Childhood size and life course weight characteristics in association with the risk of incident type 2 diabetes

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Objective: To determine how childhood overweight, in conjunction with other life course weight characteristics, relates to the development of type 2 diabetes in adulthood.

Research Design and Methods: Among 109,172 women in the Nurses’ Health Study II, body fatness at ages 5, 10, and 20 years was assessed by recall using 9-level pictorial diagrams (somatotypes) representing extreme thinness (category “1”) to obesity (category “9”). Recalled weight at age 18 years and adulthood were used to derive BMI. Self-reported type 2 diabetes cases were confirmed by supplementary questionnaire.

Results: Somatotypes at ages 5 and 10 years were positively associated with diabetes risk (p-trends <0.0001). The adjusted relative risks (RR) of women with somatotype ≥“6” (versus “2”) at age 5 years was 2.19 (95% CI: 1.79-2.67) and at age 10 years was 2.57 (2.20-3.01). Increases in size by somatotype or by weight gain since age 18 were associated with increased risk. Compared to women who were never overweight at any age, women who were overweight as an adult (BMI >25) but not previously had an adjusted RR of 8.23 (7.41-9.15). The adjusted RR was 15.10 (13.21-17.26) for women who were also overweight at age 10 (somatotype ≥“5”) and 18 (BMI >25). Increased childhood size was not associated with risk among women who did not continue to be overweight in adulthood.

Conclusions: Increased body size starting from childhood is associated with a greater risk of diabetes in adulthood. However, women who become lean in adulthood do not have an increased risk.
Large proportions of children in the US are currently at risk for or are overweight. Immediate and long term health problems have arisen due to childhood overweight, including poor lipid profile, earlier onset of type 2 diabetes, and other metabolic syndrome traits.(1) Although the rise in prevalence of type 2 diabetes in the pediatric population is cause for concern in itself, the risk as they continue into adulthood will undoubtedly be a greater public health burden.

Despite strong ties between the development of insulin resistance from increased adiposity via multiple biological mechanisms, few studies have looked at the long-term consequences of childhood overweight and the risk of type 2 diabetes in adulthood with inconsistent findings.(2-8) One study using birth and medical records data from Finland, found that BMI at ages 7-11 years in women were significantly and positively associated with future risk of diabetes.(4) However, the study did not investigate the roles of adolescent and adulthood obesity in this association and the number of cases was small (N=187).(4) By contrast, a more recent study that accounted for life-course weight, found that thinness, rather than overweight, from childhood through young adulthood was associated with increased diabetes risk.(8) However, these findings were from an older cohort (born 1925-1950) of French women, with a large percentage extremely lean in childhood and whose early nutritional status might have been affected by World War II (1939-1945). Thus, the objective of this study was to determine the longitudinal association between childhood overweight in combination with other life-course weight characteristics and the risk for type 2 diabetes in a more recent birth cohort of young women.

RESEARCH DESIGN AND METHODS

Study Population - The Nurses’ Health Study II (NHSII) is an ongoing prospective study of US female nurses aged 25 to 42 years. Follow-up is conducted using biennial questionnaires from 1989 to 2005. 109,172 participants remained after exclusion for diagnosis of any type of diabetes, cancer, or cardiovascular disease at baseline (2%), or missing information on childhood body shape (2.5%), BMI at age 18 years (0.7%), or baseline BMI (0.3%). This study was approved by the institutional review board of the Partners Health Care System (Boston, Massachusetts).

Assessment of Childhood Size and Weight Characteristics - At baseline, body fatness at ages 5, 10 and 20 years of age was assessed by recall of somatotypes, or 9-level pictorial diagrams developed by Stunkard et al(9) representing sizes ranging from extreme thinness (category “1”) to obesity (category “9”). The use of recalled somatotypes have been validated in both older(10) and younger(11) women by comparison with childhood records. Somatotypes at ages 5, 10, and 20 years correlated moderately with recorded BMI (r=0.60, 0.65, and 0.66, respectively).(10) The validity did not differ by adult BMI at the time of report.(10) Overweight was defined as somatotype ≥“5.”(12)

Weight at age 18 and adult height and weight were self-reported. Weight change was the difference between weight at age 18 years and weight at baseline in 1989. The correlation between recalled weight at age 18 and documented weight from college or nursing school records was 0.84, and the correlation between self-reported and technician measured adult weight was 0.96.(13)

