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Life course evolution of body size and breast cancer survival in the E3N cohort

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Although adult obesity has been associated with poor breast cancer survival, data on adiposity at different periods in life and its lifelong evolution are scarce. Our aims were to assess the associations between breast cancer survival and body size during childhood, puberty and early adulthood and body size trajectories from childhood to adulthood. Self-assessed body size at age 8, at puberty, at age 20–25 and at age 35–40 and trajectories of body size of 4,662 breast cancer survivors from the prospective E3N cohort were studied in relation to risk of death from any cause, death from breast cancer and second invasive cancer event using multivariate Cox regression models. Four trajectories of body size were identified (T1 "moderate increase," T2 "stable/low increase," T3 "increase at puberty" and T4 "constantly high"). Compared with stable body size, an increase in body size during adult life was associated with an increased risk of death from any cause (HR T1 *vs*. T2 = 1.27; 95% CI = 1.01–1.60) and an increased risk of second invasive cancer event (HR T1 *vs*. T2 = 1.25; 95% CI = 1.06–1.47). Silhouettes at various ages were not associated with survival. Our results suggest that the evolution of body size from childhood to adulthood has a long-term influence on breast cancer survival. Although these results need to be confirmed, this work sheds light on the need to combine lifelong approaches to current BMI to better identify breast cancer survivors who are at higher risk of recurrence or second primary cancer, or of death.

Cancer Epidemiology

Breast cancer, the most prevalent cancer among women worldwide,[1] has a good prognosis with survival rates of >80% in developed countries.[2] While understanding modifiable factors influencing breast cancer risk remains crucial, the increasing number of breast cancer survivors highlights the need to identify modifiable factors that influence risks of relapse, second cancer and death after breast cancer.

In addition to being a risk factor for postmenopausal breast cancer, obesity before and after a breast cancer diagnosis has been associated with poor survival.[3] Studies on breast cancer risk have shown that excess adiposity at several moments in life and body size trajectories could help better characterize the adiposity-breast cancer association. For instance, women with greater body size during their childhood/puberty were at decreased risk of breast cancer in several studies[4–12] while adult weight gain has been associated with an increase in breast cancer risk.[13] Despite the growing number of studies on the obesity-survival relationship, early ages body size and lifetime body size trajectories have not been much investigated.[14] One study[15] reported no association between BMI at age 16 and breast cancer-specific survival. Compared with stable weight, adult weight gain (since age 18–20) has been associated with an increased risk of death from any cause in two[16,17] out of three[16–18] studies and

Key words: breast cancer, survival, obesity, trajectory, body size change
Abbreviations: BCSS: breast cancer-specific survival; BMI: body mass index; CI: confidence interval; ER: estrogen receptor; HR: hazard ratio; iDFS: invasive disease-free survival; MHT: menopausal hormone therapy; OS: overall survival; PR: progesterone receptor; SBR: Scarff-Bloom-Richardson.
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What's new?
Obesity is a known factor affecting breast cancer survival. It remains unclear, however, whether body size in early life is associated with breast cancer survival in adulthood, or whether only adult obesity is relevant in this context. Here, analyses of life-course body size from childhood through puberty to adulthood show that an increase in body silhouette, particularly during adulthood, is associated with elevated risks of breast cancer recurrence, second primary cancer and death. The findings suggest that consideration of body size trajectory can help identify breast cancer survivors with increased likelihood of recurrence and poor outcome.

with an increased risk of death from breast cancer in two[16,17] out of five studies.[15–17,19,20] To our knowledge, no study has explored the association between body size trajectories from early childhood to adulthood in relation to breast cancer survival.

Therefore, the aims of our study were, using the data from a large prospective cohort study: (*i*) to assess the associations between body size during childhood, puberty and early adulthood and breast cancer survival; (*ii*) to characterize trajectories of prediagnostic changes in body size between childhood and adulthood in breast cancer survivors and to investigate the associations between these trajectories and breast cancer survival.

MATERIAL AND METHODS

The E3N cohort study

The "Etude Epidémiologique auprès des Femmes de la Mutuelle Générale de l'Education Nationale" (E3N) study is a prospective cohort study initiated in 1990.[21] Overall, 98,995 women aged 40–65 years were recruited from a national health insurance plan covering mostly teachers. All women gave informed consent, in compliance with the rules of the French National Commission for Data Protection and Privacy, the organization that gave ethical approval for the study. Follow-up questionnaires have been sent every 2–3 years to the participants since 1990, collecting data about lifestyle and reproductive factors as well as major health events, including cancer.

Outcome assessment

In each follow-up questionnaire, women were invited to declare any new cancer event (primary tumors and loco-regional or distant recurrences) that was then systematically investigated and validated by collecting pathological reports and/or clinical records from the patients or their doctors, up to December 7, 2011 (date when the last questionnaire was sent). Tumor characteristics such as stage, grade, nodes, distant metastases, tumor size, hormonal receptor status and histological type were extracted from the reports.

Overall survival (OS) was defined as time to death from any cause and breast cancer specific survival (BCSS) as time to death from breast cancer. Invasive disease-free survival (iDFS) after a primary invasive breast cancer was studied using second invasive cancer event or death from any cause as outcomes of interest, as defined in details previously.[22–24] We considered loco-regional invasive recurrences, distant recurrences (metastases), or second invasive cancers of any other primary sites as second invasive cancer event. Vital status of the participants was regularly updated thanks to health insurance data, doctors and families and causes of death were obtained from the French National Service on Causes of Death.

Body size assessment

In the baseline questionnaire (1990), women were invited to choose, among eight silhouette drawings (numbered 1–8, leanest to largest),[25] the one that best described their body size at age 8, at puberty, at age 20–25 and at age 35–40.

Recalled birth weight and height were collected in 2002. Birth weight was categorized in low, medium, large or missing. Birth size was categorized as small, medium, large or missing.

At baseline and in each follow up questionnaire women were asked to provide their weight in kilograms. Height (cm) was self-reported in 1990 and 1995 and in all questionnaires since 2000. BMI was then computed according to the weight reported in each questionnaire as weight (kg)/[height (m)*height (m)]. Prediagnosis BMI was the last available BMI before diagnosis (on average 1.8 years before diagnosis).

Study population

Only women with no personal history of cancer, except basal cell skin carcinoma or *in situ* colorectal cancer, prior to breast cancer diagnosis and whose first primary breast cancer had been confirmed by a pathological report before June 25, 2008 ($N = 5,991$, 94.3% of breast cancer cases reported before June 25, 2008), were included in the study. We excluded women with incomplete date of any cancer event or death ($N = 133$), *in situ* breast cancer ($n = 760$), phyllode tumors or tumors with missing morphological codes ($n = 7$) and metastatic disease at diagnosis ($n = 39$). Women with silhouette missing for at least one age period were additionally excluded ($n = 383$), as well as women without prediagnostic BMI ($n = 7$). In the end, 4,662 women diagnosed with a primary invasive nonmetastatic breast cancer between 1990 and June 25, 2008 were included in the analysis.

