Stratifying rate of disease progression by progression likelihood scores in children and adolescents with stage 1 and stage 2 type 1 diabetes in Germany

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Online-only supplemental material

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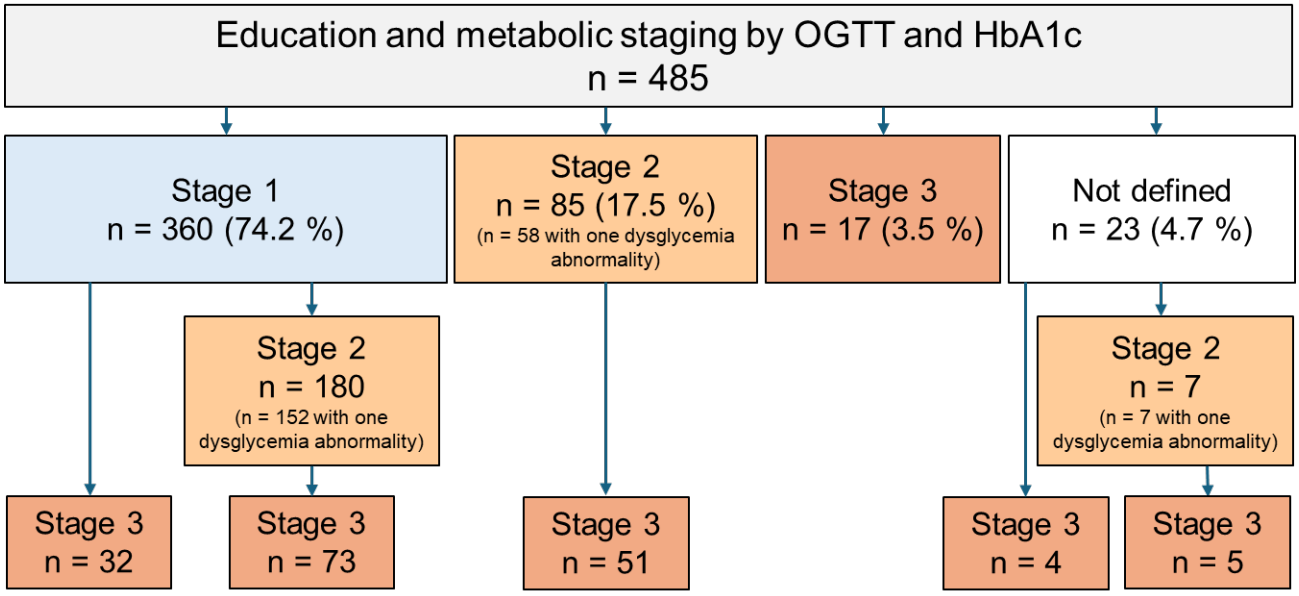
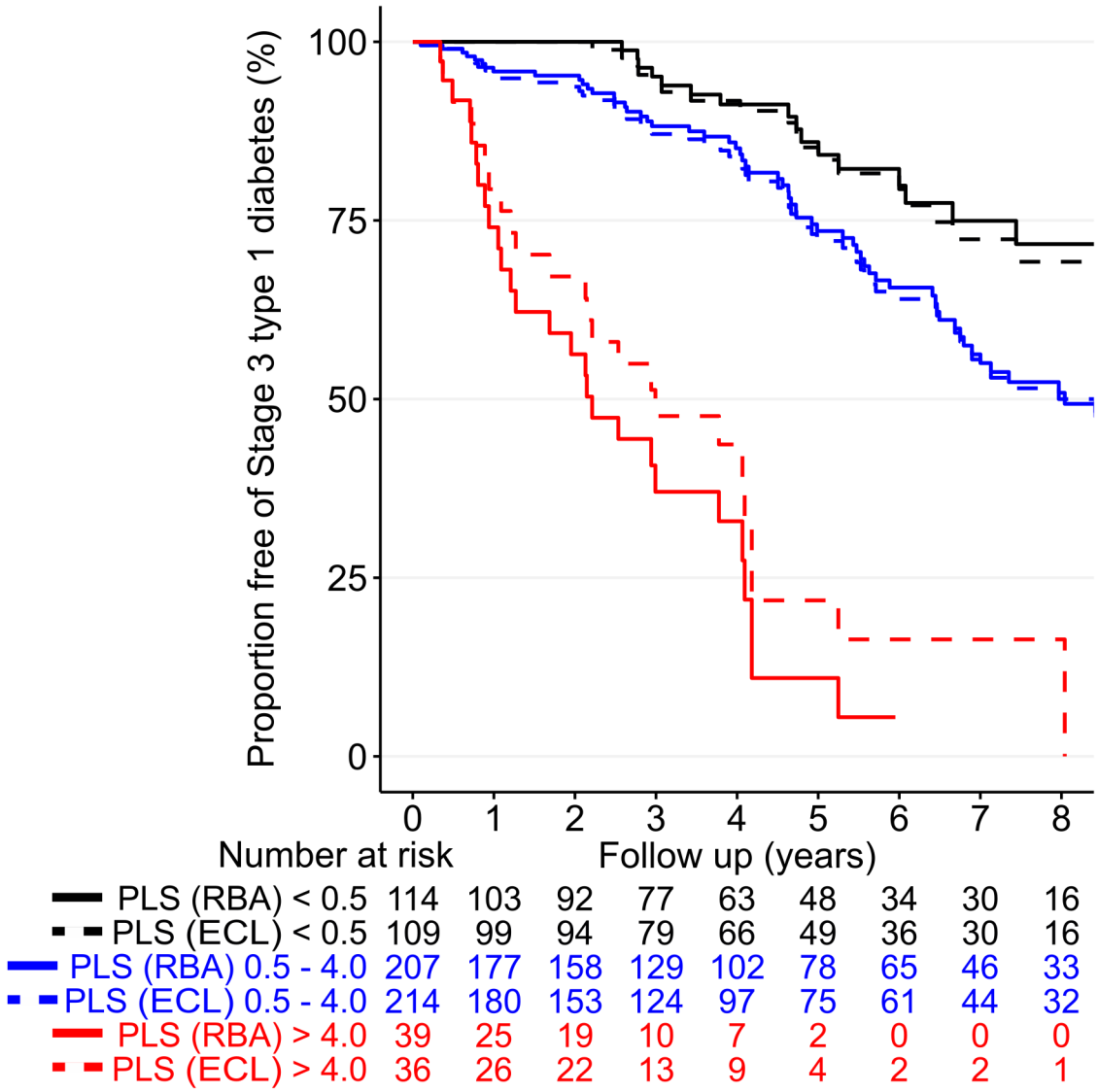
