**The M120 risk score improves identification of children at high risk of developing clinical type 1 diabetes and reports short-term response to preventative immunotherapy**

**Aim** The anti-CD3 antibody teplizumab preserves beta-cell function in type 1 diabetes (T1D) and was recently registered for use as a disease-modifying prevention therapy. This has made it challenging to validate promising new prevention therapies using the standard placebo-controlled trial powered around progression to clinical disease. We therefore sought to determine if a risk score for disease progression derived from correlates of beta-cell function could improve identification of at-risk people and report early therapeutic effects.

**Methods** The M120 risk score, calculated using age, sex, BMI, IA-2 antibody, HbA1c, blood glucose and C-peptide, was determined in TrialNet participants with multiple islet autoantibodies undergoing monitoring, including 76 in the teplizumab prevention trial. We used Cox regression to compare the abilities of M120 and OGTT (the currently used method) to predict T1D progression, and paired signed-rank and rank-sum tests to identify early teplizumab effects.

**Results** 4146 individuals with pre-clinical T1D were included. Compared to disease staging by OGTT, M120 identified 26% more children at high-risk of progression. When applied to teplizumab trial data, M120 improved after teplizumab and deteriorated after placebo, revealing a significant treatment effect after only 6 months (Figure 1).

**Conclusion** The ability of M120 to enrich for T1D risk and identify early therapeutic benefit could increase T1D prevention trial efficiency by increasing enrolment and enabling adaptive designs. The clinical utility of M120 could be readily applied to measure T1D risk and guide treatment decisions in the clinic.