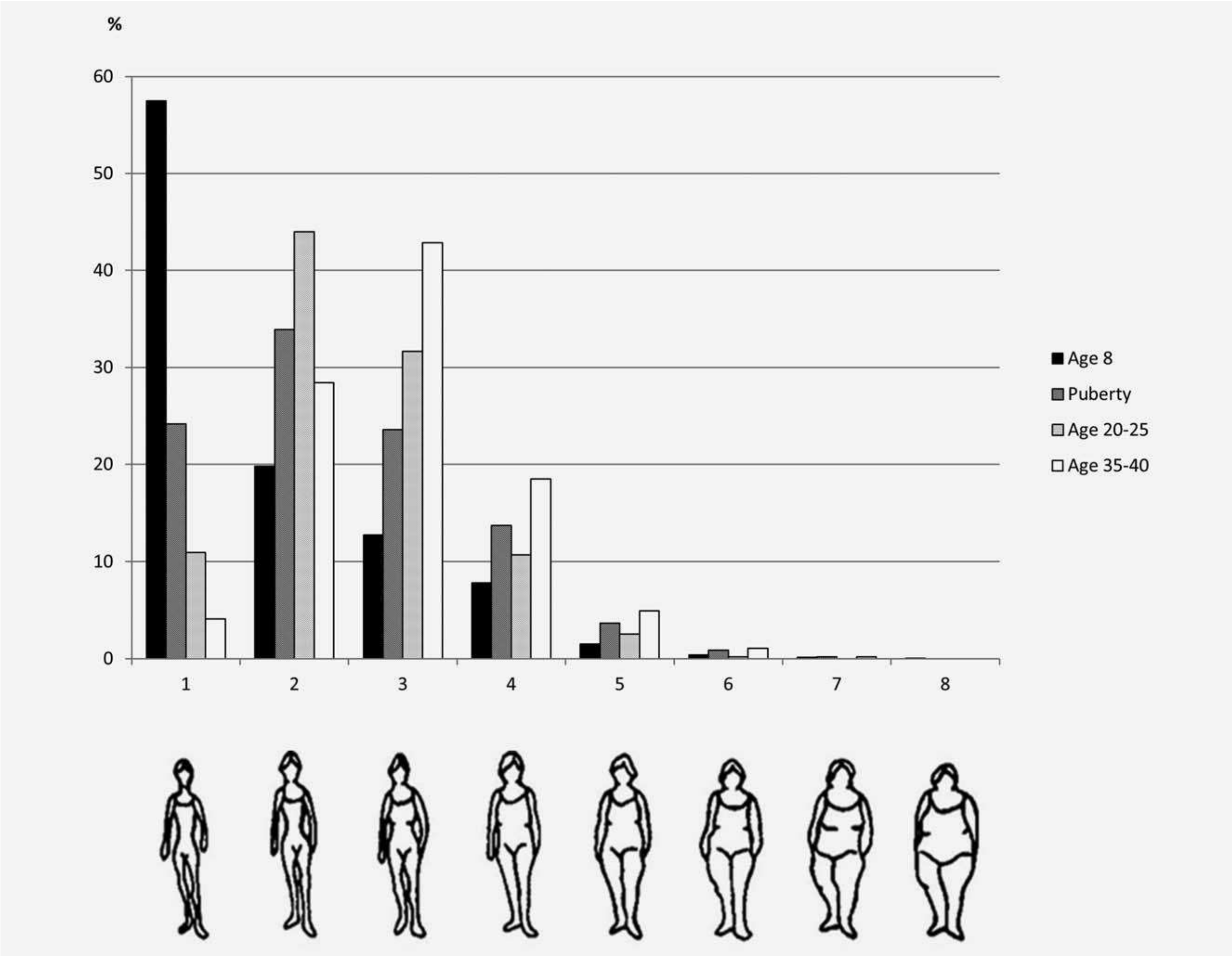

Figure 1. Distribution of silhouettes at each age ($N = 4,662$).

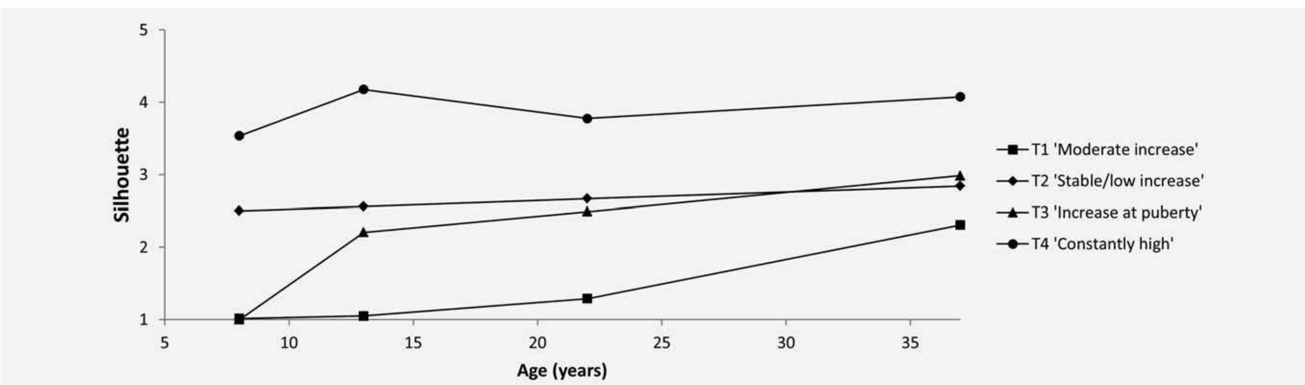

Figure 2. Estimated trajectories of body size by age.

Statistical analyses

As few women chose silhouettes 4–8 at age 8, at puberty and at age 20–25 and silhouette 1 at age 35–40, silhouettes were categorized as follows in the analyses: 1, 2, 3, 4 or more at age 8, puberty, or age 20–25; 1 or 2, 3, 4, 5 or more at age 35–40.

