**Supplementary Online Material**

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Table S1: Hyperthyroidism Read codes

|  |  |
| --- | --- |
| Read code | Read term |
| C02..00 | Thyrotoxicosis |
| C02..11 | Hyperthyroidism |
| F4G2000 | Thyrotoxic exophthalmos |
| C02z100 | Thyrotoxicosis without mention of goitre, cause with crisis |
| C020.12 | Graves' disease |
| 1431.00 | H/O: hyperthyroidism |
| 1431.11 | H/O: thyrotoxicosis |
| C02..12 | Toxic goitre |
| C022.00 | Toxic multinodular goitre |
| C02z.00 | Thyrotoxicosis without mention of goitre or other cause |
| C023.00 | Toxic nodular goitre unspecified |
| C02y300 | Thyroid crisis |
| G557500 | Thyrotoxic heart disease |
| C04z.11 | Pretibial myxoedema - hypothyroid |
| C020.00 | Toxic diffuse goitre |
| 212P.00 | Hyperthyroidism resolved |
| C02zz00 | Thyrotoxicosis NOS |
| C02z000 | Thyrotoxicosis without mention of goitre or cause no crisis |
| C020000 | Toxic diffuse goitre with no crisis |
| C021000 | Toxic uninodular goitre with no crisis |
| 4424100 | Serum T3 level high |
| 66B4.00 | Thyroid eye disease |
| C02yz00 | Thyrotoxicosis of other specified origin NOS |
| C02y.00 | Thyrotoxicosis of other specified origin |
| C020.11 | Basedow's disease |
| C022000 | Toxic multinodular goitre with no crisis |
| F381600 | Myasthenic syndrome due to thyrotoxicosis |
| F395400 | Myopathy due to thyrotoxicosis |
| C020z00 | Toxic diffuse goitre NOS |
| C023z00 | Toxic nodular goitre NOS |
| C024.00 | Thyrotoxicosis from ectopic thyroid nodule |
| C02y000 | Thyrotoxicosis of other specified origin with no crisis |
| C021.00 | Toxic uninodular goitre |
| C022z00 | Toxic multinodular goitre NOS |
| C024z00 | Thyrotoxicosis from ectopic thyroid nodule NOS |
| C020100 | Toxic diffuse goitre with crisis |
| C02y.11 | Factitia thyrotoxicosis |
| C021z00 | Toxic uninodular goitre NOS |
| 9N4T.00 | DNA - Did not attend hyperthyroidism clinic |
| C024000 | Thyrotoxicosis from ectopic thyroid nodule with no crisis |
| C02y200 | Thyrotoxicosis factitia |
| C023000 | Toxic nodular goitre unspecified with no crisis |
| FyuBD00 | [X]Dysthyroid exophthalmos |
| Cyu1300 | [X]Other thyrotoxicosis |
| C023100 | Toxic nodular goitre unspecified with crisis |
| C02y100 | Thyrotoxicosis of other specified origin with crisis |
| C025.00 | Subclinical hyperthyroidism |