Type 2 Diabetes Ascertainment - A supplementary questionnaire was mailed to confirm the self-report of diabetes diagnosis
and to distinguish different types of diabetes.(14) The National Diabetes Data Group diagnostic criteria was used for cases reported through 1997 and required confirmation of at least one the following: 1) one or more symptoms (weight loss, hunger, thirst, polyuria) and elevated glucose (fasting ≥ 7.8mmol/l [140 mg/dl], random plasma or 2 h glucose ≥ 11.1 mmol/l [200 mg/dl]), 2) no symptoms but occurrence of elevated plasma glucose as described above on at least two different occasions, or 3) use of insulin or oral hypoglycemic medication.(15) For cases occurring after 1998, the cutoff of fasting plasma glucose was changed to 7.0 mmol/l [126mg/dl] in accordance with revised criteria.(16) We excluded women classified as having only gestational or type 1 diabetes. In the Nurses’ Health Study, the supplemental questionnaire was highly reliable regarding diabetes diagnosis.(14) In a random sample of 84 women classified as being a case, medical records were available for 62 of these women and an endocrinologist confirmed the diagnosis in 61 women (98%).(14)

Assessment of Covariates- Age was calculated as months from the reported birth date to date of questionnaire return. Race, smoking status, birth weight, prematurity, multiple gestation birth, age of menarche, being breastfed, alcohol consumption, and family history of diabetes were self-reported at baseline or in 1991. Parity and age at first birth were measured biennially. Physical activity, in metabolic equivalent (MET) units, was derived from the average time spent in certain activities (e.g. jogging, running) in 1989, 1991, 1997, and 2001.

Statistical Analysis - Differences in participant characteristics by childhood somatotype at age 10 years were compared using chi-square or linear regression. Person-years were calculated based on date of return to date of diagnosis, death, or 1 July 2005, whichever came first. Multivariate Cox proportional hazard models were used to estimate the relative risk (RR) for the associations of somatotypes at ages 5, 10, and 20 years and BMI at age 18 years with type 2 diabetes risk. Somatotypes were categorized by “1” to “6”. We used category “2” as the reference due to most women having reported this category at both ages 5 and 10 years. We collapsed the uppermost categories due to few women reporting those categories.

In one multivariate model, estimates were adjusted for age (continuous), race (African American, Hispanic, Asian vs. White), parity (0, 1-2, 3+) in combination with age at first birth (>24 years), family history of diabetes (maternal, paternal, both), smoking (current, past, vs. never), and physical activity (quintiles). In a second model among participants not missing birth weight information (n=87,349, cases=2,771), estimates were adjusted for characteristics influencing childhood size including age, race, family history of diabetes, birth weight (<5.5, 5.5-6.9, 7.0-8.4, 8.5-9.9, ≥10 lbs), prematurity or multiple gestation birth status of the woman (yes/no), and age of menarche (<12, 12, 13, 14, >14 years). To test for significant trends, linear models were fitted using the median values of each category of exposure (e.g. 17.0, 19.0, 21.0, 23.5, 28.0, and 35.0 for BMI at age 18 years).

The difference in somatotype categories (between ages 5 and 10 and between ages 10 and 20) or in weight (between age 18 years and baseline), were used to assess whether change in size was associated with diabetes development. Models were additionally adjusted for starting size (e.g. adjustment for age 5 somatotype in evaluating the difference between ages 5 and 10), since where a woman began in size may reflect weight gain/loss (i.e. heavier women have the possibility to lose more weight).

The cumulative effect of overweight across the life course prior to reported diabetes was evaluated using the combination of somatotype ≥“5” at age 10, BMI ≥25 kg/m² at age 18 and BMI ≥25 kg/m² at baseline (i.e.
to represent adulthood). The reference group comprised women who reported no overweight at any of those time points. Analyses were performed using SAS, version 8.2 (SAS Institute, Cary, NC).

