

### Fertility in affected and non-affected siblings in families with type 1 diabetes: results from the type 1 diabetes genetics consortium (T1DGC)

J.C. Wiebe<sup>1</sup>, Á. Santana<sup>2</sup>, N. Medina Rodríguez<sup>2,3</sup>, M. Hernández<sup>4</sup>, J. Nóvoa<sup>1,5</sup>, D. Mauricio<sup>6</sup>, A.M. Wägner on behalf of the T1DGC<sup>1,5</sup>;

<sup>1</sup>Endocrinology Dept, Complejo Hospitalario Universitario Insular-Materno Infantil de Gran Canaria,

<sup>2</sup>Dept of Mathematics and Statistics, Universidad de Las Palmas de Gran Canaria, <sup>3</sup>Iuma, ULPGC, Las

Palmas de Gran Canaria, <sup>4</sup>Endocrinology Dept., Hospital University Arnau de Vilanova, Lleida, <sup>5</sup>Dept of Medical and Surgical Science, ULPGC, Las Palmas de Gran Canaria, <sup>6</sup>Hospital Germans Trias i Pujol, Badalona, Spain.

**Background and aims:** A recent Finnish study described reduced fertility in patients with childhood-onset type 1 diabetes (T1D). The T1DGC is an international effort aimed at the study of the genetics and pathogenesis of T1D where families with at least 2 affected siblings have been included from all over the world. The aim of our study was to assess fertility and its distribution in the T1DGC dataset available on 1st October 2009.

**Materials and methods:** Clinical information, including family history, was obtained using questionnaires at each of the participating centres. Only subjects aged 18 or more at the time of examination were included in the present analysis. Affected and unaffected siblings were compared regarding the number of offspring (chi squared and Wilcoxon's test) and stratified by gender. Non-parametric adjustments were performed for age of birth and age of onset. Additional analyses were performed in those families comprising both affected and unaffected siblings, and the number of offspring was compared within each family. Statistical analysis was performed using "R".

**Results:** A total of 2929 affected and 759 unaffected adult siblings were assessed, belonging to 1748 families. Mean age was 32.3 (11.0) years and 51% were women. Offspring were distributed as shown in the table: chi-squared= 64.33, p-value = 3.563\*10<sup>-13</sup>. This distribution was skewed at the expense of women, whereas men did not show a difference. Birth year did not significantly affect the differences seen between groups. However, there was a positive correlation between the age of onset and the number of offspring: 0.28 (0.25-0.31), p<2.2 10<sup>-16</sup>. When only families with at least one unaffected sibling were included (N=1153), the difference between the affected and unaffected sibling ranged between 0.14-0.15 children (p=7.6\*10<sup>-5</sup>).

**Conclusion:** Women with T1D have fewer children than their unaffected siblings, but such an effect is not seen in men with the disease. Birth cohort does not seem to affect this observation. Later age of onset of diabetes is associated with a higher number of offspring.

N° of offspring	0	1	2	3	≥4
Affected (%)	60.61	16.52	16.56	4.97	1.34
Non- Affected (%)	54.35	12.01	19.79	9.50	4.35

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