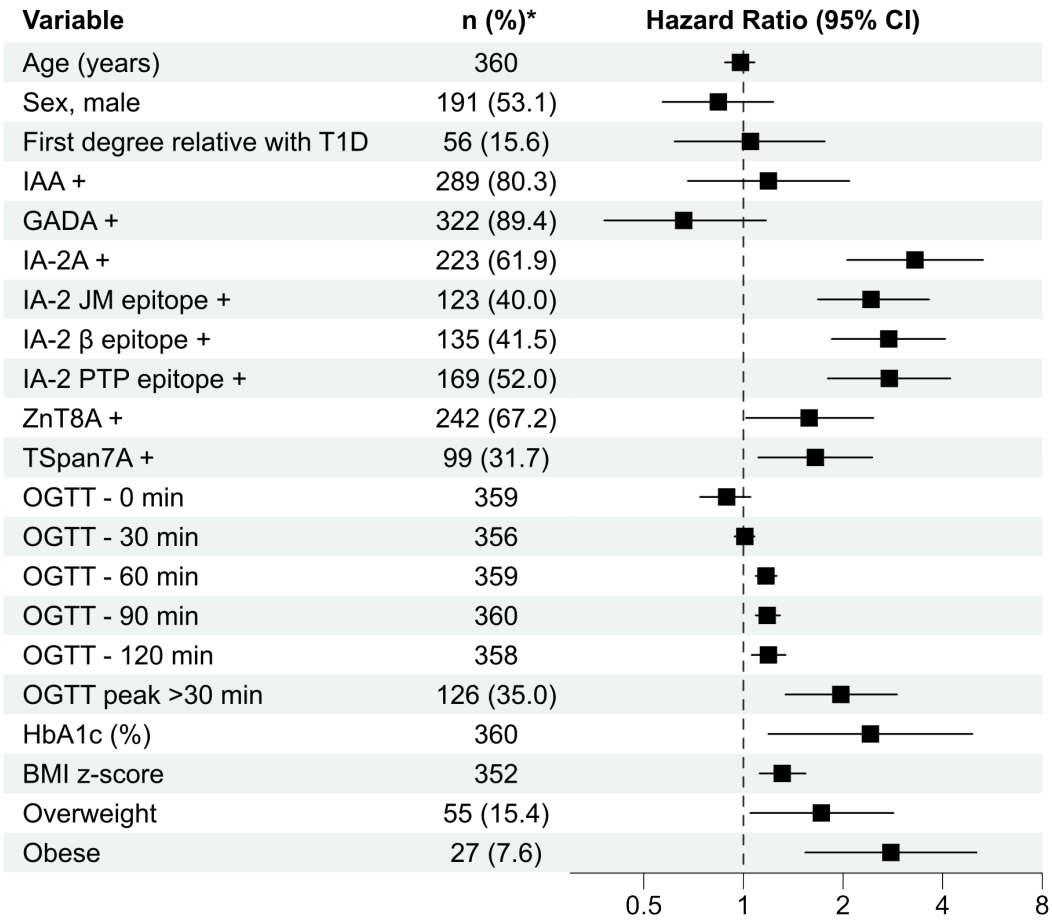


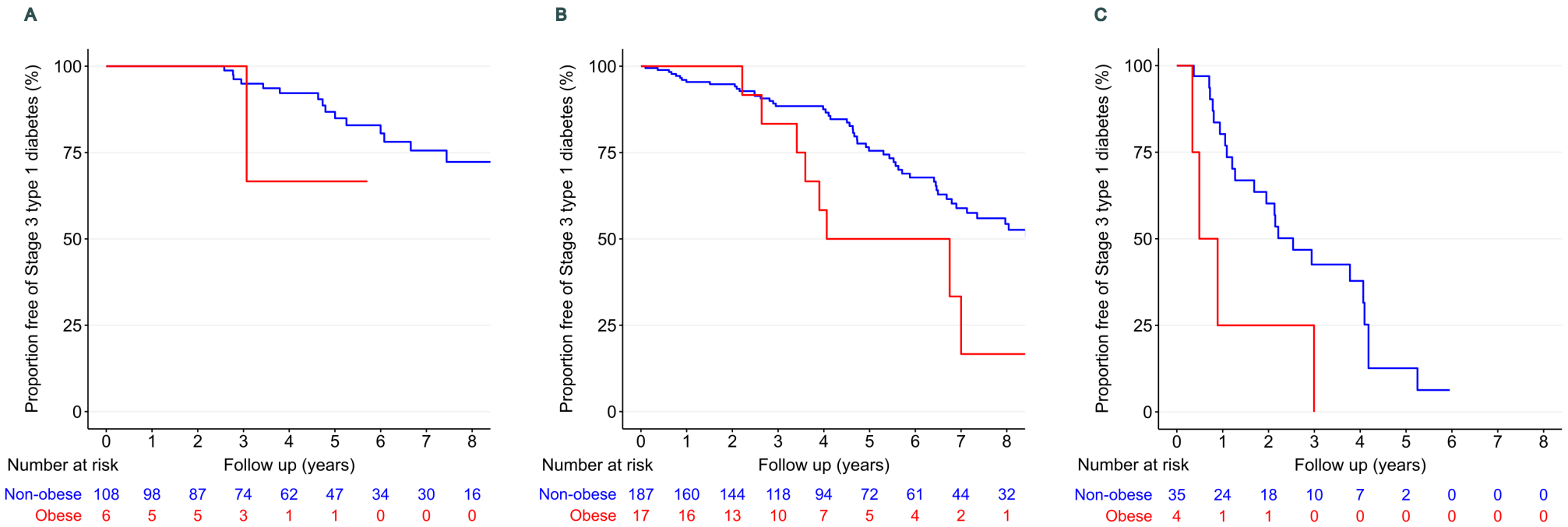
Supplemental Figure 1. Fr1da early-stage type 1 diabetes cohort and follow-up outcomes.



