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Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

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Supplemental Materials to:

Islet Autoantibody Screening in Adolescents to Predict Type 1 Diabetes

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Inverse Probability Censoring Weighting Algorithm:

The inverse probability censoring weights method accounts for right-censored subjects by using all 8,682 subjects who were type 1 diabetes free at age 10 and observed at least once at or after age 10. We weight each subject by 1/p(t) where p(t) is the probability of censoring at time point t. In this case, subjects who were diagnosed at later age are assigned higher weights to account for those who would have had diagnosed but were censored. The algorithm to define weights for each subject is defined using the following steps:

1. Estimate the probability of censoring after time t using the Kaplan Meier estimator:

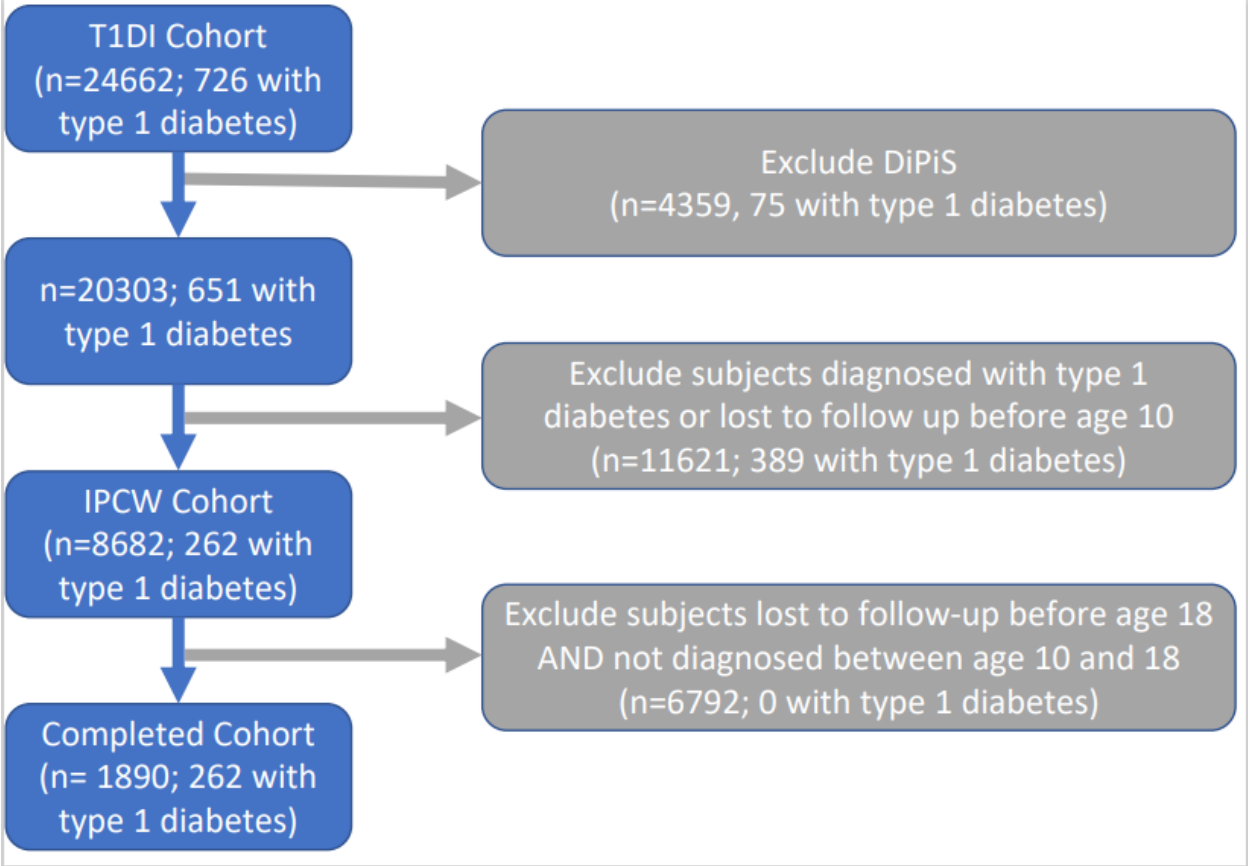
$$C(t) = \prod_{i:\, t_i < t} (1 - \frac{d_i}{n_i}) \quad \text{..... (1)}$$

   where d_i is the number of subjects censored at time t_i and n_i is the number of subjects who are not yet diagnosed or censored at time t_i.