Evolution of body size from childhood to age 35–40 was characterized using group-based trajectory modeling.[26] Body sizes at each age (before categorization) were considered as longitudinal data and used to define trajectories of women having similar evolution of body size, based on the censored normal model of SAS Proc TRAJ. To do so, we first assigned

Table 1. Baseline characteristics of the study population overall and according to trajectories of body size evolution

	Overall	T1 "Moderate increase"	T2 "Stable/ low increase"	T3 "Increase at puberty"	T4 "Constantly high"	*p* Value*
	N = 4,662	*N* = 997	*N* = 1,379	*N* = 1,671	*N* = 615	
	Mean ± SD or *N* (%)	Mean ± SD or *N* (%)	Mean ± SD or *N* (%)	Mean ± SD or *N* (%)	Mean ± SD or *N* (%)	
Follow-up for OS and BCSS (years)	11.1 ± 4.9	11.2 ± 5.0	11.1 ± 4.9	11.0 ± 4.9	11.2 ± 5.1	0.6
Follow-up for iDFS (years)	9.2 ± 5.1	9.2 ± 5.2	9.3 ± 5.0	9.1 ± 5.0	9.3 ± 5.1	0.5
Age at cancer diagnosis (years)	59.1 ± 7.7	59.6 ± 7.7	58.7 ± 7.6	59.2 ± 7.8	58.7 ± 7.6	0.02
Year of diagnosis						
1990–1994	925 (19.8%)	218 (21.8%)	258 (18.7%)	324 (19.4%)	125 (20.3%)	0.8
1995–1999	1,335 (28.6%)	286 (28.7%)	397 (28.8%)	474 (28.4%)	178 (28.9%)	
2000–2004	1,540 (33.0%)	309 (31.0%)	468 (33.9%)	564 (33.7%)	199 (32.4%)	
2005–2008	862 (18.5%)	184 (18.5%)	256 (18.6%)	309 (18.5%)	113 (18.4%)	
TNM stage at diagnosis						
I	2,748 (61.4%)	581 (60.5%)	831 (63.4%)	979 (60.9%)	357 (59.7%)	0.3
II	1,375 (30.7%)	312 (32.5%)	377 (28.8%)	501 (31.1%)	185 (30.9%)	
III	354 (7.9%)	67 (7.0%)	102 (7.8%)	129 (8.0%)	56 (9.4%)	
SBR grade						
1	1,377 (33.5%)	297 (33.4%)	428 (35.0%)	467 (32.1%)	185 (33.9%)	0.6
2	2,002 (48.7%)	435 (48.9%)	574 (47.0%)	717 (49.4%)	276 (50.6%)	
3	732 (17.8%)	158 (17.8%)	220 (18.0%)	269 (18.5%)	85 (15.6%)	
ER status						
ER–	746 (19.1%)	159 (19.2%)	234 (20.2%)	251 (17.9%)	102 (19.6%)	0.5
ER+	3,164 (80.9%)	669 (80.8%)	922 (79.8%)	1,155 (82.1%)	418 (80.4%)	
ER status						
PR–	1,326 (35.1%)	288 (36.0%)	395 (35.4%)	473 (34.8%)	170 (34.1%)	0.9
PR+	2,448 (64.9%)	511 (64.0%)	722 (64.6%)	886 (65.2%)	329 (65.9%)	
Histological subtypes						
Ductal	3,355 (72.0%)	737 (73.9%)	979 (71.0%)	1,176 (70.4%)	463 (75.3%)	0.01
Lobular	764 (16.4%)	149 (14.9%)	222 (16.1%)	312 (18.7%)	81 (13.2%)	
Mixed	117 (2.5%)	19 (1.9%)	41 (3.0%)	47 (2.8%)	10 (1.6%)	
Other	426 (9.1%)	92 (9.2%)	137 (9.9%)	136 (8.1%)	61 (9.9%)	
Birth weight						
Low	322 (8.2%)	93 (11.5%)	48 (4.1%)	150 (10.6%)	31 (6.0%)	<0.001
Medium	3,335 (85.1%)	673 (83.2%)	1,041 (88.2%)	1,191 (84.2%)	430 (83.2%)	
Large	264 (6.7%)	43 (5.3%)	91 (7.7%)	74 (5.2%)	56 (10.8%)	
Birth height						
Small	337 (9.3%)	92 (12.2%)	67 (6.1%)	138 (10.6%)	40 (8.3%)	<0.001
Medium	2,937 (81.0%)	579 (76.8%)	920 (83.9%)	1,043 (80.5%)	395 (82.5%)	
Large	351 (9.7%)	83 (11.0%)	109 (10.0%)	115 (8.9%)	44 (9.2%)	
Age of menarche (years)	12.8 ± 1.4	13.1 ± 1.4	12.7 ± 1.3	12.8 ± 1.4	12.4 ± 1.4	<0.001
Use of oral contraceptive						
Ever	2,798 (60.0%)	603 (60.5%)	840 (60.9%)	997 (59.7%)	358 (58.2%)	0.7
Never	1,864 (40.0%)	394 (39.5%)	539 (39.1%)	674 (40.3%)	257 (41.8%)	

Table 1. Baseline characteristics of the study population overall and according to trajectories of body size evolution (Continued)

	Overall	T1 "Moderate increase"	T2 "Stable/ low increase"	T3 "Increase at puberty"	T4 "Constantly high"	*p* Value*
	N = 4,662	*N* = 997	*N* = 1,379	*N* = 1,671	*N* = 615	
	Mean ± SD or *N* (%)	Mean ± SD or *N* (%)	Mean ± SD or *N* (%)	Mean ± SD or *N* (%)	Mean ± SD or *N* (%)	
Number of children and age at first full-term pregnancy						
No child	610 (13.2%)	136 (13.7%)	183 (13.4%)	205 (12.4%)	86 (14.2%)	0.8
One child before age 30	500 (10.8%)	121 (12.2%)	141 (10.3%)	166 (10.1%)	72 (11.9%)	
One child after age 30	280 (6.1%)	62 (6.3%)	75 (5.5%)	106 (6.4%)	37 (6.1%)	
>1 child, first before age 30	2,871 (62.2%)	596 (60.2%)	868 (63.4%)	1,042 (63.2%)	365 (60.2%)	
>1 child, first after age 30	354 (7.7%)	75 (7.6%)	102 (7.4%)	131 (7.9%)	46 (7.6%)	
Breastfeeding among women with children						
Less than 6 months	2,076 (53.7%)	439 (53.1%)	634 (55.0%)	729 (52.8%)	274 (54.5%)	0.1
More than 6 months	560 (14.5%)	101 (12.2%)	168 (14.6%)	223 (16.1%)	68 (13.5%)	
No breastfeeding	1,228 (31.8%)	287 (34.7%)	350 (30.4%)	430 (31.1%)	161 (32.0%)	
Menopausal status at diagnosis, age at menopause and ever use of MHT						
Menopausal after age 50 not using MHT	684 (16.6%)	122 (14.0%)	214 (17.2%)	248 (16.8%)	100 (18.4%)	0.1
Menopausal after age 50 using MHT	1,476 (35.7%)	346 (39.6%)	439 (35.3%)	508 (34.4%)	183 (33.7%)	
Menopausal before age 50 not using MHT	248 (6.0%)	55 (6.3%)	66 (5.3%)	87 (5.9%)	40 (7.4%)	
Menopausal before age 50 using MHT	795 (19.2%)	174 (19.9%)	227 (18.3%)	289 (19.6%)	105 (19.3%)	
Premenopausal	931 (22.5%)	176 (20.2%)	297 (23.9%)	343 (23.3%)	115 (21.2%)	
Family history of breast cancer						
In first degree relatives only	308 (7.1%)	76 (8.1%)	88 (6.8%)	104 (6.7%)	40 (7.1%)	0.7
In first and second degree relatives	125 (2.9%)	32 (3.4%)	38 (3.0%)	39 (2.5%)	16 (2.8%)	
None	3,922 (90.0%)	834 (88.5%)	1,162 (90.2%)	1,415 (90.8%)	511 (90.1%)	
Education level						
Undergraduate	516 (11.4%)	141 (14.6%)	131 (9.8%)	200 (12.4%)	44 (7.5%)	0.001
0–2 years postgraduation	2,242 (49.8%)	483 (49.9%)	649 (48.7%)	799 (49.3%)	311 (53.3%)	
3–4 years postgraduation	819 (18.2%)	163 (16.8%)	270 (20.3%)	285 (17.6%)	101 (17.3%)	
≥ 5 years postgraduation	928 (20.6%)	181 (18.7%)	283 (21.2%)	336 (20.7%)	128 (21.9%)	
Marital status before diagnosis						
Single	1,039 (22.5%)	239 (24.4%)	299 (21.9%)	368 (22.2%)	133 (22.1%)	0.5
Couple	3,572 (77.5%)	740 (75.6%)	1,069 (78.1%)	1,293 (77.8%)	470 (77.9%)	
Smoking status before diagnosis						
Current	531 (11.4%)	99 (9.9%)	179 (13.0%)	175 (10.5%)	78 (12.7%)	0.04
Past	1,664 (35.7%)	335 (33.6%)	487 (35.3%)	613 (36.7%)	229 (37.2%)	
Never	2,465 (52.9%)	563 (56.5%)	712 (51.7%)	882 (52.8%)	308 (50.1%)	