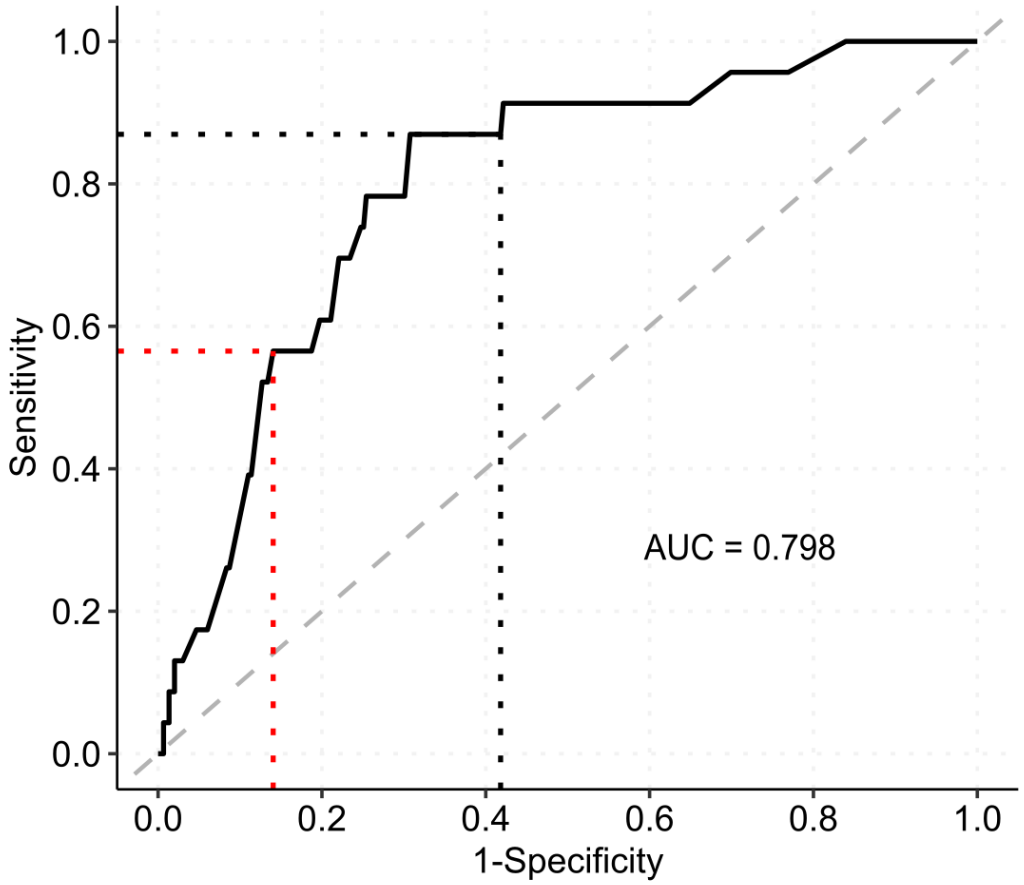
Supplemental Figure 2. Stratification of progression from stage 1 to stage 3 type 1 diabetes by the progression likelihood score (PLS) calculated using IA-2A units measured by radiobinding assay (RBA, solid lines) and electrochemiluminescence (ECL, dashed lines) assay. Children were categorized using previously defined PLS thresholds as <0.5 (low, black line), 0.5 – 4.0 (intermediate, blue line) and >4.0 (high, red line). The IA-2A categories for the ECL assay were matched to the centiles of the RBA categories and corresponded to 6.5 units (negative), >6.5 – 82 units, >82 – 1250 units, and >1250 units. Progression differed significantly among categories in both the PLS derived from the ECL IA-2A units (p<0.0001) and the RBA IA-2A units (p=0.0001). The numbers underneath the x axis indicate the number remaining at each year of follow-up.