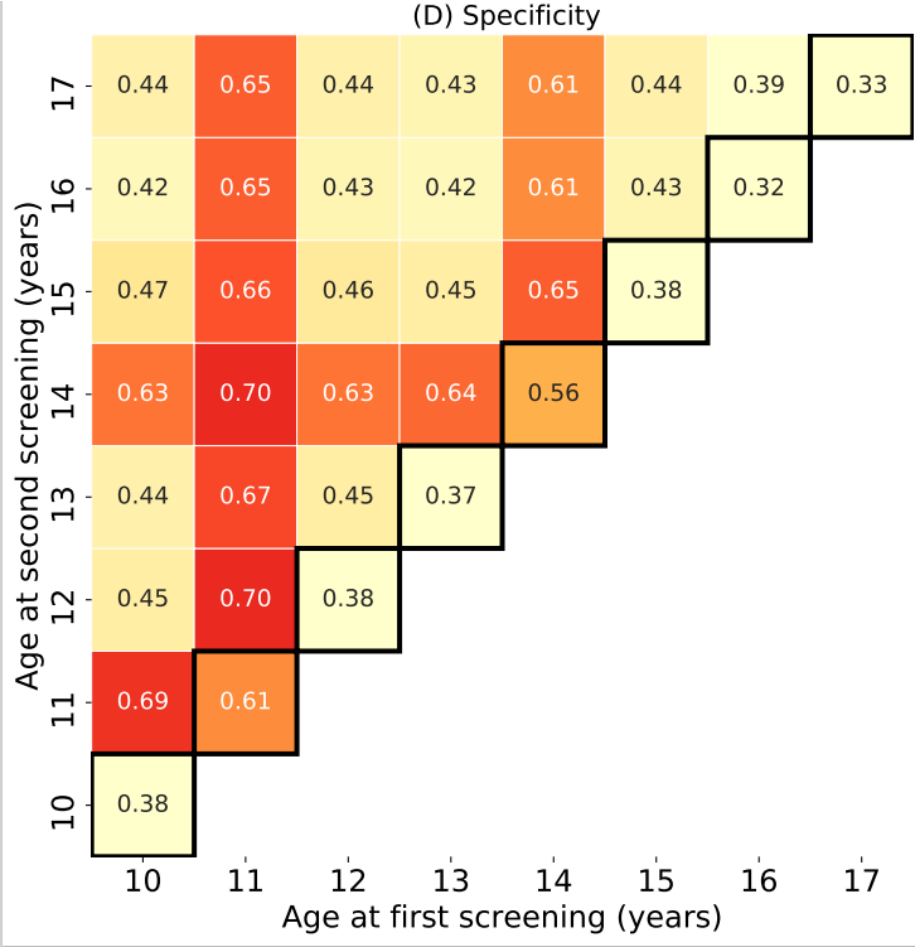
2. Each subject i is assigned a weight w_i as follows:

$$w_i = \begin{cases} \frac{1}{C(\theta)}, & diagnosed\ at\ time\ \theta < \tau \\ \frac{1}{C(\tau)}, & followed\ up\ until\ time\ \tau \\ 0, & otherwise \end{cases} \quad \text{..... (2)}$$