Table S2: Characteristics of the full cohort

|  |  |
| --- | --- |
| Characteristic | Pregnancies among women with hyperthyroidism (N=4712 pregnancies)  |
|  |  |
| Maternal age (years) |  |
| <24 | 434 (9.2%) |
| 25-29 | 1001 (21.2%) |
| 30-34 | 1656 (35.1%) |
| 35+ | 1621 (34.4%) |
| median (IQR) | 33 (29-36) |
|  |  |
| Calendar year of pregnancy |  |
| 2000-2002 | 548 (11.6%) |
| 2003-2005 | 840 (17.8%) |
| 2006-2008 | 971 (20.6%) |
| 2009-2011 | 1009 (21.4%) |
| 2012-2014 | 900 (19.1%) |
| 2015-2017 | 444 (9.4%) |
|  |  |
| Pregnancy outcome |  |
| Delivery | 3398 (72.1%) |
| Pregnancy loss | 1314 (27.9%) |
|  |  |
| Multiple pregnancy  | 41 (.9%) |
|  |  |
| Definitive treatment before pregnancy |  |
| Thyroid surgery | 658 (14%) |
| Radioiodine  | 174 (3.7%) |
| Both thyroid surgery and radioiodine | 9 (0.2%) |
|  |  |
| On antithyroid drug treatment at start of pregnancy |  |
| Carbimazole | 361 (7.7%) |
| Propylthiouracil | 264 (5.6%) |
|  |  |
| Antithyroid drug treatment during pregnancy |  |
| Carbimazole only | 302 (6.4%) |
| Propylthiouracil only | 379 (8%) |
| Both drugs at different stages | 156 (3.3%) |
|  |  |
| Index of Multiple Deprivation quintile |  |
| 1 (Least deprived) | 1018 (21.6%) |
| 2 | 811 (17.2%) |
| 3 | 905 (19.2%) |
| 4 | 996 (21.1%) |
| 5 (Most deprived) | 982 (20.8%) |
|  |  |
| Body Mass Index (kg/m2) |  |
| <18.5 Underweight | 155 (3.3%) |
| 18.5-24.9 Normal | 2295 (48.7%) |
| 25-29.9 Overweight | 1169 (24.8%) |
| 30+ Obese | 802 (17%) |
| Missing | 291 (6.2%) |
| median (IQR) | 24 (22-28) |
|  |  |
| Smoking status |  |
| Non-smoker | 2251 (47.8%) |
| Current smoker | 1033 (21.9%) |
| Ex-smoker | 1419 (30.1%) |
| Missing | 9 (.2%) |
|  |  |
| Pre-existing diabetes  | 678 (14.4%) |
|  |  |
| Pre-existing hypertension  | 191 (4.1%) |
|  |  |

Table S3: Characteristics of pregnancies with and without a TSH record

|  |  |  |  |
| --- | --- | --- | --- |
| Characteristic | Pregnancies in the analysis cohort (N=2502)  | Pregnancies excluded from analysis cohort due to no TSH records (N=2210)  | Standardized difference |
|  |  |  |  |
| Treatment status at start of pregnancy |  |  |  |
| Prior definitive treatment | 543 (21.7%) | 289 (13.1%) | 0.45 |
| Taking ATDs | 454 (18.1%) | 161 (7.3%) |  |
| No prior definitive treatment and not taking ATDs | 1505 (60.2%) | 1760 (79.6%) |  |
|  |  |  |  |
| Maternal age (years) |  |  |  |
| <24 | 210 (8.4%) | 224 (10.1%) | 0.05 |
| 25-29 | 549 (21.9%) | 452 (20.5%) |  |
| 30-34 | 919 (36.7%) | 737 (33.3%) |  |
| 35+ | 824 (32.9%) | 797 (36.1%) |  |
| median (IQR) | 33 (29-36) | 33 (29-37) |  |
|  |  |  |  |
| Calendar year of pregnancy |  |  |  |
| 2000-2002 | 209 (8.4%) | 339 (15.3%) | 0.12 |
| 2003-2005 | 462 (18.5%) | 378 (17.1%) |  |
| 2006-2008 | 548 (21.9%) | 423 (19.1%) |  |
| 2009-2011 | 562 (22.5%) | 447 (20.2%) |  |
| 2012-2014 | 480 (19.2%) | 420 (19%) |  |
| 2015-2017 | 241 (9.6%) | 203 (9.2%) |  |
|  |  |  |  |
| Pregnancy outcome |  |  |  |
| Delivery | 2109 (84.3%) | 1289 (58.3%) | 0.60 |
| Pregnancy loss | 393 (15.7%) | 921 (41.7%) |  |
|  |  |  |  |
| Multiple pregnancy  | 25 (1%) | 16 (.7%) | 0.03 |
|  |  |  |  |
| Index of Multiple Deprivation quintile |  |  |  |
| 1 (Least deprived) | 578 (23.1%) | 440 (19.9%) | 0.18 |
| 2 | 457 (18.3%) | 354 (16%) |  |
| 3 | 507 (20.3%) | 398 (18%) |  |
| 4 | 514 (20.5%) | 482 (21.8%) |  |
| 5 (Most deprived) | 446 (17.8%) | 536 (24.3%) |  |
|  |  |  |  |
| Body Mass Index (kg/m2) |  |  |  |
| <18.5 Underweight | 68 (2.7%) | 87 (3.9%) | 0.12 |
| 18.5-24.9 Normal | 1263 (50.5%) | 1032 (46.7%) |  |
| 25-29.9 Overweight | 632 (25.3%) | 537 (24.3%) |  |
| 30+ Obese | 407 (16.3%) | 395 (17.9%) |  |
| Missing | 132 (5.3%) | 159 (7.2%) |  |
| median (IQR) | 24 (22-28) | 24 (22-29) |  |
|  |  |  |  |
| Smoking status |  |  |  |
| Non-smoker | 1229 (49.1%) | 1022 (46.2%) | 0.15 |
| Current smoker | 488 (19.5%) | 545 (24.7%) |  |
| Ex-smoker | 784 (31.3%) | 635 (28.7%) |  |
| Missing | 1 (0%) | 8 (.4%) |  |
|  |  |  |  |
| Pre-existing diabetes  | 393 (15.7%) | 285 (12.9%) | 0.08 |
|  |  |  |  |
| Pre-existing hypertension  | 82 (3.3%) | 109 (4.9%) | 0.08 |

