**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 education 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** |  |  |  |  |  |
| Relative weight to peers at age 10 |  |  |  |  |  |
| 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 relative to peers at age 10 |  |  |  |  |  |
| 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 | — | — |
| Weight relative to peers during teen years |  |  |  |  |  |
| 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 |
| 12-13 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 |
| Age started using 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 | 0.73 | 0.49, 1.07 |
| Started at 20 years of age or older3 | 19,099 (39.9%) | 87 | 232,996 | — | — |
| Unknown birth control status2 | 1,003 (2.1%) | 4 | 11,984 | — | — |
| **Lifestyle factors** |  |  |  |  |  |
| Physical activity between age 5 and 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 between age 5 and 20 (MET-hours/week, continuous) | 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 | 0.88 | 0.46, 1.68 |
| 20 years of age or older3 | 13,128 (27.4%) | 56 | 156,659 | — | — |
| Unknown2 | 31 (0.1%) | 0 | 359 | — | — |
| Number of drinks per year between age 5 and 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 and number of pack-years |  |  |  |  |  |
| Never smoked before baseline | 27,105 (56.6%) | 131 | 335,087 | 1 | — |
| Before 20 years of age | 15,874 (33.1%) | 83 | 189,859 | 1.12 | 0.85, 1.48 |
| Started before 20, 5 pack-years or less | 14,852 (31.0%) | 78 | 177,875 | 1.13 | 0.85, 1.49 |
| 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 older3 | 4,915 (10.3%) | 25 | 57,971 | — | — |
| Unknown smoking status | 19 (0.0%) | 0 | 218 | — | — |
| Total years of secondhand smoking under age 18 from household member |  |  |  |  |  |
| 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 | | | | | |
| *3* Individuals started at 20 years of age or older were excluded from the analyses | | | | | |

**Table 3: Mutually adjusted associations between for selected factors and differentiated thyroid cancer incidence**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Characteristic** | **DTC cases, N** | **Model 1** | | **Model 2** | |
| **HR** | **95% CI** | **HR** | **95% CI** |
| Height relative to peers at age 10 |  |  |  |  |  |
| 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 | — | — | — | — |
| Weight relative to peers during teen years |  |  |  |  |  |
| 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 education 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, relative height vs. peers at age 10, and relative weight vs. peers during teen years, ever not having enough to eat during childhood, and highest household education 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 weight relative to peers during teen years and baseline BMI with differentiated thyroid cancer incidence

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**Supplementary materials**

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

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## Supplementary table 1: The joint associations of weight relative to peers during teen years and baseline BMI with differentiated thyroid cancer incidence

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Baseline BMI** | **Weight relative to peers during teen years** | **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 used attained age as the timescale and were adjusted for race/ethnicity | | | | |

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

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Baseline BMI** | **Weight relative to peers at age 10** | **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 used attained age as the timescale and were adjusted for race/ethnicity | | | | |

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

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Characteristic** | **Early-onset cancers** | | | **Late-onset cancers** | | | **Medically confirmed DTC cases** | | | **Papillary thyroid cancer** | | | **E-values** | |
|  | **Cases** | **HR** | **95% CI** | **Cases** | **HR** | **95% CI** | **Cases** | **HR** | **95% CI** | **Cases** | **HR** | **95% CI** | **E-values for HR** | **E-values for CI1** |
| Height relative to peers at age 10 | | | |  |  |  |  |  |  |  |  |  |  |  |
| Shorter | 9 | 1.18 | 0.50, 2.75 | 36 | 0.89 | 0.60, 1.33 | 43 | 1.05 | 0.72, 1.54 | 41 | 1.1 | 0.74, 1.62 | 1.31 | 1 |
| Same height | 13 | 1 | — | 73 | 1 | — | 72 | 1 | — | 66 | 1 | — |  |  |
| Taller | 17 | 2.05 | 0.99, 4.23 | 51 | 1.15 | 0.80, 1.64 | 60 | 1.34 | 0.95, 1.88 | 57 | 1.38 | 0.97, 1.97 | 2.18 | 1.31 |
| Unknown2 | 0 | — | — | 0 | — | — | 0 | — | — | 0 | — | — |  |  |
| Weight relative to peers during teen years | | |  |  |  |  |  |  |  |  |  |  |  |  |
| Lighter | 14 | 1.17 | 0.57, 2.41 | 61 | 1.36 | 0.95, 1.93 | 71 | 1.52 | 1.08, 2.12 | 67 | 1.56 | 1.10, 2.21 | 1.88 | 1 |
| Same weight | 16 | 1 | — | 63 | 1 | — | 65 | 1 | — | 60 | 1 | — |  |  |
| Heavier | 9 | 1.26 | 0.56, 2.85 | 36 | 1.54 | 1.03, 2.33 | 39 | 1.53 | 1.03, 2.27 | 37 | 1.56 | 1.04, 2.36 | 2.07 | 1 |
| Unknown2 | 0 | — | — | 0 | — | — | 0 | — | — | 0 | — | — |  |  |
| Ever not having enough to eat during childhood | | | |  |  |  |  |  |  |  |  |  |  |  |
| No | 32 | 1 | — | 138 | 1 | — | 155 | 1 | — | 146 | 1 | — |  |  |
| Yes | 7 | 2.05 | 0.87, 4.79 | 22 | 1.69 | 1.07, 2.67 | 20 | 1.36 | 0.85, 2.19 | 18 | 1.32 | 0.80, 2.17 | 2.73 | 1.56 |
| Unknown2 | 0 | — | — | 0 | — | — | 0 | — | — | 0 | — | — |  |  |
| Highest household education level at age 13 | | | |  |  |  |  |  |  |  |  |  |  |  |
| Highschool or GED or less | 21 | 1 | — | 93 | 1 | — | 98 | 1 | — | 92 | 1 | — |  |  |
| Some college or associate or technical degree | 9 | 1.08 | 0.49, 2.39 | 30 | 0.92 | 0.61, 1.40 | 31 | 0.86 | 0.58, 1.30 | 29 | 0.86 | 0.56, 1.30 | 1.38 | 1 |
| Bachelor's degree or higher | 8 | 0.58 | 0.26, 1.28 | 34 | 0.77 | 0.52, 1.14 | 43 | 0.78 | 0.54, 1.13 | 40 | 0.77 | 0.53, 1.12 | 1.99 | 1.22 |
| Unknown2 | 0 | — | — | 3 | — | — | 3 | — | — | 3 | — | — | — | — |
| HR = Hazard Ratio, CI = Confidence Interval. The risk estimates are shown when there were at least 5 cases.  Multivariable models used attained age as the timescale and were adjusted for race/ethnicity  *1* E-values for the limit of the confidence interval closest to the null  2 Results for “Unknown” categories of are not shown | | | | | | | | | | | | | | |