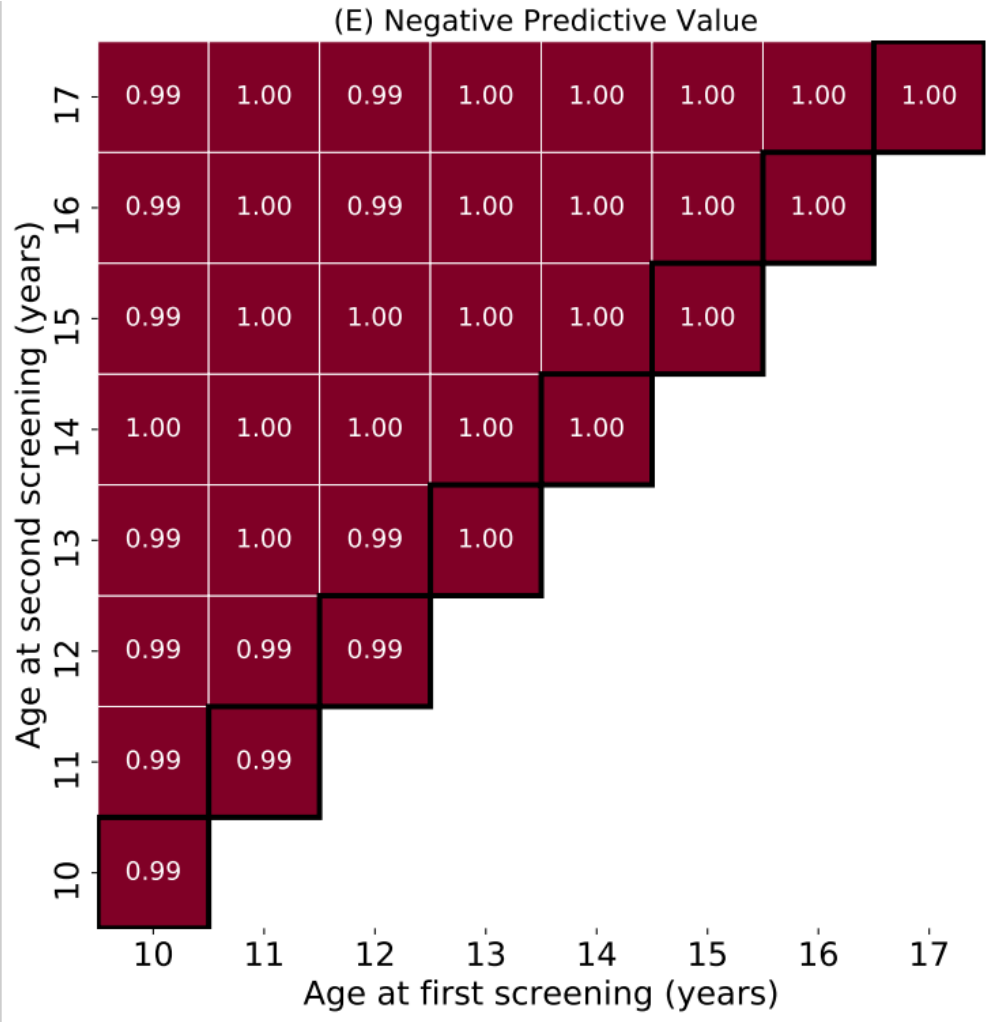
Subjects who are censored and not diagnosed before time τ will be assigned weight 0 and excluded from the analysis. However, their information is used in computing the probability of censoring and the corresponding weights assigned to other subjects. For example, if the probability of censoring after age 10 years is 0.2, this means that for any subject diagnosed at age 10, there are on average 4 other subjects censored before age 10 plus that one subject followed through age 10. In this example IPCW would assign a 5-times weight to the completely followed subject to account for 4 subjects censored before age 10 plus the followed subject (main manuscript reference #17 Vock DM et al.).