ATD, antithyroid drug

Table S4: Additional adjustment for BMI. Association between treatment status at start of pregnancy and thyroid status during pregnancy among 2370 pregnant women with hyperthyroidism in UK, 2000-2017

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Treatment status at start of pregnancy | Number of pregnancies (column %) | Number with suboptimal thyroid status (row %) | Crude OR (95% CI), p-value | Adjusted OR (95% CI), p-value | Fully adjusted OR (95% CI), p-value |
| Taking antithyroid drugs  | 428 (18.1) | 85 (19.9) | ref | ref | ref |
| Prior definitive treatment | 513 (21.7) | 266 (51.9) | 4.35 (3.19-5.92), p<0.001 | 4.54 (3.35-6.17), p<0.001 | 4.54 (3.35-6.17), p<0.001 |
| No prior definitive treatment and not taking antithyroid drugs | 1429 (60.3) | 314 (22.0) | 1.14 (0.85-1.51), p=0.380 | 1.17 (0.89-1.55), p=0.265 | 1.16 (0.88-1.54), p=0.286 |

Notes: Adjusted and fully adjusted models include maternal age, year of pregnancy start, multiple pregnancy, index of multiple deprivation (IMD), smoking status, pre-existing diabetes, pre-existing hypertension. Fully adjusted model also includes BMI. All models exclude 132 pregnancies with missing BMI.

Table S5: Preconception TSH by treatment status at conception

|  |  |  |
| --- | --- | --- |
| Treatment status at conception  | Pregnancies in the analysis cohort with a TSH record <90 days before conception N (column %) | Number (row %) with TSH >2.5 mU/L before conception |
| Any treatment status | 1013 (100) | 284 (28.0) |
| Taking antithyroid drugs | 283 (27.9) | 47 (16.6) |
| Prior definitive treatment | 208 (20.5) | 94 (45.2) |
| No prior definitive treatment and not taking antithyroid drugs | 522 (51.5) | 143 (27.4) |