RESULTS

There were 3,307 incident cases of type 2 diabetes over 16 years of follow-up, for an incidence rate of 197 cases per 100,000 person-years. Table 1 shows the characteristics for all women and by reported childhood somatotype at age 10 years categorized from “1” to “6+”. Women with somatotype of “1” at age 10 years were more likely of minority race, have birth weight <5.5 lbs, were born premature, and had a later age at menarche; whereas women with somatotype ≥ “6” were more likely to have birth weight >10 lbs, to actively smoke, were nulliparous, and had positive parental history of diabetes. Similar associations for “1” and “6+” were found at age 5 years. Somatotypes at ages 5, 10, and 20 years were associated with each other. Of the women reporting somatotype ≥ “6” at age 10 years, 41% reported somatotype ≥ “6” at age 5 years, and 28% at age 20 years. Weight and BMI were also positively associated with somatotype; a 1-2 kg/m² increase in adolescent or adult BMI was observed per increase in somatotype category.

Somatotypes at ages 5, 10 and 20 years and BMI at age 18 years (Table 2) were all significantly and positively associated with diabetes risk (all p-trends <0.0001). Compared to having a somatotype of “2,” RR of diabetes associated with a somatotype ≥ “6” at age 5 was 2.19 (95% CI: 1.79-2.67), at age 10 years was 2.57 (95% CI: 2.20-3.01), and at age 20 years was 5.67 (95% CI: 4.92-6.54). The risk among women who reported a BMI at age 18 >30 kg/m² was 8.72 (95% CI: 7.58-10.02) compared to women with BMI of 18-19 kg/m². Among a subgroup not missing birth weight information (n=87,175), adjusting for childhood factors including birth weight, did not substantially change these estimates.

Type 2 diabetes risk slightly increased among women who reported increases in size whether by somatotype between ages 5 and 10 and between ages 10 and 20 or by weight gain since age 18 (Table 3). Compared to women reporting no change in somatotype, one or more unit increases in somatotype at these ages were associated with approximately twice the risk whereas decreases in somatotype at these ages were associated with reduced risk. These associations were strengthened after adjusting for earlier somatotype. Weight gain since age 18, which is the difference between baseline weight and weight at age 18, was also significantly associated with risk of diabetes. Compared with women who had little change in weight (i.e. ±4.9 lbs), even a weight gain of 5-8 lbs doubled risks; while weight gain of >25 lbs increased risk by over twenty times. Weight loss was associated with increased risk until after adjusting for BMI at age 18 to account for greater weight loss being associated with larger adolescent body size. In analyses stratified by BMI at age 18 years, weight loss of 10 pounds or more was significantly associated with a reduced risk of diabetes among women who were overweight (RR 0.45, 95% CI: 0.22-0.91) or obese (RR 0.45, 95% CI: 0.28-0.72) in adolescence but not among those who were lean (RR 1.72, 95% CI: 0.76-3.90).

The prevalences of overweight by somatotype ≥ “5” at ages 5, 10, and 20 years were 7%, 12%, and 11%, respectively. Most of the cases (83%) in the cohort occurred among women who were overweight (BMI≥25) at baseline with an incidence rate of 562 per 100,000 person-years. Among these women, the prevalences of overweight by somatotype ≥ “5” were 12%, 21%, and 23%, respectively.
To evaluate the cumulative effect of being overweight across the life course, women were jointly categorized as being overweight using somatotype at age 10, BMI at age 18 years and BMI at baseline (with mean age of 34 years) (Figure 1). Women who were overweight only as an adult (BMI >25) had an adjusted RR of 8.23 (95% CI: 7.41-9.15) compared to women who were never overweight at any age. The adjusted RR increased to 15.10 (95% CI: 13.21-17.26) for women who were also overweight at age 10 (somatotype ≥“5”) and age 18 (BMI >25). However, women who were overweight at age 10 but came off of the trajectory and became lean in adulthood (i.e. not being overweight in adulthood) did not have a significantly increased risk of diabetes (RR of 1.02, 95% CI: 0.74-1.40).

CONCLUSIONS
Among 109,172 women followed over 16 years, somatotypes at ages 5 and 10 years were positively associated with the risk of incident type 2 diabetes after adjusting for major risk factors. However, women who were overweight at age 10 but were lean in adulthood did not have an increased risk of diabetes associated with childhood overweight, underscoring the importance of continued efforts to control adiposity among overweight children.

