**Main Tables and Figures**

**Figure 1: Flowchart of study population**

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**Table 1: Baseline characteristics of the study sample (n=47,913)**

|  |  |
| --- | --- |
| **Characteristic** |  |
| Age (median, interquartile range) | 55.4 (48.9, 62.1) |
| Race/ethnicity |  |
| Non-Hispanic White | 39,947 (83.4%) |
| Non-Hispanic Black | 4,304 (9.0%) |
| Hispanic | 2,416 (5.0%) |
| Non-Hispanic all other races | 1,231 (2.6%) |
| Unknown | 15 (<0.1%) |
| BMI |  |
| <25.0 | 18,331 (38.3%) |
| 25.0-29.9 | 15,205 (31.7%) |
| 30.0+ | 14,361 (30.0%) |
| Unknown | 16 (<0.1%) |
| Benign thyroid disease | 10,308 (21.5%) |
| Personal educational level |  |
| High school, GED, or less | 7,290 (15.2%) |
| Some college or associate or technical degree | 16,161 (33.7%) |
| Bachelor’s degree or more | 24,450 (51.0%) |
| Unknown | 12 (<0.1%) |
| Annual household income |  |
| <$50000 | 12,228 (25.5%) |
| $50000-$99999 | 19,552 (40.8%) |
| $100000+ | 16,133 (33.7%) |