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Table 1. Baseline characteristics of the study population overall and according to trajectories of body size evolution (Continued)

	Overall	T1 "Moderate increase"	T2 "Stable/ low increase"	T3 "Increase at puberty"	T4 "Constantly high"	*p* Value*
	N = 4,662	*N* = 997	*N* = 1,379	*N* = 1,671	*N* = 615	
	Mean ± SD or *N* (%)	Mean ± SD or *N* (%)	Mean ± SD or *N* (%)	Mean ± SD or *N* (%)	Mean ± SD or *N* (%)	
High blood pressure before diagnosis						
No	2,698 (57.9%)	559 (56.1%)	840 (60.9%)	950 (56.9%)	349 (56.7%)	0.06
Yes	1,964 (42.1%)	438 (43.9%)	539 (39.1%)	721 (43.1%)	266 (43.3%)	
Prediagnosis BMI (kg/m^2)	23.6 ± 3.6	22.6 ± 2.8	23.1 ± 3.2	23.7 ± 3.7	25.7 ± 4.4	<0.001

Abbreviations: BMI: body mass index; ER: estrogen receptors; PR: progesterone receptors; MHT: menopause hormone therapy; OS: overall survival; BCSS: breast cancer-specific survival; iDFS: invasive disease-free survival.
**p*-values for comparison across trajectories by analysis of variance on log-transformed continuous variables and χ^2 test for categorical variables.
Numbers of missing values were 185 (4.0%) for TNM stage, 551 (11.8%) for SBR grade, 752 (16.1%) for ER status, 888 (19.0%) for PR status, 741 (15.9%) for birth weight, 1,037 (22.2%) for birth height, 86 (1.8%) for age at menarche, 188 (4.6%) for breast-feeding, 528 (11.3%) for age at menopause and MHT use, 307 (6.6%) for family history of breast cancer, 157 (3.4%) for education level, 51 (1.1%) for marital status before diagnosis, 2 (<0.1%) for smoking status before diagnosis.

a single age to each silhouette: age 13 years (rounded age at menarche) for puberty, age 22.5 years for silhouette at age 20–25 and age 37.5 years for silhouette at age 35–40. As recommended,[27,28] the optimal number of trajectories in the study population was determined based on the Bayesian information criterion and the percentage of subjects across trajectories, with a maximum of five groups tested given the available data. The shape of each trajectory was then determined. As birth weight and size were likely to influence trajectories, models adjusted for both factors were examined, but only adjustment for birth weight was included in the final model because including birth size did not influence trajectories. For each trajectory, the mean posterior probability for each individual belonging to this trajectory was calculated.

For descriptive analyses, heterogeneity between groups of women defined according to their body size trajectories was assessed using chi^2 tests or analyses of variance.

For survival analyses, follow-up started at the date of diagnosis of the first primary invasive breast cancer. For OS and BCSS analyses, women were followed until the event of interest or until December 7, 2011. In the iDFS analyses, women who did not answer the last questionnaire before date of death or December 7, 2011 (11.0%) were considered lost to follow-up, and censored at the date of the last completed questionnaire plus 6 months. Otherwise, women were followed until the date of diagnosis of a second invasive cancer event, date of death, or December 7, 2011, whichever occurred first. Cox proportional hazards models with time since diagnosis as the timescale were used to estimate hazard ratios (HRs) and 95% confidence intervals (CI) associated with body size at each age and with trajectories. Proportional hazards assumption was assessed using log-log plots. For tests of linear trend across categories, we assigned to the participants the median value of each category and modeled the corresponding variable as a continuous term. Adjustment variables were selected in univariate analyses and included age at diagnosis, tumor characteristics (Scarff-Bloom-Richardson (SBR) grade of the tumor, estrogen receptor (ER) status, progesterone receptor (PR) status, TNM stage and histological subtype), age at menarche, age at first full-term pregnancy, number of children, total duration of breast-feeding, ever use of oral contraceptive, menopausal status at diagnosis, age at menopause and menopause hormone therapy (MHT) use before diagnosis, family history of breast cancer, high blood pressure, smoking status before diagnosis, education level, marital status at diagnosis and prediagnosis BMI. The model was also stratified according to the period of diagnosis. For covariates with <5% missing values, missing values were imputed to the modal category or the median value. For SBR grade (11.8% missing values) and hormone receptor status (ER: 16.1% missing values, PR: 19.0%), we created a missing category.

Analyses were stratified according to menopausal status at diagnosis, hormone receptor status, age at menarche and overweight status at diagnosis.

We performed a sensitivity analysis excluding women born preterm (born at least one month before due delivery date). Adjustments for dietary factors such as daily energy and alcohol intakes in 1993 were examined on the subpopulation for which dietary data was available, after exclusion of subjects with extreme energy intakes (in the 1st or 99th percentile for the ratio between total energy intake and energy requirement).

All statistical tests were two-sided, and *p*-values below 0.05 were considered statistically significant. All analyses were performed with the Statistical Analyses Systems (SAS) version 9.4 (SAS Institute, Cary, NC).