Limited studies have investigated the long-term consequences of childhood overweight and the risk of type 2 diabetes in adulthood, with inferences hindered by small number of cases and/or lack of differentiation of diabetes type.(2-8) In addition, some studies included cases of young age at onset (<30 years old). (3,5,7) One study using data based on records (185 cases) found that the cumulative incidence of diabetes was doubled (4.2% to 8.4%) among women in the largest BMI group at age 11 years (>17.4 kg/m²) compared to those in the smallest (≤15.3 kg/m²). (4) We found a similar increase in risk using recalled somatotypes. By contrast, a study of older French women using recalled body shape, found an association between childhood thinness and diabetes risk.(8) However, this birth cohort vastly differed from the NHSII as demonstrated by over 60% of their cases having reported extreme leanness (somatotype “1”) at age 8 years; possibly due to their nutritional status having been affected by World War II. (8) Thus, our findings among a more recent birth cohort may be more relevant.

In addition to absolute size, longitudinal changes through different ages are also relevant to the risk of diabetes.(17,18) Under normal development, infants lose weight after 6 months of age and continue doing so until ~ 5 years of age when their adiposity rebounds.(18) Although we were unable to assess age at adiposity rebound, earlier rebound has been associated with increased risk of type 2 diabetes(17) and there is some suggestion that age at rebound matters more than the absolute size of the child at any point in time because it corresponds to weight gain. Our findings of increased risk associated with increases in somatotype and weight gain support the importance of change in size in addition to absolute size. These findings offer support for continued weight reduction efforts across the life span.

Moreover, in analyses of the cumulative effect of overweight through childhood, adolescence, and adulthood, the risk for type 2 diabetes was greatest among women reporting overweight by all three measures, even though the difference was marginal when compared to adolescent overweight. However, women who became lean in adulthood did not have an increased risk of diabetes associated with childhood overweight. Similar observations have been made from other studies of youth overweight and type 2 diabetes or related traits, with findings becoming non-significant after
accounting for adult BMI.(6,19,20) Tracking of metabolic risk factors (e.g. HDL, triglycerides) has also been observed after 21 years of follow-up from childhood,(21) supporting that cumulative overweight is linked with prolonged exposure to metabolic irregularities, putting children on the path to beta cell dysfunction earlier. It should be noted that although there is tracking of overweight to obesity from childhood to adulthood, the trajectory is not fixed from youth.(18,22) It has been shown that about 10-30% of overweight children do not go on to be overweight as adults with conflicting evidence as to whether there is greater tracking in girls compared to boys.(22) Conversely, the majority of adults who are overweight were not in childhood(22) as confirmed here with only 12-20% of the overweight women reporting childhood overweight.

Our study had some limitations. Though experts have recommended BMI for the measurement of childhood size,(18,23) we used recalled somatotype. Misclassification of childhood size is inevitable. However, two previous studies have shown that the accuracy of recall between childhood somatotypes and recorded childhood BMI did not differ by adult BMI.(10,11) The misclassification of childhood size is thus more likely to be nondifferential, which cannot explain the observed positive association between childhood size and type 2 diabetes risk. In addition, our findings were in agreement with other studies which used childhood measures of weight and height.(4,20) Generalizability of our findings may be limited to Caucasian women who were over 95% of our study population. More research is needed in minority populations who have higher rates of overweight and diabetes.(1,24) Lastly, we cannot rule out the possibility of residual confounding by unmeasured confounders due to the observational nature of the study.

As for strengths, NHSII included a large number of women (>3000 cases) and adjusted for many risk factors. Follow-up for previous studies required re-contacting participants in adulthood with low to moderate success rates (20-60%),(5,7,19,20) whereas we evaluated somatotypes at baseline and >90% of the women remained for follow-up.

In conclusion, our findings demonstrate that the importance of childhood overweight stems largely from adult overweight. Women who do not continue to be overweight in adulthood do not have increased risks. It remains important then to promote lifestyle changes from youth so that the adverse trajectory could be avoided. Multiple interventions that childhood overweight can be addressed have been suggested(23), but these remain to be fully tested.