GED: General Educational Development

**Table 2: Association between childhood and adolescent factors and differentiated thyroid cancer incidence in the Sister Study cohort**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Characteristic** |  | **Multivariable models** | | | |
| **Total cohort, N (%)** | **DTC cases, N** | **Person-years** | **HR***1* | **95% CI***1* |
| **Growth and reproductive factors** |  |  |  |  |  |
| Weight at age 10 vs. peers |  |  |  |  |  |
| Lighter | 16,793 (35.0%) | 80 | 203,318 | 1.03 | 0.77, 1.38 |
| Same weight | 22,324 (46.6%) | 105 | 271,626 | 1 | — |
| Heavier | 8,644 (18.0%) | 52 | 106,503 | 1.25 | 0.90, 1.75 |
| Unknown2 | 152 (0.3%) | 2 | 1,688 | — | — |
| Height at age 10 vs. peers |  |  |  |  |  |
| Shorter | 12,285 (25.6%) | 53 | 150,199 | 0.94 | 0.68, 1.32 |
| Same height | 21,984 (45.9%) | 99 | 266,794 | 1 | — |
| Taller | 13,556 (28.3%) | 87 | 165,201 | 1.41 | 1.06, 1.89 |
| Unknown2 | 88 (0.2%) | 0 | 941 | — | — |
| Teenage weight vs. peers |  |  |  |  |  |
| Lighter | 16,658 (34.8%) | 90 | 201,757 | 1.28 | 0.96, 1.71 |
| Same weight | 22,461 (46.9%) | 97 | 273,839 | 1 | — |
| Heavier | 8,735 (18.2%) | 52 | 106,906 | 1.37 | 0.97, 1.91 |
| Unknown2 | 59 (0.1%) | 0 | 634 | — | — |
| Age reached full adult height (continuous) | 47,742 | 239 | 581,202 | 0.98 | 0.94, 1.03 |
| Age at breast development |  |  |  |  |  |
| Less than 11 years of age | 6,352 (13.3%) | 32 | 76,904 | 1.04 | 0.71, 1.52 |
| 11-13 years of age | 32,749 (68.4%) | 160 | 399,844 | 1 | — |
| 14 years of age or more | 8,233 (17.2%) | 44 | 99,796 | 1.11 | 0.79, 1.55 |
| Unknown2 | 579 (1.2%) | 3 | 6,591 | — | — |
| Age at breast development (continuous) | 47,334 | 236 | 576,545 | 1.01 | 0.93, 1.09 |
| Age at menarche |  |  |  |  |  |
| Less than 12 years of age | 9,735 (20.3%) | 55 | 117,128 | 1.16 | 0.85, 1.59 |
| 12-14 years of age | 26,875 (56.1%) | 134 | 328,470 | 1 | — |
| 14 years of age or more | 11,246 (23.5%) | 50 | 136,821 | 0.89 | 0.64, 1.23 |
| Unknown2 | 57 (0.1%) | 0 | 716 | — | — |
| Age at menarche (continuous) | 47,856 | 239 | 582,419 | 0.97 | 0.89, 1.06 |
| Start age for hormonal birth control |  |  |  |  |  |
| Never used birth control | 6,947 (14.5%) | 43 | 82,008 | 1 | — |
| Started before 20 years of age | 20,864 (43.5%) | 105 | 256,147 | 0.72 | 0.50, 1.05 |
| Started at 20 years of age or older | 19,099 (39.9%) | 87 | 232,996 | 0.69 | 0.48, 1.00 |
| Unknown birth control status2 | 1,003 (2.1%) | 4 | 11,984 | — | — |
| **Lifestyle factors** |  |  |  |  |  |
| Physical activity before age 20 (MET hours/week) |  |  |  |  |  |
| Less than 21 MET-hours/week | 41,526 (86.7%) | 209 | 506,471 | 1 | — |
| 21-<42 MET-hours/week | 3,964 (8.3%) | 22 | 47,968 | 1.09 | 0.70, 1.69 |
| 42 MET-hours/week or more | 2,100 (4.4%) | 5 | 25,155 | 0.47 | 0.19, 1.14 |
| Unknown2 | 323 (0.7%) | 3 | 3,542 | — | — |
| Physical activity before age 20 (MET hours/week) | 47,590 | 236 | 579,593 | 0.99 | 0.98, 1.00 |
| Age started drinking regularly |  |  |  |  |  |
| Never drinker | 1,849 (3.9%) | 10 | 21,453 | 1 | — |
| Before 20 years of age | 32,905 (68.7%) | 173 | 404,665 | 0.9 | 0.47, 1.72 |
| 20 years of age or older | 13,128 (27.4%) | 56 | 156,659 | 0.8 | 0.41, 1.58 |
| Unknown2 | 31 (0.1%) | 0 | 359 | — | — |
| Alcohol consumption under 20 (drinks/year) |  |  |  |  |  |
| 0 drink/year | 15,136 (31.6%) | 66 | 179,860 | 1 | — |
| Less than 60 drinks/year | 14,083 (29.4%) | 74 | 174,500 | 1.11 | 0.79, 1.55 |
| 60-229 drinks/year | 8,983 (18.7%) | 38 | 111,049 | 0.86 | 0.57, 1.30 |
| 230 drinks/year or more | 5,269 (11.0%) | 33 | 64,920 | 1.25 | 0.80, 1.93 |
| Unknown2 | 4,442 (9.3%) | 28 | 52,806 | — | — |
| Age started smoking |  |  |  |  |  |
| Never smoked before baseline | 27,105 (56.6%) | 131 | 335,087 | 1 | — |
| Before 20 years of age | 15,874 (33.1%) | 83 | 189,859 | 1.13 | 0.86, 1.50 |
| Started before 20, 5 pack-years or less | 14,852 (31.0%) | 78 | 177,875 | 1.14 | 0.86, 1.51 |
| Started before 20, more than 5 pack-years | 914 (1.9%) | 5 | 10,802 | 1.17 | 0.48, 2.87 |
| 20 years of age or older | 4,915 (10.3%) | 25 | 57,971 | 1.16 | 0.76, 1.79 |
| Unknown smoking status | 19 (0.0%) | 0 | 218 | — | — |
| Total years of secondhand smoking under 18 |  |  |  |  |  |
| No secondhand smoking during childhood | 13,867 (28.9%) | 72 | 169,783 | 1 | — |
| 10 years or less | 6,258 (13.1%) | 30 | 76,550 | 0.94 | 0.61, 1.44 |
| More than 10 years | 26,919 (56.2%) | 133 | 326,740 | 0.99 | 0.74, 1.32 |
| Unknown2 | 869 (1.8%) | 4 | 10,061 | — | — |
| **Socioeconomic factors** |  |  |  |  |  |
| Family income while growing up |  |  |  |  |  |
| Well off | 3,066 (6.4%) | 13 | 37,935 | 0.78 | 0.44, 1.37 |
| Middle income | 28,582 (59.7%) | 152 | 351,548 | 1 | — |
| Low income | 12,350 (25.8%) | 56 | 148,793 | 0.91 | 0.67, 1.24 |
| Poor | 3,799 (7.9%) | 17 | 43,676 | 0.96 | 0.58, 1.61 |
| Unknown2 | 116 (0.2%) | 1 | 1,183 | — | — |
| Ever not having enough to eat during childhood |  |  |  |  |  |
| No | 43,388 (90.6%) | 206 | 531,069 | 1 | — |
| Yes | 4,492 (9.4%) | 33 | 51,706 | 1.67 | 1.15, 2.43 |
| Unknown2 | 33 (0.1%) | 0 | 361 | — | — |
| Highest household education level at age 13 |  |  |  |  |  |
| Highschool or GED or less | 25,729 (53.7%) | 134 | 307,924 | 1 | — |
| Some college or associate or technical degree | 8,889 (18.6%) | 45 | 109,360 | 0.93 | 0.66, 1.30 |
| Bachelor's degree or higher | 12,736 (26.6%) | 56 | 159,924 | 0.75 | 0.55, 1.03 |
| Unknown2 | 559 (1.2%) | 4 | 5,928 | — | — |
| Household composition at age 13 |  |  |  |  |  |
| Two parents | 42,700 (89.1%) | 220 | 522,033 | 1 | — |
| Single parent | 4,669 (9.7%) | 15 | 54,984 | 0.68 | 0.40, 1.15 |
| Unknown2 | 544 (1.1%) | 4 | 6,118 | — | — |
| Childhood residence |  |  |  |  |  |
| Urban, suburban, small town | 36,184 (75.5%) | 180 | 442,597 | 1 | — |
| Rural areas | 11,024 (23.0%) | 57 | 132,358 | 1.07 | 0.79, 1.44 |
| Unknown2 | 705 (1.5%) | 2 | 8,180 | — | — |
| HR = Hazard Ratio, CI = Confidence Interval |  |  |  |  |  |
| *1* Multivariable models used attained age as the timescale and were adjusted for race/ethnicity | | | | | |
| *2* Results for “Unknown” categories are not shown | | | | | |