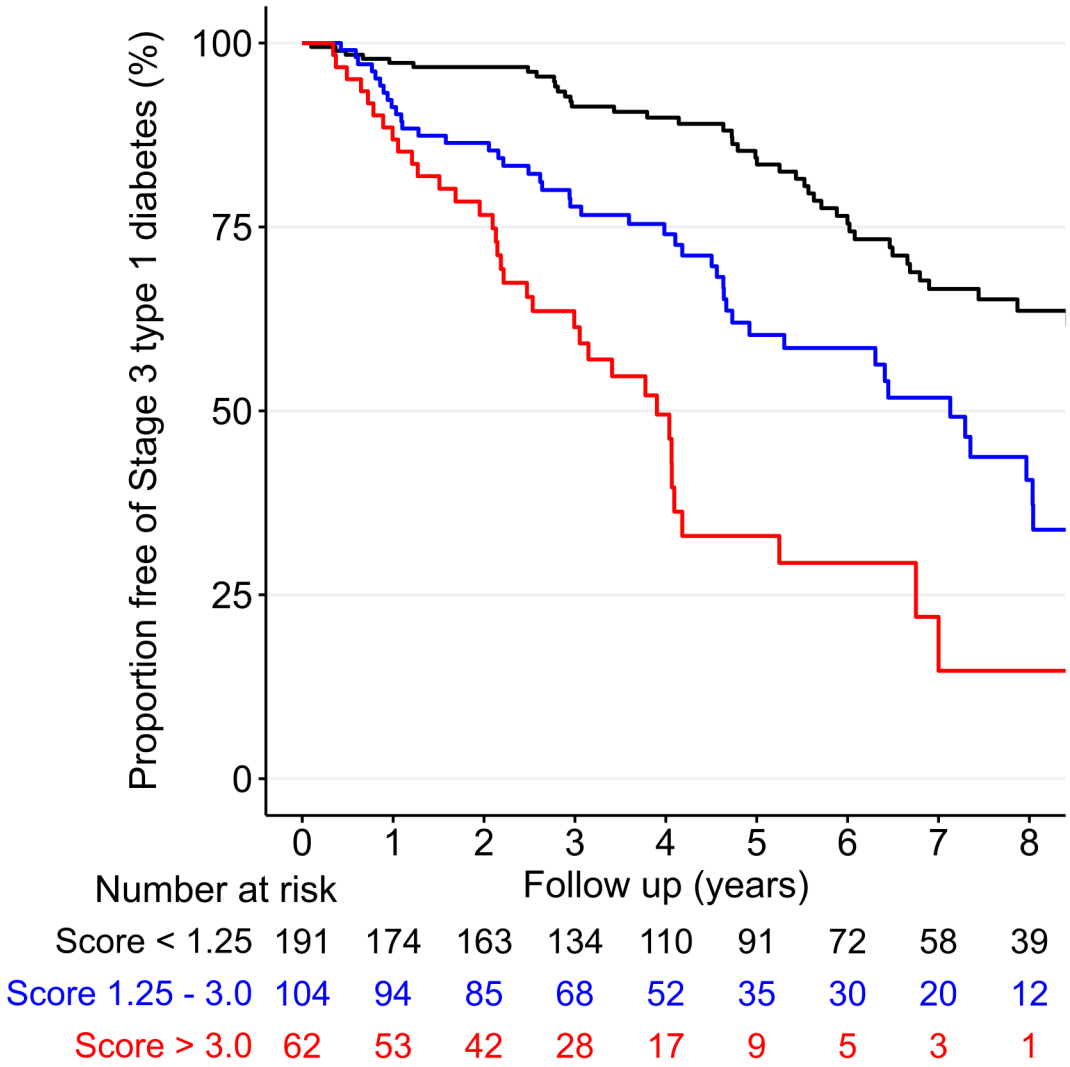
Supplemental Figure 3. Association of demographic, autoantibody and metabolic variables with progression rate to stage 3 type 1 diabetes. Shown are the hazard ratios (black squares) and the 95% confidence intervals (lines) from univariable Cox proportional hazards models analyzing progression to stage 3 type 1 diabetes in the 360 children with stage 1 in the Fr1da cohort. The variables age, OGTT glucose values at 0, 30, 60, 90, 120 minutes, HbA1c and BMI z-score were continuous variables. The remainder were categorical and expressed as a hazard ratio against the relative reference comparator. *Numbers for continuous variables represent the numbers with information; numbers (%) for categorical variables represent the number and frequency in the category.



