

THE LANCET

Diabetes & Endocrinology

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Thomas N J, Jones S E, Weedon M N, Shields B M, Oram R A, Hattersley A T. Frequency and phenotype of type 1 diabetes in the first six decades of life: a cross-sectional, genetically stratified survival analysis from UK Biobank. *Lancet Diabetes Endocrinol* 2017; published online Nov 30. [http://dx.doi.org/10.1016/S2213-8587\(17\)30362-5](http://dx.doi.org/10.1016/S2213-8587(17)30362-5).

Supplementary

Excluded cases

Subjects with diabetes who were likely to have filled inappropriately the age of diagnosis with the duration of diabetes were excluded. These 92 individuals who were stated to be diagnosed younger than 20 years of age (median age 10) and did not go straight to insulin treatment (78% were still not on insulin therapy). The alternative diagnosis would be childhood or adolescent Type 2 diabetes which was not recognised in children in the UK until 2000 and still is extremely rare in British White subjects²⁵.

Diabetes diagnosed by doctor?

There were four possible options: “yes”, “no”, “do not know” or “prefer not to answer”. 431 individuals who answered “do not know” or “prefer not to answer” were coded as missing.

Did you start insulin within one year of your diagnosis of diabetes?

Individuals were only shown this question if they answered “yes” to the previous question indicating that a doctor had told them they have diabetes. Female individuals who indicated they had diabetes only during pregnancy were not shown this question. The respondents who replied that they did have diabetes were then asked if they started insulin within a year, 93 Individuals who answered “do not know” or “prefer not to answer” were coded as missing.

What was your age when the diabetes was first diagnosed?

If the answer was more than the participants age it was rejected. If participants answered less than 10 they were asked to confirm.

Self-reported diabetes type

If the participant was uncertain of the type of illness they had, then they described it to the interviewer (a trained nurse) who attempted to place it within the coding tree. If the illness could not be located in the coding tree then the interviewer entered a free-text description of it. These free-text descriptions were subsequently examined by a doctor and, where possible, matched to entries in the coding tree. Two individuals were coded as missing who answered “yes” to having both T1D and T2D.

Hospital admission data

Data on hospital episode statistics (HES) for participants resident in England are provided to UK Biobank by the Administrative Data Liaison Service (ADLS). Records date back to 01 April 1997 and contain coded data on admissions, operations and procedures. UK Biobank has kept the data in its original format, according to HES specification. HES use the World Health Organization’s ICD (International Classification of Diseases and Related Health Problems) to record diagnosis information.

Calculating Clinical characteristics

Our group clinical characteristics were calculated as below.

$$\sigma_{AI}^2 = \frac{1}{N_{AI} - 1} ([N_{ALL} - 1]\sigma_{ALL}^2 - N_{AI}\mu_{AI}^2 - [N_{NAI} - 1]\sigma_{NAI}^2 - N_{NAI}\mu_{NAI}^2 + [N_{ALL}]\mu_{ALL}^2)$$

σ_{AI}^2 is the variance of the autoimmune group

N_{AI} is the total number of patients in the autoimmune group

N_{NAI} is the total number of patients in the non-autoimmune group

N_{ALL} is the total number of patients in the whole

σ_{NAI}^2 is the variance of the non-autoimmune group

σ_{ALL}^2 is the variance of the whole group

μ_{AI} is the mean of the autoimmune group

μ_{NAI} is the mean of the non-autoimmune group

μ_{ALL} is the mean of the whole group

Supplementary Table 1: T1D SNPs included in the genetic risk score with weights. Effect allele is the risk increasing allele on the positive strand.

| SNP | Gene | Odds Ratio | Weight | Effect Allele |
|-------------------------|-------------|------------|--------|---------------|
| rs2187668, rs7454108 | DR3/DR4 | 48.18 | 3.87 | |
| | DR3/DR3 | 21.12 | 3.05 | |
| | DR4/DR4 | 21.98 | 3.09 | |
| | DR4/X | 7.03 | 1.95 | |
| | DR3/X | 4.53 | 1.51 | |
| rs1264813 | HLA_A_24 | 1.54 | 0.43 | T |
| rs2395029 | HLA_B_5701 | 2.5 | 0.92 | T |
| rs3129889 | HLA_DRB1_15 | 14.88 | 2.70 | A |
| rs2476601 | PTPN22 | 1.96 | 0.67 | A |
| rs689 | INS | 1.75 | 0.56 | T |
| rs12722495 | IL2RA | 1.58 | 0.46 | T |
| rs2292239 | ERBB3 | 1.35 | 0.30 | T |
| rs10509540 | C10orf59 | 1.33 | 0.29 | T |
| rs4948088 | COBL | 1.3 | 0.26 | C |
| rs7202877 | | 1.28 | 0.25 | G |

| | | | | |
|------------|----------|------|------|---|
| rs12708716 | CLEC16A | 1.23 | 0.21 | A |
| rs3087243 | CTLA4 | 1.22 | 0.20 | G |
| rs1893217 | PTPN2 | 1.2 | 0.18 | G |
| rs11594656 | IL2RA | 1.19 | 0.17 | T |
| rs3024505 | IL10 | 1.19 | 0.17 | G |
| rs9388489 | C6orf173 | 1.17 | 0.16 | G |
| rs1465788 | | 1.16 | 0.15 | C |
| rs1990760 | IFIH1 | 1.16 | 0.15 | T |
| rs3825932 | CTSH | 1.16 | 0.15 | C |
| rs425105 | | 1.16 | 0.15 | T |
| rs763361 | CD226 | 1.16 | 0.15 | T |
| rs4788084 | IL27 | 1.16 | 0.15 | C |
| rs17574546 | | 1.14 | 0.13 | C |
| rs11755527 | BACH2 | 1.13 | 0.12 | G |
| rs3788013 | UBASH3A | 1.13 | 0.12 | A |
| rs2069762 | IL2 | 1.12 | 0.11 | A |
| rs2281808 | | 1.11 | 0.10 | C |
| rs5753037 | | 1.1 | 0.10 | T |