Adult onset type 1 diabetes: trying to find the needle in the haystack, my Biobank story

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Background

• “Type 1 diabetes predominantly affects children and young adults”.

• Can affect patients of all ages – how common over 30 years of age? Characteristics?

• Epidemiological data on Type 1 diabetes in later life limited

• Most studies focus on childhood
Current limitations

• Age is a key predictor for diabetes type
  – In childhood Type 1 predominates so cases “stand out”
  – In older age the sea of type 2 diabetes means cases “drowned out”.

• Cases difficult to identify
  – Clinicians classification and prescribing insulin therapy is not systematic
  – No defined clinical criteria
The circle of difficulty

Difficult to identify in clinical practice

Difficult to study
Approach 1:- Genetic predisposition

• T1D strong genetic susceptibility

• Captured 30 SNPS (single nucleotide polymorphisms) as a Type 1 diabetes genetic risk score (T1D–GRS).

• Sum of risk-increasing alleles weighted by risk
Method

Kaplan-Meier curve of diabetes free survival in high vs low T1D GRS halves
The number of cases of autoimmune diabetes remains constant from birth to 60 years of age.

Calculated clinical characteristics of those diagnosed from 31 to 60 years of age

<table>
<thead>
<tr>
<th>Mean/ Proportion (95% CI)</th>
<th>Type 1 diabetes diagnosed 31-60 years</th>
<th>Type 2 diabetes diagnosed 31-60 years</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>537</td>
<td>11,696</td>
<td></td>
</tr>
<tr>
<td>Current age (years)</td>
<td>56 (55-57)</td>
<td>59 (59-59)</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>Age at diagnosis (years)</td>
<td>42 (41-43)</td>
<td>52 (52-52)</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.4 (26.7-28.0)</td>
<td>32.4 (32.2-32.5)</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>Insulin at a year (%)</td>
<td>89 (86-91)</td>
<td>6 (5-6)</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>n</td>
<td>476/537</td>
<td>648/11696</td>
<td></td>
</tr>
<tr>
<td>Insulin now (%)</td>
<td>100 (100-100)</td>
<td>16 (15-17)</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>n</td>
<td>537/537</td>
<td>1924/11696</td>
<td></td>
</tr>
<tr>
<td>DKA as a discharge diagnosis (%)</td>
<td>11 (9-14)61/537</td>
<td>0.3 (0.1-0.4)</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>n</td>
<td>30/11696</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Conclusion

- 42% of type 1 diabetes occurs after 30 years of age

- Difficult to identify as type 2 diabetes predominates later in life

- Similar characteristics when diagnosed above and below 30 years of age

- Only possible because of large population dataset with genetic and linked data which allows novel approach's to answer important questions
Thank you for listening

Andrew Hattersley
Richard Oram
Sam Jones
Mike Weedon
Tim McDonald
Angus Jones
Bev Shields