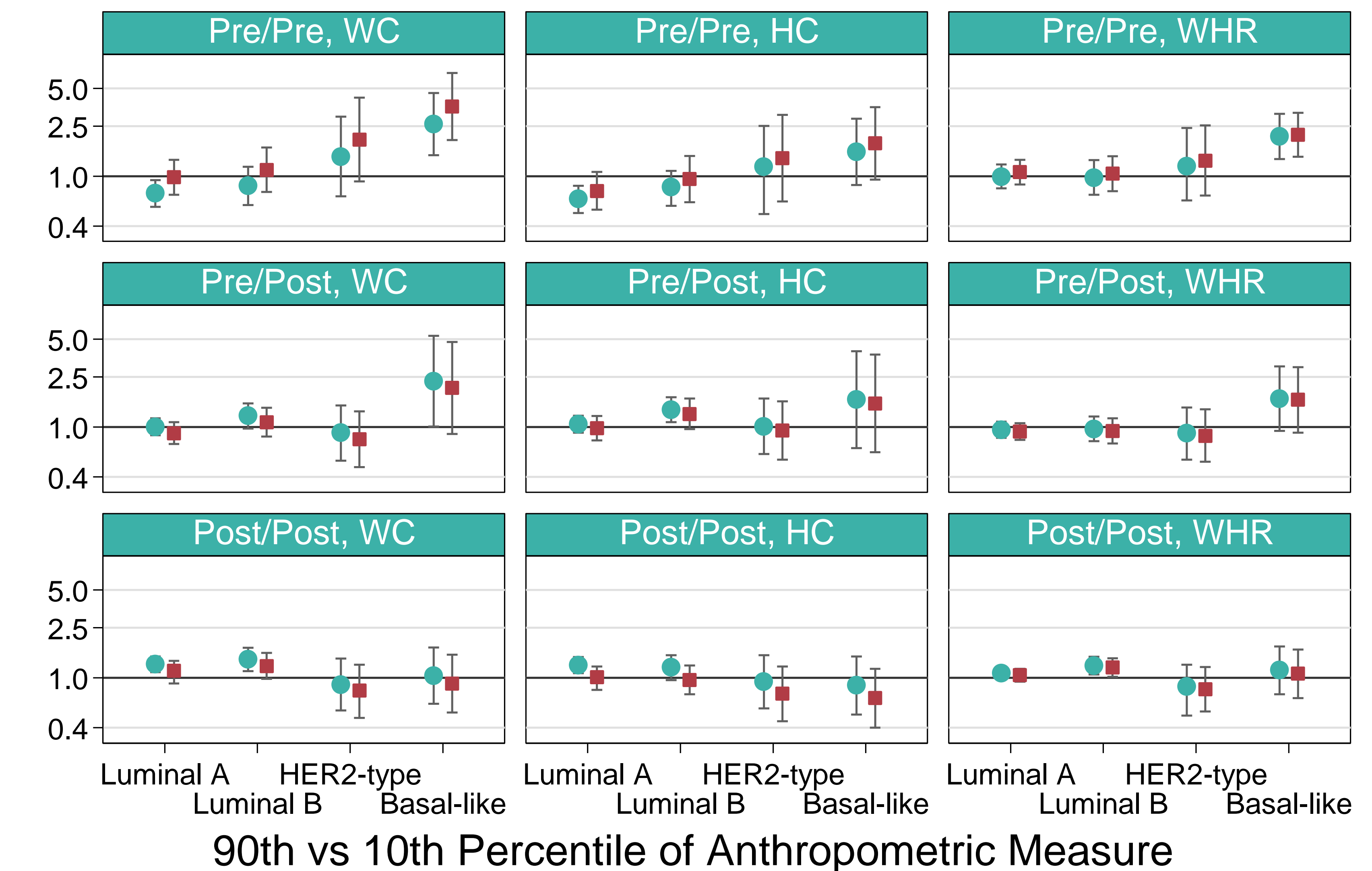
Figure 2. Hazard ratio (HR) and 95% confidence intervals (CI) of invasive breast cancer by molecular subtype comparing the 90th with the 10th percentile of anthropometric measures

Conclusions

- Women with greater central adiposity had higher risk of both premenopausal and postmenopausal breast cancers, independent of BMI
- This suggests that maintaining a healthy waist circumference may decrease risk of breast cancer even among premenopausal women

Acknowledgements