RESULTS

Silhouettes and trajectories

As shown in Figure 1, whereas silhouette 1 was the most frequently reported silhouette at age 8 (57.5%), silhouette 2 was

Table 2. Associations between body sizes categories and survival after breast cancer in the E3N cohort study

	OS			Breast cancer-specific survival			Invasive disease-free survival		
	Events[1]	HR[4]	95% CI	Events[2]	HR	95% CI	Events[3]	HR	95% CI
Body size at age 8									
1	366	1.00	(ref)	246	1.00	(ref)	719	1.00	(ref)
2	111	0.86	(0.70–1.07)	83	0.89	(0.69–1.15)	228	0.88	(0.76–1.03)
3	68	0.90	(0.69–1.17)	51	0.98	(0.72–1.33)	138	0.85	(0.70–1.02)
≥4	57	1.06	(0.79–1.41)	42	1.12	(0.79–1.58)	112	0.87	(0.71–1.07)
p-trend			0.74			0.80			0.04
Body size at puberty									
1	163	1.00	(ref)	108	1.00	(ref)	315	1.00	(ref)
2	208	0.95	(0.77–1.17)	144	0.95	(0.73–1.22)	411	0.95	(0.82–1.10)
3	126	0.96	(0.76–1.22)	97	1.10	(0.83–1.46)	264	0.89	(0.75–1.05)
≥4	105	0.98	(0.76–1.26)	73	0.96	(0.70–1.31)	207	0.84	(0.70–1.01)
p-trend			0.86			0.90			0.04
Body size at age 20–25									
1	70	1.00	(ref)	44	1.00	(ref)	128	1.00	(ref)
2	269	0.97	(0.74–1.27)	193	1.10	(0.78–1.53)	533	1.06	(0.88–1.29)
3	167	0.88	(0.66–1.17)	124	0.98	(0.69–1.40)	366	1.01	(0.82–1.24)
≥4	96	1.16	(0.84–1.60)	61	1.11	(0.74–1.67)	170	1.05	(0.82–1.33)
p-trend			0.64			0.98			0.93
Body size at age 35–40									
1–2	189	1.00	(ref)	126	1.00	(ref)	387	1.00	(ref)
3	253	0.94	(0.77–1.14)	189	0.98	(0.77–1.24)	506	0.95	(0.83–1.09)
4	113	1.01	(0.78–1.31)	78	0.95	(0.70–1.31)	217	0.98	(0.81–1.18)
≥5	47	0.85	(0.58–1.24)	29	0.66	(0.41–1.06)	87	0.90	(0.69–1.19)
p-trend			0.62			0.20			0.56

Abbreviations: HR: hazard ratio; CI: confidence interval.
[1]Deaths (all causes).
[2]Deaths from breast cancer.
[3]Second cancer event or death from any cause.
[4]Model is adjusted for birth weight (low/medium/large/missing) and height (small/medium/large/missing), age at diagnosis (continuous), SBR grade of the tumor (1/2/3/missing), ERs status (positive/negative/missing), PRs status (positive/negative/missing),TNM stage (I/II/III), histological subtype (ductal/lobular/mixed/other) age at menarche (continuous), number of children and age at first full-term pregnancy (no child/one child before age 30/one child after age 30/>1 child, first before age 30/>1 child, first after age 30), breastfeeding (<6 months/>6 months/no breast-feeding), use of oral contraceptive (ever/never), menopausal status at diagnosis, age at menopause and ever use of MHT (menopausal after age 50 not using MHT/menopausal after age 50 using MHT/menopausal before age 50 not using MHT/menopausal before age 50 using MHT/premeno-pausal/missing), family history of breast cancer (no/in first degree relatives only/in 1rst and second degree relatives), high blood pressure before diagnosis (yes/no), smoking status before diagnosis (current/past/never), education level (undergraduate/0–2 years postgraduation/3–4 years post-graduation/≥ 5 years postgraduation), marital status before diagnosis (single/couple), prediagnosis BMI (continuous) and stratified on year of diagnosis (1990–1994/1995–1999/2000–2004/2005–2008).

the most frequent at puberty (33.9%) and 20–25 (44.0%) and silhouette 3 was the most frequent at 35–40 (42.8%). Figure 2 shows the four identified trajectories of body size evolution. The model with two trajectories following linear trends (T1, T2) and two trajectories following cubic trends (T3, T4) showed the best fit to data. The first trajectory (T1) can be described as a continuous increase in body size over time, especially between ages 20–25 and 35–40, and was named "moderate increase". The second trajectory (T2 is characterized by a stable body size from childhood until age 35–40 ("stable/low increase"). The third trajectory (T3) is characterized by a strong increase in body size at puberty ("increase at puberty"). The fourth trajectory (T4) described a constantly high body size ("constantly high"). Percentages of women following the T1, T2, T3 and T4 trajectories were 21.4; 29.6, 35.8 and 13.2%, respectively, and posterior group membership probabilities were 0.84, 0.93, 0.94 and 0.90, respectively.

Population characteristics

Among the 4,662 women included in the analyses, 602 women died before the end of follow up (422 deaths from

Table 3. Associations between trajectories of body size evolution and survival after breast cancer in the E3N cohort study

	OS			Breast cancer-specific survival			Invasive disease-free survival		
	Events[1]	HR[4]	95% CI	Events[2]	HR	95% CI	Events[3]	HR	95% CI
Trajectories									
T2 "Stable/low increase"	149	1.00	(ref)	115	1.00	(ref)	317	1.00	(ref)
T1 "Moderate increase"	145	1.27	(1.01–1.60)	101	1.19	(0.91–1.57)	285	1.25	(1.06–1.47)
T3 "Increase at puberty"	220	1.16	(0.94–1.43)	145	1.00	(0.78–1.28)	427	1.13	(0.97–1.31)
T4 "Constantly high"	88	1.32	(1.00–1.74)	61	1.16	(0.84–1.61)	168	1.17	(0.96–1.42)

Abbreviations: HR: hazard ratio; CI: confidence interval.
[1]Deaths (all causes).
[2]Deaths from breast cancer.
[3]Second cancer event or death from any cause.
[4]Model is adjusted for age at diagnosis (continuous), SBR grade of the tumor (1/2/3/missing), ERs status (positive/negative/missing), PRs status (positive/negative/missing),TNM stage (I/II/III), histological subtype (ductal/lobular/mixed/other) age at menarche (continuous), number of children and age at first full-term pregnancy (no child/one child before age 30/one child after age 30/>1 child, first before age 30/>1 child, first after age 30), breastfeeding (<6 months/>6 months/no breastfeeding), use of oral contraceptive (ever/never), menopausal status at diagnosis, age at menopause and ever use of MHT (menopausal after age 50 not using MHT/menopausal after age 50 using MHT/menopausal before age 50 not using MHT/menopausal before age 50 using MHT/premenopausal/missing), family history of breast cancer (no/in first degree relatives only/in first and second degree relatives), high blood pressure before diagnosis (yes/no), smoking status before diagnosis (current/past/never), education level (undergraduate/0–2 years postgraduation/3–4 years postgraduation/≥ 5 years postgraduation), marital status before diagnosis (single/couple), prediagnosis BMI (continuous) and stratified on year of diagnosis (1990–1994/1995–1999/2000–2004/2005–2008).

breast cancer). The number of second invasive cancer events was 1,185 (434 metastases, 394 loco-regional recurrences, 198 sec primary cancers, 6 uncertain whether primary tumor or metastatic disease and 153 unclassified cancer event without any pathological report). Mean follow up for the overall population was 11.1 years for OS and BCSS and 9.2 years for iDFS.