**Table 3: Mutually adjusted associations between differentiated thyroid cancer risk factors**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Characteristic** | **DTC cases, N** | **Model 1** | | **Model 2** | |
| **HR** | **95% CI** | **HR** | **95% CI** |
| Height at age 10 vs. peers |  |  |  |  |  |
| Shorter | 53 | 0.9 | 0.64, 1.26 | 0.9 | 0.64, 1.26 |
| Same height | 99 | 1 | — | 1 | — |
| Taller | 87 | 1.39 | 1.04, 1.86 | 1.39 | 1.04, 1.85 |
| Unknown | 0 | — | — | — | — |
| Teenage weight vs. peers |  |  |  |  |  |
| Lighter | 90 | 1.29 | 0.96, 1.72 | 1.29 | 0.97, 1.74 |
| Same weight | 97 | 1 | — | 1 | — |
| Heavier | 52 | 1.3 | 0.93, 1.83 | 1.31 | 0.93, 1.83 |
| Unknown | 0 | — | — | — | — |
| Ever not having enough to eat during childhood |  |  |  |  |  |
| No | 206 | 1 | — | 1 | — |
| Yes | 33 | 1.58 | 1.08, 2.31 | 1.92 | 1.26, 2.90 |
| Unknown | 0 | — | — | — | — |
| Highest household educational level at age 13 |  |  |  |  |  |
| Highschool or GED or less | 134 | 1 | — | 1 | — |
| Some college or associate or technical degree | 45 | 0.94 | 0.67, 1.32 | 0.9 | 0.64, 1.27 |
| Bachelor's degree or higher | 56 | 0.77 | 0.56, 1.07 | 0.72 | 0.51, 1.01 |
| Unknown | 4 | 1.8 | 0.66, 4.88 | 1.72 | 0.62, 4.77 |
| HR = Hazard Ratio, CI = Confidence Interval |  |  |  |  |  |
| Model 1 was simultaneously adjusted for attained age (timescale), self-identified race/ethnicity, height at age 10 vs. peers, and teenage weight vs. peers, ever not having enough to eat during childhood, and highest household educational level at age 13. Model 2 was simultaneously adjusted for all covariates of model 1 and family income while growing up, household composition at age 13, and childhood residence | | | | | |

