Type 1 diabetes risk assessment: improvement by follow-up measurements in young islet autoantibody-positive relatives.

AIMS/HYPOTHESIS: Combinations of autoantibody characteristics, including antibody number, titre, subclass and epitope have been shown to stratify type 1 diabetes risk in islet autoantibody-positive relatives. The aim of this study was to determine whether autoantibody characteristics change over time, the nature of such changes, and their implications for the development of diabetes. METHODS: Five-hundred and thirteen follow-up samples from 141 islet autoantibody-positive first-degree relatives were tested for islet autoantibody titre, IgG subclass, and GAD and IA-2 antibody epitope. All samples were categorised according to four risk stratification models. Relatives had a median follow-up of 6.8 years and 48 developed diabetes during follow-up. Survival analysis was used to determine the probability of change in risk category and of progression to diabetes. RESULTS: For each stratification model, the majority of relatives (71-81%) remained in the same risk category throughout follow-up. In the remainder, changes occurred both from lower to higher and from higher to lower risk categories. For all four models, relatives aged 15 years (0.001 < p < 0.03). Relatives whose autoantibody status changed from low- to high-risk categories had a higher risk of diabetes than relatives who remained in low-risk categories, and inclusion of autoantibody status
during follow-up improved diabetes risk stratification in Cox proportional hazards models (p < 0.001).

CONCLUSIONS/INTERPRETATION: Changes in islet autoantibodies are relevant to pathogenesis, and are likely to signal alterations in the disease process. Detection of changes through follow-up measurement will improve diabetes risk stratification, particularly in young individuals.