As shown in Table 1, tumor characteristics did not materially differ across trajectories, except for the "stable/low increase" (T2) and the "constantly high" (T4) trajectories, among which ductal subtype was more frequent. Prediagnosis BMI was the highest for women with the "constantly high" trajectory and the lowest for women with the "moderate increase" trajectory.

Survival analysis

Silhouettes were not associated with survival, except for a borderline significant inverse association between risk of second invasive cancer event and silhouette at puberty (HR silh. ≥4 *vs.* silh. 1 = 0.84; 95% CI = 0.70–1.01; p-trend = 0.04; Table 2).

Compared with the "stable/low increase" trajectory (T2), women in the "moderate increase" trajectory (T1) were at increased risk of death from any cause (HR T1 *vs.* T2 = 1.27; 95% CI = 1.01–1.60) and of second invasive cancer event (HR T1 *vs.* T2 = 1.25; 95% CI = 1.06–1.47; Table 3). The "constantly high" trajectory (T4) was also associated with an increased risk of death from any cause (HR T4 *vs.* T2 = 1.32; 95% CI = 1.00–1.74), but not with iDFS (HR T4 *vs.* T2 = 1.17; 95% CI = 0.96–1.42). No trajectory was associated with BCSS.

No interaction was detected with menopausal status, hormone receptor status, prediagnostic BMI or age at menarche (Table 4, all p-interaction > 0.14).

In stratified analyses, statistically significant associations between T4 and OS were confined to premenopausal women and women older than 13 years at menarche. T1 was significantly associated with OS in ER + PR+ and women with BMI >25 kg/m^2 and with iDFS in premenopausal and postmenopausal women, in ER + PR+ cases, in women with BMI lower than 25 kg/m^2 and older than 13 years at menarche.

Excluding women who were born prematurely ($n = 158$) did not change the results. Including only women with daily alcohol and overall energy intake available ($N = 3741$) and adjusting for these two factors did not change materially change the findings.

DISCUSSION

In this population of breast cancer survivors, an increase in body size during adult life was associated with an increased risk of death from any cause and of second invasive cancer event, compared with women whose body size remained stable until age 35–40. A constantly large body size was also associated with an increased risk of second invasive cancer event.

To our knowledge, no study examined the association between body size during childhood and survival after breast cancer. One study on 166 breast cancer patients examined BMI at age 16 and showed no association with BCSS.[15]

Although no previous study has explored the association between body size trajectories and breast cancer survival, our results are consistent with some of the previous reports that investigated adult weight gain. In a meta-analysis (14), two[16,17] out of three[16–18] studies reported an increased risk of death from any cause in women with the highest weight gain between age 20–30 and diagnosis, compared with women with stable weight and two[16,17] out of four[16,17,19,20] studies

Table 4. Associations between trajectories survival by menopausal and hormone receptor status, prediagnostic BMI and age at menarche

	N	OS					Invasive disease-free survival				
		T2	T1	T3	T4		T2	T1	T3	T4	
		"Stable/ low increase"	"Moderate increase"	"Increase at puberty"	"Constantly high"		"/Stable/ low increase"	"Moderate increase"	"Increase at puberty"	"Constantly high"	
		Events[1]/ BC cases	Events[1]/ BC cases	Events[1]/ BC cases	Events[1]/ BC cases	*p-int.*	Events[2]/ BC cases	Events[2]/ BC cases	Events[2]/ BC cases	Events[2]/ BC cases	*p-int.*
Premenopausal	931					0.54					0.77
		42/297	32/176	55/343	25/115		76/297	95/176	119/343	40/115	
HR (95% CI)		1.00 (ref.)	1.43 (0.88–2.33)	1.28 (0.84–1.93)	1.97 (1.16–3.37)		1.00 (ref.)	1.50 (1.09–2.06)	1.17 (0.88–1.54)	1.26 (0.85–1.87)	
Postmenopausal	3,731										
		107/1,082	113/821	165/1,328	63/500		209/1,082	222/821	308/1,328	128/500	
HR (95% CI)		1.00 (ref.)	1.26 (0.97–1.65)	1.11 (0.87–1.43)	1.20 (0.86–1.66)		1.00 (ref.)	1.21 (1.00–1.47)	1.11 (0.93–1.33)	1.17 (0.94–1.47)	
ER+PR+	2,294					0.34					0.35
		50/677	61/476	84/832	38/309		126/677	118/476	187/832	73/309	
HR (95% CI)		1.00 (ref.)	1.79 (1.22–2.63)	1.27 (0.89–1.82)	1.48 (0.95–2.29)		1.00 (ref.)	1.39 (1.08–1.80)	1.20 (0.96–1.51)	1.21 (0.90–1.63)	
ER-PR-	590										
		39/188	22/126	42/196	16/80		63/188	45/126	65/196	33/80	
HR (95% CI)		1.00 (ref.)	0.71 (0.41–1.23)	0.91 (0.57–1.47)	0.92 (0.49–1.75)		1.00 (ref.)	1.03 (0.69–1.54)	0.99 (0.68–1.43)	1.33 (0.84–2.12)	
BMI <25 kg/m^2	3,349					0.57					0.97
		117/1,048	116/810	146/1,171	43/320		244/1,048	232/810	303/1,171	85/320	
HR (95% CI)		1.00 (ref.)	1.16 (0.89–1.50)	1.06 (0.83–1.35)	1.31 (0.92–1.87)		1.00 (ref.)	1.21 (1.01–1.46)	1.10 (0.93–1.31)	1.19 (0.92–1.52)	
BMI ≥25 kg/m^2	1,313										
		32/331	29/187	74/500	45/295		73/331	53/187	124/500	83/295	
HR (95% CI)		1.00 (ref.)	1.74 (1.03–2.94)	1.51 (0.98–2.32)	1.47 (0.93–2.34)		1.00 (ref.)	1.42 (0.98–2.04)	1.18 (0.87–1.59)	1.15 (0.84–1.59)	
Age at menarche <13 y	2,159					0.16					0.14
		67/670	48/371	100/763	45/355		168/670	96/371	192/763	101/355	
HR (95% CI)		1.00 (ref.)	1.33 (0.91–1.95)	1.30 (0.95–1.78)	1.10 (0.74–1.64)		1.00 (ref.)	1.00 (0.78–1.30)	1.03 (0.83–1.27)	1.08 (0.83–1.40)	