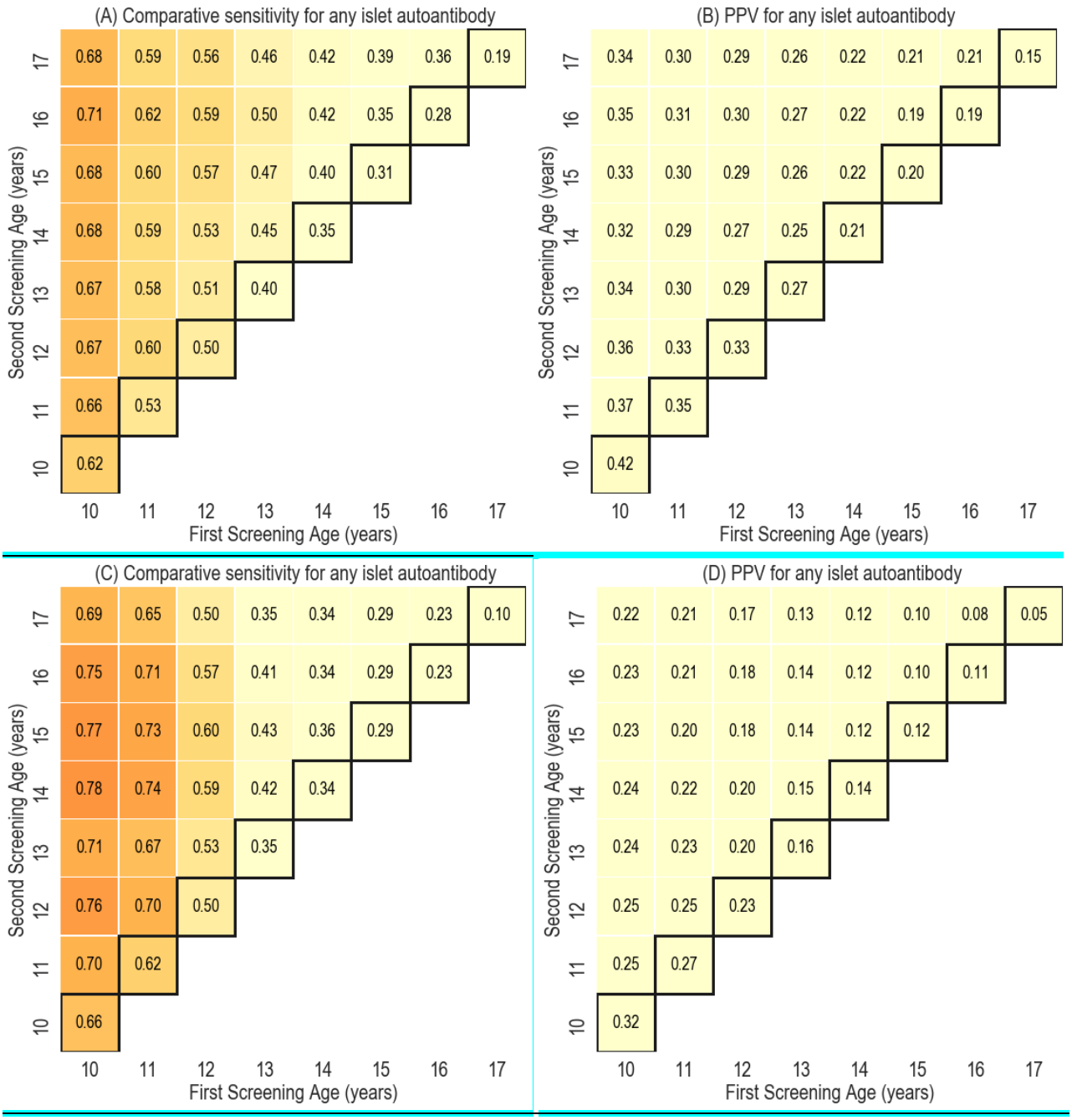
Supplemental figure S1. Flow chart describing the study population derived from the total T1DI cohort (n=24,662). DiPiS subjects were excluded because of scarce follow-up data after age 10 years. In addition, subjects who were diagnosed with type 1 diabetes or lost to follow-up before age 10 were excluded. The data of 8,682 subjects who had at least one visit after age 10 were used in the analysis by utilizing the IPCW (inverse probability censoring weighting) technique. The completed cohort included 1890 subjects who were either followed up to age 18 years or diagnosed with type 1 diabetes between ages 10 and 18.



Supplemental figure S2. Specificity from screening any islet autoantibody at single ages (diagonal numbers highlighted within black squares) and at all combinations of two ages between 10 and 17 years for risk of type 1 diabetes in subjects followed beyond age 10.



Supplemental figure S3. Negative predictive value from screening any islet autoantibody at single ages (diagonal numbers highlighted within black squares) and at all combinations of two ages between 10 and 17 years for risk of type 1 diabetes in subjects followed beyond age 10.



Supplemental figure S4. Comparative sensitivity (A) and PPV (B) for the 972 boys from screening any islet autoantibody at single ages (diagonal numbers highlighted within black squares) and at all combinations of two ages between 10 and 17 years for risk of type 1 diabetes in subjects followed beyond age 10. Similarly, panels C and D present comparative sensitivities and PPVs for the 918 girls. The highest comparative sensitivity indicates the optimum screening age or age pair to detect the maximum number of subjects developing type 1 diabetes during follow-up. The PPV at single age or age pair indicates the likelihood that autoantibody positive subjects develop type 1 diabetes during the follow-up.