## Figure 2: The joint associations of teenage weight vs. peers and baseline BMI with differentiated thyroid cancer incidence

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**Supplementary materials**

## Supplementary Figure 1: Association between height at age 10 vs peers, teenage weight vs peers, ever not having enough to eat during childhood, and highest household education level at age 13 and thyroid cancer incidence in the Sister Study participants stratified according to potential modifying factors

Chart

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## Supplementary table 1: The joint associations of teenage weight vs. peers and baseline BMI with differentiated thyroid cancer incidence

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Baseline BMI** | **Teenage weight vs. peers** | **Number of events** | **HR***1* | **95% CI***1* |
| <25 | Lighter | 54 | 2.7 | 1.61, 4.50 |
|  | Same weight | 20 | 1 | — |
|  | Heavier | 9 | 2.34 | 1.06, 5.13 |
| 25.0-29.9 | Lighter | 27 | 2.5 | 1.40, 4.47 |
|  | Same weight | 36 | 2.12 | 1.23, 3.67 |
|  | Heavier | 11 | 1.89 | 0.91, 3.95 |
| 30.0+ | Lighter | 9 | 1.55 | 0.70, 3.41 |
|  | Same weight | 41 | 3 | 1.75, 5.12 |
|  | Heavier | 32 | 3.13 | 1.79, 5.48 |
| 1HR = Hazard Ratio, CI = Confidence Interval  Multivariable models were adjusted for attained age (timescale), and self-identified race/ethnicity | | | | |

## Supplementary table 2: The joint associations of weight at age 10 vs. peers and baseline BMI with differentiated thyroid cancer incidence

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Baseline BMI** | **Weight at age 10 vs. peers** | **Number of events** | **HR***1* | **95% CI***1* |
| <25 | Lighter | 49 | 2.04 | 1.25, 3.32 |
|  | Same weight | 24 | 1 | — |
|  | Heavier | 9 | 1.51 | 0.70, 3.25 |
| 25.0-29.9 | Lighter | 21 | 1.52 | 0.84, 2.73 |
|  | Same weight | 36 | 1.80 | 1.07, 3.02 |
|  | Heavier | 16 | 2.14 | 1.14, 4.04 |
| 30.0+ | Lighter | 10 | 1.29 | 0.62, 2.71 |
|  | Same weight | 45 | 2.53 | 1.54, 4.16 |
|  | Heavier | 27 | 2.45 | 1.41, 4.25 |
| 1HR = Hazard Ratio, CI = Confidence Interval  Multivariable models were adjusted for attained age (timescale), and self-identified race/ethnicity | | | | |