Table 4. Associations between trajectories survival by menopausal and hormone receptor status, prediagnostic BMI and age at menarche (Continued)

	N	OS					Invasive disease-free survival				
		T2	T1	T3	T4		T2	T1	T3	T4	
		"Stable/ low increase"	"Moderate increase"	"Increase at puberty"	"Constantly high"		"/Stable/ low increase"	"Moderate increase"	"Increase at puberty"	"Constantly high"	
		Events[1]/ BC cases	Events[1]/ BC cases	Events[1]/ BC cases	Events[1]/ BC cases	*p-int.*	Events[2]/ BC cases	Events[2]/ BC cases	Events[2]/ BC cases	Events[2]/ BC cases	*p-int.*
Age at menarche ≥13 y	2,503										
		82/709	97/626	120/908	43/260		149/709	189/626	235/908	67/260	
HR (95% CI)		1.00 (ref.)	1.25 (0.92–1.69)	1.08 (0.81–1.43)	1.62 (1.10–2.38)		1.00 (ref.)	1.49 (1.20–1.86)	1.28 (1.04–1.57)	1.29 (0.96–1.73)	

Abbreviations: BC: breast cancer; HR, hazard ratio; CI, confidence interval.
[1]Deaths (all causes).
[2]Second cancer event or death from any cause.
*Model is adjusted for birth weight (low/medium/large/missing) and height (small/medium/large/missing) (except for trajectories), age at diagnosis (continuous), SBR grade of the tumor (1/2/3/missing), ERs status (positive/negative/missing), PRs status (positive/negative/missing), TNM stage (I/II/III), histological subtype (ductal/lobular/mixed/other) age at menarche (continuous), number of children and age at first full-term pregnancy (no child/one child before age 30/one child after age 30/>1 child, first before age 30/>1 child, first after age 30), breastfeeding (<6 months/>6 months/no breastfeeding), use of oral contraceptive (ever/never), menopausal status at diagnosis, age at menopause and ever use of MHT (menopausal after age 50 not using MHT/menopausal after age 50 using MHT/menopausal before age 50 not using MHT/menopausal before age 50 using MHT/premenopausal/missing), family history of breast cancer (no/in first degree relatives only/in first and second degree relatives), high blood pressure before diagnosis (yes/no), smoking status before diagnosis (current/past/never), education level (undergraduate/0–2 years postgraduation/3–4 years postgraduation/≥ 5 years postgraduation), marital status before diagnosis (single/couple), prediagnosis BMI (continuous) and stratified on year of diagnosis z(1990–1994/1995–1999/2000–2004/2005–2008). Models stratified for each factor are not adjusted for this factor.

reported an association between such weight gain and risk of death from breast cancer. Moreover, adult weight gain (>17 kg) has also been associated with an increased risk of second primary breast cancer.[29] We similarly reported that the "moderate increase" trajectory, which corresponds to the greatest change in body size during adulthood (between ages 20–25 and 35–40), was associated with an increased risk of death from any cause and second invasive cancer event. Additionally, women in the "constantly high" trajectory (T4) were at increased risk of death from any cause, while large body size during adulthood was not associated with survival, suggesting that long-term excess adiposity might be as deleterious as adult weight gain and that duration of excess adiposity should be accounted for, as recently suggested also by studies on breast cancer risk.[30]

Previous studies that examined the association between weight gain from age 18–20 to 1 year before diagnosis[16,18] or usual adult weight[20] and breast cancer survival by menopausal status and did not report any heterogeneity. However, one study[16] that was able to distinguish between premenopausal and postmenopausal weight gain showed that only postmenopausal weight gain was associated with an increased all-cause and breast cancer-specific mortality. In our study, women were aged 40–65 years old in 1990. This 25 years age range when silhouettes representing body size were assessed for the last time prevented us from evaluating postmenopausal body size trajectories.

Only one study on weight gain and survival investigated the heterogeneity by hormone receptor status and reported no difference in the associations.[16] In our study, associations between trajectories and survival tended to be stronger among ER + PR+ tumors, the most frequent subtype in our population. This could suggest a specific role of steroid hormones, however this difference might also result from a lack of statistical power in the ER-PR- subgroup ($N = 590$, 119 deaths).

One study[20] did not report any difference according to adult BMI in the association between adult weight gain and BCSS, consistently with what we observed for iDFS. Despite the absence of any interaction, our results suggest however that the association between body size trajectories and OS could be driven or increased by overweight status, with stronger estimates in overweight women.

The associations between the "moderate increase" in body size and "constantly high" trajectories and lower breast cancer survival may be related to the systemic inflammation associated with weight gain[31] and excess adiposity.[32] Indeed, together with pathways involving growth factors and insulin resistance, inflammation was previously related to poor survival outcomes.[33]

Strengths of this work include detailed information on breast cancer characteristics and available data regarding factors likely to influence the evolution of body size over the life course, such as birth size and weight.[34,35] Furthermore, all data were collected prospectively among a large number of breast cancer survivors, with long-term follow-up. However, several limitations must be acknowledged. First, the silhouette scale that was used to assess body size is not an objective measure of adiposity. A validation study within the E3N cohort[36] showed that women with the leanest silhouette tended to overestimate their body size, while women with the largest silhouette tended to underestimate their body size, which is a common issue with self-declared data.[37] However, such a classification bias would only attenuate the risk estimates. In addition, because adults are unlikely to precisely recall their body weight during childhood, silhouettes were shown to be a useful tool for lifelong approaches.[38] Few women reported silhouettes corresponding to the highest levels of adiposity. Yet, our results suggest that body size trajectories might influence survival even at relatively low levels of adiposity. Thus, we expect the observed associations to be stronger in populations with more obese women and a wider range of silhouette variations. Another limitation is that, as the E3N cohort was not originally designed to study survival, some information on tumor characteristics and treatments were incomplete or missing. However, all our analyses were stratified by periods of diagnosis to account for the evolution of cancer treatments and evaluation of prognostic and predictive factors over the 18 years of the study period.

This work shows, for the first time, the importance for women of maintaining a healthy weight over the life course not only because weight gain influences risk of cancer and other chronic diseases, but also because maintaining a healthy weight might, once the disease has occurred, improve breast cancer survival. Although these results need to be confirmed, this work sheds light on the need to combine lifelong approach to current BMI, with a focus on key periods of the women reproductive life (puberty, menopause) and duration of excess adiposity, to better identify breast cancer survivors who are at higher risk of recurrence or second primary cancer, or of death.

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References

1. Ferlay J, Soerjomataram I, Dikshit R, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int J Cancer* 2015;136:E359–E86.
2. Coleman MP, Quaresma M, Berrino F, et al. Cancer survival in five continents: a worldwide population-based study (CONCORD). *Lancet Oncol* 2008;9:730–56.
3. Chan DS, Vieira AR, Aune D, et al. Body mass index and survival in women with breast cancer-systematic literature review and meta-analysis of 82 follow-up studies. *Ann Oncol* 2014;25:1901–14.