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Table 1. Characteristics of Nurses’ Health Study II participants (n=109,172) by somatotype at age 10 years

| Characteristic (1989) | Total | “1”  | “2”  | “3”  | “4”  | “5”  | “6+” |
|----------------------|-------|------|------|------|------|------|------|
| Women, %             | 100   | 18.9 | 30.7 | 22.5 | 15.8 | 9.0  | 3.1  |
| Age, years           | 34.31 (5) | 34.67 (5) | 34.02 (5) | 34.14 (5) | 34.36 (5) | 34.67 (5) | 34.79 (5) |
| White, %             | 95.2  | 92.0 | 95.0 | 96.4 | 96.7 | 96.7 | 95.6 |
| Birth weight <5.5 lbs, %* | 7.9  | 10.2 | 7.8  | 7.1  | 6.9  | 7.4  | 7.2  |
| Birth weight >10 lbs, %* | 1.3  | 0.9  | 0.9  | 1.3  | 1.5  | 1.9  | 3.1  |
| Premature, %*        | 6.5   | 7.1  | 6.4  | 6.2  | 6.3  | 6.5  | 6.4  |
| Multiple gestation, %* | 1.4  | 1.5  | 1.5  | 1.3  | 1.2  | 0.9  | 0.7  |
| Breastfed, %*        | 34.0  | 33.0 | 34.2 | 35.5 | 33.4 | 33.1 | 31.9 |
| Menarche at age 12 years, %* | 30.2 | 27.1 | 29.8 | 32.5 | 31.4 | 30.7 | 29.6 |
| Menarche at age ≥15 years, %* | 7.6  | 12.1 | 8.7  | 5.7  | 4.7  | 4.6  | 4.9  |
| Nulliparous, %       | 30.4  | 29.6 | 29.3 | 29.3 | 31.5 | 34.4 | 37.9 |
| Age at first birth >24 yrs, % | 41.0 | 40.5 | 42.1 | 42.3 | 40.6 | 37.3 | 34.7 |
| Parental history of diabetes, % | 15.2 | 15.0 | 13.6 | 14.4 | 16.6 | 18.7 | 22.1 |
| Active Smoker, %      | 13.4  | 13.4 | 11.6 | 12.4 | 14.4 | 17.8 | 20.8 |
| Non-drinker, %        | 35.0  | 33.4 | 34.5 | 36.0 | 35.9 | 35.3 | 36.2 |
| Physical Activity, METs/wk | 24.91 (37) | 26.27 (40) | 25.01 (37) | 24.25 (36) | 24.09 (34) | 24.43 (35) | 25.96 (41) |
| Somatotype ≥“6” @5 years, % | 1.6  | 0.1  | 0.1  | 0.1  | 0.4  | 2.3  | 41.0 |
| Somatotype ≥“6” @20 years, % | 3.3  | 0.3  | 0.5  | 1.5  | 4.4  | 13.9 | 27.7 |
| BMI at age 18, kg/m²  | 21.25 (3) | 19.33 (2) | 20.18 (2) | 21.55 (3) | 22.84 (3) | 23.85 (4) | 25.57 (6) |
| Adult weight, kg      | 65.37 (14) | 59.90 (10) | 61.80 (11) | 66.34 (14) | 70.75 (17) | 73.24 (18) | 76.49 (19) |
| Adult height, m       | 1.65 (0.07) | 1.65 (0.07) | 1.65 (0.07) | 1.65 (0.07) | 1.65 (0.07) | 1.65 (0.07) | 1.66 (0.07) |
| Adult BMI, kg/m²      | 24.05 (5) | 22.02 (3) | 22.75 (4) | 24.48 (5) | 26.05 (6) | 26.88 (6) | 27.86 (7) |
| Weight change since age 18, kg | 7.61 (11) | 7.31 (8) | 6.94 (9) | 7.92 (11) | 8.74 (13) | 8.26 (14) | 6.30 (16) |

*Reported in 1991 questionnaire (rather than at baseline in 1989 for all other covariates)
Mean (SD) presented unless indicated. Abbreviation: METs/wk, metabolic equivalents per week
Table 2. Childhood and adolescent size and relative risk (95% CI) of type 2 diabetes in adulthood in the Nurses’ Health Study (n=109,172)