**Supplementary table 3: Association between childhood and adolescent factors and differentiated thyroid cancer incidence in the Sister Study participants: sensitivity analyses**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Characteristic** | **Competing risks** | | | **Medically confirmed cases only** | | | **Papillary thyroid cancer only** | | | **Complete case analysis** | | | **E-values** | | |
| **Number of cases** | **HR***1* | **95% CI***1* | **Number of cases** | **HR***1* | **95% CI***1* | **Number of cases** | **HR***1* | **95% CI***1* | **Number of cases** | **HR***1* | **95% CI***1* | **E-values for HR** | **E-values for CI2** | |
| **Maternal pregnancy characteristics** |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |
| Pre-pregnancy or gestational diabetes |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |
| Probably not/Definitely not | 230 | 1 | — | 168 | 1 | — | 157 | 1 | — | 230 | 1 | — |  |  | |
| Definitely/Probably | 5 | 2.53 | 1.05, 6.12 | 5 | 3.3 | 1.35, 8.05 | 5 | 3.56 | 1.46, 8.70 | 5 | 2.38 | 0.98, 5.79 | 4.16 | 1 | |
| Unknown3 | 4 | - | - | 2 | - | - | 2 | - | - | 0 |  |  | - | - | |
| Gestational hypertension or hypertension-related disorders |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |
| Probably not/Definitely not | 199 | 1 | — | 145 | 1 | — | 138 | 1 | — | 199 | 1 | — |  |  | |
| Definitely/Probably | 16 | 1.94 | 1.17, 3.23 | 12 | 2.07 | 1.15, 3.73 | 9 | 1.63 | 0.83, 3.21 | 16 | 2 | 1.20, 3.33 | 3.4 | 1.68 | |
| Unknown3 | 24 | - | - | 18 | - | - | 17 | - | - | 0 |  |  | - | - | |
| **Birth and infancy characteristics** |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |
| Birth weight (g) |  |  |  | 6 | 0.48 | 0.21, 1.09 |  |  |  |  |  |  |  |  | |
| < 2500 | 10 | 0.59 | 0.31, 1.13 | 106 | 1 | — | 5 | 0.42 | 0.17, 1.03 | 10 | 0.6 | 0.32, 1.15 | 2.72 | 1 | |
| Between 2500 and 3999 | 140 | 1 | — | 16 | 1.39 | 0.82, 2.35 | 101 | 1 | — | 140 | 1 | — |  |  | |
| 4000+ | 23 | 1.54 | 0.99, 2.39 | 47 | - | - | 14 | 1.28 | 0.73, 2.24 | 23 | 1.5 | 0.96, 2.33 | 2.36 | 1 | |
| Unknown3 | 66 | - | - | 127 | 1.34 | 0.99, 1.82 | 44 | - | - | 0 |  |  | - | - | |
| Birth weight (per kg, continuous) | 172 | 1.26 | 0.97, 1.63 |  |  |  | 119 | 1.37 | 1.00, 1.87 | 172 | 1.24 | 0.95, 1.60 | 1.78 | 1 | |
| Gestational age at birth |  |  |  | 91 | 1 | — |  |  |  |  |  |  |  |  | |
| Born post-term or less than 2 weeks before due date | 116 | 1 | — | 6 | 0.45 | 0.20, 1.03 | 84 | 1 | — | 116 | 1 | — |  |  | |
| Born at least 2 weeks before due date | 8 | 0.48 | 0.23, 0.98 | 78 | - | - | 5 | 0.41 | 0.17, 1.01 | 8 | 0.48 | 0.23, 0.97 | 3.65 | 1.22 | |
| Unknown3 | 115 | - | - | 168 | 1 | — | 75 | - | - | 0 |  |  | - | - | |
| HR = Hazard Ratio, CI = Confidence Interval. The risk estimates are shown when there were at least 5 cases.  *1* Multivariable models used attained age as the timescale and were adjusted for self-reported race/ethnicity  *2* E-values for the limit of the confidence interval closest to the null  3 Results for “Unknown” categories of are not shown | | | | | | | | | | | | | | |