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4. Weiderpass E, Braaten T, Magnusson C, et al. A prospective study of body size in different periods of life and risk of premenopausal breast cancer. *Cancer Epidemiol Biomarkers Prev* 2004;13:1121–7.
5. Ahlgren M, Melbye M, Wohlfahrt J, et al. Growth patterns and the risk of breast cancer in women. *N Engl J Med* 2004;351:1619–26.
6. Baer HJ, Tworoger SS, Hankinson SE, et al. Body fatness at young ages and risk of breast cancer throughout life. *Am J Epidemiol* 2010;171:1183–94.
7. Fuemmeler BF, Pendzich MK, Tercyak KP. Weight, dietary behavior, and physical activity in childhood and adolescence: implications for adult cancer risk. *Obes Facts* 2009;2:179–86.
8. Bardia A, Vachon CM, Olson JE, et al. Relative weight at age 12 and risk of postmenopausal breast cancer. *Cancer Epidemiol Biomarkers Prev* 2008;17:374–8.
9. Fagherazzi G, Guillas G, Boutron-Ruault MC, et al. Body shape throughout life and the risk for breast cancer at adulthood in the French E3N cohort. *Eur J Cancer Prev* 2013;22:29–37.
10. Berkey CS, Frazier AL, Gardner JD, et al. Adolescence and breast carcinoma risk. *Cancer* 1999;85: 2400–9.
11. Le Marchand L, Kolonel LN, Earle ME, et al. Body size at different periods of life and breast cancer risk. *Am J Epidemiol* 1988;128:137–52.
12. Hilakivi-Clarke L, Forsen T, Eriksson JG, et al. Tallness and overweight during childhood have opposing effects on breast cancer risk. *Br J Cancer* 2001;85:1680–4.
13. World Cancer Research Fund/American Institute for Cancer Research. Continuous Update Project Report. Food, Nutrition, Physical Activity, and the Prevention of Breast Cancer. Washington DC: AICR, 2010.
14. World Cancer Research Fund/American Institute for Cancer Research. Continuous Update Project Report: Systematic review on diet, nutrition, physical activity and survival and second cancers in breast cancer survivors. Washington DC: AICR, 2014.
15. Kumar NB, Cantor A, Allen K, et al. Android obesity at diagnosis and breast carcinoma survival: Evaluation of the effects of anthropometric variables at diagnosis, including body composition and body fat distribution and weight gain during life span, and survival from breast carcinoma. *Cancer* 2000;88:2751–7.
16. Cleveland RJ, Eng SM, Abrahamson PE, et al. Weight gain prior to diagnosis and survival from breast cancer. *Cancer Epidemiol Biomarkers Prev* 2007;16:1803–11.
17. Dal Maso L, Zucchetto A, Talamini R, et al. Effect of obesity and other lifestyle factors on mortality in women with breast cancer. *Int J Cancer* 2008;123:2188–94.
18. Bernstein JL, Lapinski R, Lynch C, et al. Factors influencing mortality among young women with second primary breast carcinoma. *Cancer* 2002; 95:2051–8.
19. Enger SM, Bernstein L. Exercise activity, body size and premenopausal breast cancer survival. *Br J Cancer* 2004;90:2138–41.
20. Whiteman MK, Hillis SD, Curtis KM, et al. Body mass and mortality after breast cancer diagnosis. *Cancer. Epidemiol Biomarkers Prev* 2005;14:2009–14.
21. Clavel-Chapelon F. Cohort profile: the French E3N Cohort Study. *Int J Epidemiol* 2015;44:801–9.
22. His M, Fagherazzi G, Mesrine S, et al. Pre-diagnostic body size and breast cancer survival in the E3N cohort study. *Int J Cancer* 2016;139:1053–64.
23. Gourgou-Bourgade S, Cameron D, Poortmans P, et al. Guidelines for time-to-event endpoint definitions in Breast cancer trials: Results of the DATECAN initiative (Definition for the Assessment of Time-to-event Endpoints in CANcer trials). *Ann Oncol* 2015;26:873–9.
24. Hudis CA, Barlow WE, Costantino JP, et al. Proposal for standardized definitions for efficacy end points in adjuvant breast cancer trials: the STEEP system. *J Clin Oncol* 2007;25:2127–32.
25. Sørensen TI, Stunkard AJ, Teasdale TW, et al. The accuracy of reports of weight: children's recall of their parents' weights 15 years earlier. *Int J Obes* 1983; 7:115–22.
26. Jones B, Nagin DS. Advances in group-based trajectory modeling and an SAS procedure for estimating them. *Stat Methods Res* 2007;35:542–71.
27. Nagin DS. Analyzing developmental trajectories: a semiparametric, group-based approach. *Psychol Methods* 1999;4:139–57.
28. Andruff H, Carraro N, Thompson A, et al. Latent class growth modelling: a tutorial. *Tutor Quant Methods Psychol* 2009;5:11–24.
29. Trentham-Dietz A, Newcomb PA, Nichols HB, et al. Breast cancer risk factors and second primary malignancies among women with breast cancer. *Breast Cancer Res Treat* 2007;105:195–207.
30. Arnold M, Jiang L, Stefanick ML, et al. Duration of adulthood overweight, obesity, and cancer risk in the women's health initiative: a longitudinal study from the United States. *PLoS Med.* 2016;13: e1002081.
31. Fogarty AW, Glancy C, Jones S, et al. A prospective study of weight change and systemic inflammation over 9 y. *Am J Clin Nutr* 2008;87: 30–5.
32. Renehan AG, Zwahlen M, Egger M. Adiposity and cancer risk: new mechanistic insights from epidemiology. *Nat Rev Cancer* 2015;15: 484–98.
33. Jiralerspong S, Goodwin PJ. Obesity and breast cancer prognosis: evidence, challenges, and opportunities. *J Clin Oncol* 2016;34:4203–16.
34. Rogers I. The influence of birthweight and intrauterine environment on adiposity and fat distribution in later life. *Int J Obes Relat Metab Disord* 2003;27:755–77.
35. Schellong K, Schulz S, Harder T, et al. Birth weight and long-term overweight risk: systematic review and a meta-analysis including 643,902 persons from 66 studies and 26 countries globally. *PLoS One* 2012;7:e47776.
36. Tehard B, van Liere MJ, Com NC, et al. Anthropometric measurements and body silhouette of women: validity and perception. *J Am Diet Assoc* 2002;102:1779–84.
37. Krul AJ, Daanen HA, Choi H. Self-reported and measured weight, height and body mass index (BMI) in Italy, the Netherlands and North America. *Eur J Public Health* 2011;21:414–9.
38. Must A, Willett WC, Dietz WH. Remote recall of childhood height, weight, and body build by elderly subjects. *Am J Epidemiol* 1993;138:56–64.