Table S6: Suboptimal thyroid status in the first trimester by preconception TSH among pregnancies with prior radioiodine or thyroid surgery

|  |  |  |
| --- | --- | --- |
| Preconception TSH  | Pregnancies with a TSH record in the first trimester and <90 days before conception N (column %) | Number (row %) with suboptimal thyroid status in the first trimester |
| Any preconception TSH  | 158 (100) | 77 (48.7) |
| TSH>2.5 mU/L before conception | 73 (46.2) | 42 (57.5) |
| TSH <=2.5 mU/L before conception | 85 (53.8) | 35 (41.2) |

Table S7: Sensitivity analysis i) restricted to women with both TSH and FT4 records (plus FT4 reference range) in pregnancy. Association between treatment status at start of pregnancy and thyroid status during pregnancy among 1435 pregnant women with hyperthyroidism in UK, 2000-2017

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Treatment status at start of pregnancy | Number of pregnancies (column %) | Number with suboptimal thyroid status (row %) | Crude OR (95% CI), p-value | Adjusted OR (95% CI), p-value |
| Taking antithyroid drugs  | 284 (19.8) | 76 (26.8) | ref | ref |
| Prior definitive treatment | 333 (23.2) | 199 (59.8) | 4.06 (2.83-5.83), p<0.001 | 4.25 (2.97-6.10), p<0.001 |
| No prior definitive treatment and not taking antithyroid drugs | 818 (57.0) | 251 (30.7) | 1.21 (0.88-1.66), p=0.236 | 1.27 (0.93-1.73), p=0.133 |

Notes: Adjusted model includes maternal age, year of pregnancy start, multiple pregnancy, index of multiple deprivation (IMD), smoking status, pre-existing diabetes, pre-existing hypertension.

Table S8: Sensitivity analysis ii) restricted to women eligible for HES linkage. Association between treatment status at start of pregnancy and thyroid status during pregnancy among 1529 pregnant women with hyperthyroidism in UK, 2000-2017

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Treatment status at start of pregnancy | Number of pregnancies (column %) | Number with suboptimal thyroid status (row %) | Crude OR (95% CI), p-value | Adjusted OR (95% CI), p-value |
| Taking antithyroid drugs  | 283 (18.5) | 53 (18.7) | ref | ref |
| Prior definitive treatment | 356 (23.3) | 189 (53.1) | 4.91 (3.32-7.27), p<0.001 | 5.32 (3.61-7.83), p<0.001 |
| No prior definitive treatment and not taking antithyroid drugs | 890 (58.2) | 194 (21.8) | 1.21 (0.84-1.75), p=0.313 | 1.26 (0.88-1.81), p=0.201 |

Notes: Adjusted model includes maternal age, year of pregnancy start, multiple pregnancy, index of multiple deprivation (IMD), smoking status, pre-existing diabetes, pre-existing hypertension.

Table S9: Sensitivity analysis iii) using a lower TSH threshold of 2.5 mU/L to determine thyroid status. Association between treatment status at start of pregnancy and thyroid status during pregnancy among 2502 pregnant women with hyperthyroidism in UK, 2000-2017

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Treatment status at start of pregnancy | Number of pregnancies (column %) | Number with suboptimal thyroid status (row %) | Crude OR (95% CI), p-value | Adjusted OR (95% CI), p-value |
| Any treatment status  | 2502 (100) | 1003 (40.1) |  |  |
| Taking antithyroid drugs  | 454 (18.2) | 129 (28.4) | ref | ref |
| Prior definitive treatment | 543 (21.7) | 365 (67.2) | 5.15 (3.86-6.87), p<0.001 | 5.35 (4.01-7.14), p<0.001 |
| No prior definitive treatment and not taking antithyroid drugs | 1505 (60.1) | 509 (33.8) | 1.28 (1.00-1.64), p=0.045 | 1.30 (1.02-1.65), p=0.034 |

Notes: Adjusted model includes maternal age, year of pregnancy start, multiple pregnancy, index of multiple deprivation (IMD), smoking status, pre-existing diabetes, pre-existing hypertension.