| Age 5 Somatotype | PY   | cases | age-adjusted | model 2* | model 3† |
|------------------|------|-------|--------------|----------|----------|
| 1                | 417996 | 756   | 1.13 (1.02-1.25) | 1.05 (0.95-1.16) | 1.01 (0.90-1.13) |
| 2                | 533990 | 807   | 1.00         | 1.00     | 1.00     |
| 3                | 396742 | 774   | 1.28 (1.15-1.41) | 1.25 (1.14-1.38) | 1.20 (1.08-1.34) |
| 4                | 212080 | 568   | 1.72 (1.54-1.91) | 1.65 (1.48-1.84) | 1.63 (1.45-1.84) |
| 5                | 88885  | 289   | 2.04 (1.78-2.33) | 1.85 (1.62-2.12) | 1.80 (1.55-2.09) |
| 6+               | 26619  | 113   | 2.61 (2.14-3.18) | 2.19 (1.79-2.67) | 2.00 (1.59-2.51) |

| p-trend < .0001 | p-trend < .0001 | p-trend < .0001 |
|-----------------|-----------------|-----------------|

| Age 10 Somatotype | PY   | cases | age-adjusted | model 2* | model 3† |
|-------------------|------|-------|--------------|----------|----------|
| 1                 | 317663 | 441   | 1.04 (0.92-1.17) | 0.98 (0.87-1.11) | 0.96 (0.83-1.10) |
| 2                 | 516959 | 649   | 1.00         | 1.00     | 1.00     |
| 3                 | 377995 | 716   | 1.50 (1.35-1.67) | 1.49 (1.34-1.66) | 1.49 (1.32-1.67) |
| 4                 | 262795 | 765   | 2.27 (2.05-2.52) | 2.17 (1.95-2.41) | 2.15 (1.92-2.42) |
| 5                 | 149808 | 525   | 2.68 (2.39-3.01) | 2.45 (2.18-2.75) | 2.52 (2.21-2.86) |
| 6+                | 51091  | 211   | 3.09 (2.64-3.61) | 2.57 (2.20-3.01) | 2.41 (2.02-2.88) |

| p-trend < .0001 | p-trend < .0001 | p-trend < .0001 |
|-----------------|-----------------|-----------------|

| Age 20 Somatotype | PY   | cases | age-adjusted | model 2* | model 3† |
|-------------------|------|-------|--------------|----------|----------|
| 1                 | 75871 | 83    | 0.97 (0.77-1.23) | 0.91 (0.72-1.15) | 0.96 (0.73-1.25) |
| 2                 | 443762 | 443   | 1.00         | 1.00     | 1.00     |
| 3                 | 633117 | 928   | 1.54 (1.37-1.72) | 1.52 (1.36-1.70) | 1.55 (1.36-1.76) |
| 4                 | 346718 | 924   | 2.83 (2.53-3.17) | 2.71 (2.42-3.04) | 2.78 (2.44-3.16) |
| 5                 | 122949 | 564   | 4.85 (4.28-5.49) | 4.42 (3.90-5.01) | 4.79 (4.16-5.51) |
| 6+                | 53897  | 365   | 7.24 (6.30-8.32) | 5.67 (4.92-6.54) | 6.17 (5.26-7.23) |

| p-trend < .0001 | p-trend < .0001 | p-trend < .0001 |
|-----------------|-----------------|-----------------|

| BMI @ 18 | PY   | cases | age-adjusted | model 2* | model 3† |
|----------|------|-------|--------------|----------|----------|
| <18      | 158206 | 164   | 1.13 (0.94-1.35) | 1.06 (0.88-1.26) | 1.06 (0.86-1.30) |
| 18-<19   | 507641 | 458   | 1.00         | 1.00     | 1.00     |
| 20-<22   | 530083 | 727   | 1.52 (1.35-1.71) | 1.49 (1.32-1.67) | 1.51 (1.32-1.72) |
| 22-<25   | 312876 | 848   | 3.02 (2.69-3.38) | 2.79 (2.49-3.13) | 2.86 (2.51-3.25) |
| 25-<30   | 127826 | 721   | 6.32 (5.62-7.11) | 5.32 (4.72-5.99) | 6.10 (5.35-6.97) |
| 30+      | 39682  | 389   | 11.55 (10.08-13.23) | 8.72 (7.58-10.02) | 9.26 (7.92-10.82) |

| p-trend < .0001 | p-trend < .0001 | p-trend < .0001 |
|-----------------|-----------------|-----------------|

Abbreviations: CI, confidence interval; PY, person-years
Childhood size & adulthood diabetes risk