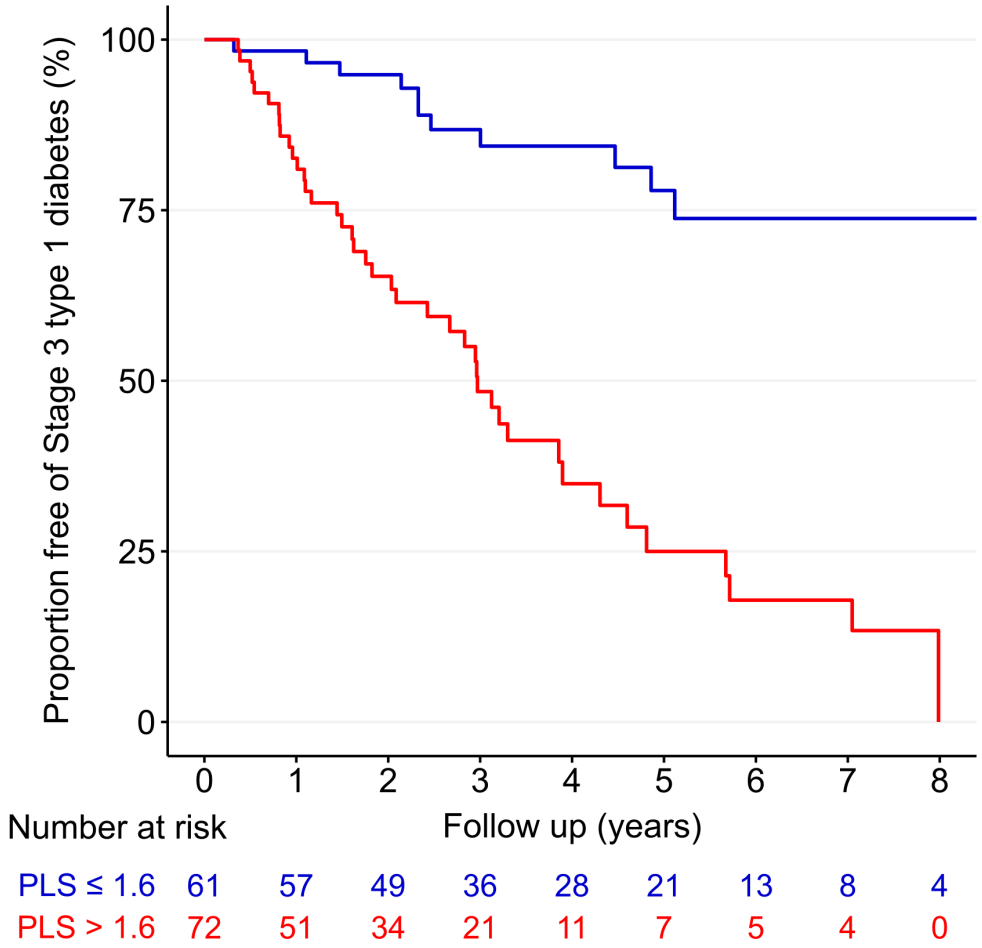
Supplemental Figure 4. Stratification of progression from stage 1 to stage 3 type 1 diabetes by the progression likelihood score (PLS) and obesity in children in the Fr1da cohort. Kaplan-Meier survival curves for progression to stage 3 in A) children with a low PLS (p=0.83), B) intermediate PLS (p=0.007), C) high PLS (p=0.017) for children who are obese (red lines) and not obese (blue lines). The numbers underneath the x axis indicate the number remaining at each year of follow-up.



Supplemental Figure 5. Receiver operator characteristic (ROC) curve for non-OGTT based progression score for its ability to discriminate the Fr1da cohort children with stage 1 who developed stage 3 type 1 diabetes within 2 years of follow-up (sensitivity) from those who were followed for at least 2 years without developing stage 3 (1 – specificity). The vertical/horizontal dashed lines show the performance at the PLS thresholds of 1.25 (black) and 3 (red). The diagonal dashed line represents no discrimination.



Supplemental Figure 6. Sensitivity analysis of a non-OGTT-based progression score for stratification of progression from stage 1 to stage 3 type 1 diabetes. Stage 1 type 1 diabetes was classified on the basis of a normal HbA1c value without considering OGTT measurements. Kaplan-Meier survival curves for progression to stage 3 type 1 diabetes are shown for children with scores <1.25 (black line), 1.25 to 3.0 (blue line) and >3.0 (red line). Progression differed significantly among categories ($p<0.0001$). The numbers underneath the x axis indicate the number remaining at each year of follow-up.



Supplemental Figure 7. Stratification of progression from stage 2 to stage 3 type 1 diabetes by the progression likelihood score (PLS) in children who progressed to stage 2 during follow-up. Kaplan-Meier survival curves for progression to stage 3 type 1 diabetes in 133 children diagnosed with stage 2 type 1 diabetes in follow-up in the Fr1da cohort, having only one dysglycemic value. Children were categorized as those with a PLS ≤1.6 (n= 61, blue line) and those with a PLS >1.6 (n=72, red line). Progression differed significantly among categories ($p<0.0001$). The numbers underneath the x axis indicate the number remaining at each year of follow-up.