**Main Tables and Figures**

**Figure 1: Flowchart of study population**

**Graphical user interface, text, application, chat or text message

Description automatically generated**

**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 vs. 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 | — | — |
| Relative height vs. 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 | — | — |
| Relative weight vs. 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 |
| 12-14 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 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 | 0.9 | 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 | — | — |
| 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 | 1.13 | 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 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 | | | | | |

**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** |
| Relative height vs. 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 | — | — | — | — |
| Relative weight vs. 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 relative weight vs. peers during teen years and baseline BMI with differentiated thyroid cancer incidence

A picture containing text, antenna

Description automatically generated

**Supplementary materials**

## Supplementary Figure 1: Association between relative height vs peers at age 10, relative weight vs 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

A picture containing graphical user interface

Description automatically generated

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

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Baseline BMI** | **Relative weight vs. 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 were adjusted for attained age (timescale), and self-identified race/ethnicity | | | | |

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

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Baseline BMI** | **Relative weight vs. 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 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** | **Early-onset cancers** | | | **Late-onset cancers** | | | **Competing risks** | | | **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** | **Cases** | **HR** | **95% CI** | **E-values for HR** | **E-values for CI1** |
| Relative height vs. peers at age 10 | | | |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Shorter | 9 | 1.18 | 0.50, 2.75 | 26 | 0.95 | 0.59, 1.52 | 53 | 0.92 | 0.66, 1.29 | 43 | 1.05 | 0.72, 1.54 | 41 | 1.1 | 0.74, 1.62 | 1.31 | 1 |
| Same height | 13 | 1 | — | 50 | 1 | — | 99 | 1 | — | 72 | 1 | — | 66 | 1 | — |  |  |
| Taller | 1ss7 | 2.05 | 0.99, 4.23 | 36 | 1.17 | 0.77, 1.80 | 87 | 1.29 | 0.96, 1.72 | 60 | 1.34 | 0.95, 1.88 | 57 | 1.38 | 0.97, 1.97 | 2.18 | 1.31 |
| Unknown2 | 0 | — | — | 0 | — | — | 0 | — | — | 0 | — | — | 0 | — | — |  |  |
| Relative weight vs. peers during teen years | | |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Lighter | 14 | 1.17 | 0.57, 2.41 | 44 | 1.45 | 0.95, 2.20 | 90 | 1.34 | 1.00, 1.80 | 71 | 1.52 | 1.08, 2.12 | 67 | 1.56 | 1.10, 2.21 | 1.88 | 1 |
| Same weight | 16 | 1 | — | 43 | 1 | — | 97 | 1 | — | 65 | 1 | — | 60 | 1 | — |  |  |
| Heavier | 9 | 1.26 | 0.56, 2.85 | 25 | 1.55 | 0.95, 2.54 | 52 | 1.39 | 0.99, 1.95 | 39 | 1.53 | 1.03, 2.27 | 37 | 1.56 | 1.04, 2.36 | 2.07 | 1 |
| Unknown2 | 0 | — | — | 0 | — | — | 0 | — | — | 0 | — | — | 0 | — | — |  |  |
| Ever not having enough to eat during childhood | | | |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| No | 32 | 1 | — | 99 | 1 | — | 206 | 1 | — | 155 | 1 | — | 146 | 1 | — |  |  |
| Yes | 7 | 2.05 | 0.87, 4.79 | 13 | 1.45 | 0.81, 2.60 | 33 | 1.62 | 1.10, 2.38 | 20 | 1.36 | 0.85, 2.19 | 18 | 1.32 | 0.80, 2.17 | 2.73 | 1.56 |
| Unknown2 | 0 | — | — | 0 | — | — | 0 | — | — | 0 | — | — | 0 | — | — |  |  |
| Highest household education level at age 13 | | | |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Highschool or GED or less | 21 | 1 | — | 64 | 1 | — | 134 | 1 | — | 98 | 1 | — | 92 | 1 | — |  |  |
| Some college or associate or technical degree | 9 | 1.08 | 0.49, 2.39 | 20 | 0.88 | 0.53, 1.45 | 45 | 0.92 | 0.66, 1.29 | 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 | 26 | 0.83 | 0.52, 1.31 | 56 | 0.68 | 0.49, 0.93 | 43 | 0.78 | 0.54, 1.13 | 40 | 0.77 | 0.53, 1.12 | 1.99 | 1.22 |
| Unknown2 | 0 | — | — | 2 | 1.82 | 0.44, 7.47 | 4 | 1.98 | 0.72, 5.41 | 3 | 1.88 | 0.59, 5.95 | 3 | 2.07 | 0.65, 6.57 | 2.95 | 1 |
| 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 self-reported 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 | | | | | | | | | | | | | | | | | |