*Model 2 adjusted for age, race, smoking status, parental history of diabetes, parity, age at first birth, and adult physical activity
†Model 3 adjusted for age, race, parental history of diabetes, birth weight, multiple birth, prematurity, age of menarche (n=87,175, cases=2,681 in subgroup not missing birth weight information)

Table 3. Changes in size and relative risk (95% CI) of type 2 diabetes in Nurses’ Health Study II (n=109,172)

| Age 5 to 10 | PY cases | age-adjusted | model 2* | model 2 + age 5 size† |
|-------------|---------|--------------|----------|----------------------|
| decrease    | 19572   | 0.93 (0.65-1.35) | 0.95 (0.65-1.37) | 0.63 (0.43-0.91) |
| no change   | 1235621 | 1.00          | 1.00     | 1.00                 |
| +1          | 310086  | 2.00 (1.85-2.16) | 1.86 (1.72-2.01) | 1.89 (1.75-2.05) |
| ≥2          | 111033  | 2.16 (1.93-2.41) | 1.95 (1.75-2.18) | 2.19 (1.95-2.45) |

| Age 10 to 20 | PY cases | age-adjusted | model 2* | model 2 + age 10 size† |
|--------------|---------|--------------|----------|------------------------|
| decrease     | 109956  | 1.04 (0.89-1.21) | 1.00 (0.86-1.17) | 0.53 (0.45-0.62) |
| no change    | 758071  | 1.00          | 1.00     | 1.00                   |
| +1           | 621736  | 1.27 (1.18-1.37) | 1.22 (1.12-1.31) | 1.86 (1.71-2.02) |
| ≥2           | 186550  | 1.89 (1.70-2.08) | 1.72 (1.55-1.90) | 2.87 (2.58-3.20) |

| Weight change since age 18 | PY cases | age-adjusted | model 2* | model 2 + BMI @18† |
|---------------------------|---------|--------------|----------|-------------------|
| Loss ≥10 lbs              | 31322   | 5.44 (4.11-7.20) | 4.48 (3.38-5.94) | 1.26 (0.93-1.71) |
| Loss 5-<10 lbs            | 58170   | 2.02 (1.45-2.82) | 1.84 (1.32-2.56) | 1.17 (0.84-1.63) |
| No change (+/- 5 lbs)     | 714230  | 1.00 (ref)    | 1.00 (ref) | 1.00 (ref)        |
| Gain 5-<8 lbs             | 226283  | 2.05 (1.69-2.49) | 1.99 (1.64-2.42) | 2.10 (1.73-2.55) |
| Gain 8-<11 lbs            | 182828  | 3.24 (2.70-3.88) | 3.05 (2.54-3.66) | 3.10 (2.58-3.72) |
| Gain 11-<15 lbs           | 177159  | 6.54 (5.60-7.65) | 5.99 (5.12-7.00) | 5.78 (4.94-6.77) |
| Gain 15-<20 lbs           | 114008  | 10.92 (9.36-12.74) | 9.67 (8.28-11.30) | 8.74 (7.48-10.20) |
| Gain 20-<25 lbs           | 76539   | 15.72 (13.46-18.36) | 13.42 (11.48-15.70) | 11.11 (9.49-13.00) |
| Gain ≥25 lbs              | 95774   | 32.28 (28.11-37.06) | 27.13 (23.57-31.23) | 20.41 (17.70-23.52) |

Abbreviation: PY person-years
*Model 2 adjusted for age, race, smoking status, parental history of diabetes, parity, age at first birth, and adult physical activity
† Model 2 variables with additional adjustment for earlier size; i.e. somatotype at age 5 and 10 years and BMI at age 18 years
Figure legends

Figure 1: Adjusted relative risks (95% confidence intervals) of type 2 diabetes by somatotype ≥ “5” at age 10, BMI ≥ 25 at age 18 years and BMI ≥ 25 at baseline (average age of 34 years), after adjusting for age, race, smoking status, parental history of diabetes, parity, age at first birth, and physical activity. Number of type 2 diabetes cases for each category: 503 for “none”, 50 for “10yrs”, 21 for “18 yrs”, 10 for “10&18yrs”, 1469 for “34yrs”, 260 for “10&34yrs”, 664 for “18&34yrs”, and 441 for “all ages.”