SUPPLEMENTARY DATA

Online-only Supplemental Material

Autoantibody reversion: Changing risk categories in multiple-autoantibody positive individuals.

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Short running title: Loss of multiple antibody status in at-risk

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Supplementary Table 1. Models describing risk of type 1 diabetes diagnosis.

		Unadjusted			Adjusted		
Variable	**Level**	**HR***	**95% CI**	**P-value**	**HR***	**95% CI**	**P-value**
HLA-DR3	Present vs. Absent	1.12	0.95 – 1.32	0.161	1.14	0.97 – 1.33	0.119
HLA-DR4	Present vs. Absent	1.22	1.02 – 1.46	0.033	1.19	0.97 – 1.45	0.102
Protective HLA†	Present vs. Absent	0.45	0.25 – 0.83	0.011	0.68	0.34 – 1.36	0.274
Gender	Female vs. Male	1.00	0.85 – 1.16	0.949	1.10	0.92 – 1.31	0.316
Age by decade‡		0.75	0.69 – 0.82	<0.001	0.73	0.60 – 0.87	0.004
BMI (z-score) ‡		1.12	1.04 – 1.21	0.004	1.18	1.05 – 1.32	0.007
Autoantibody maintenance	Reverted vs. Maintained	0.47	0.31 – 0.71	<0.001	0.54	0.35 – 0.83	0.005
Baseline OGTT	Abnormal glucose tolerance vs. Normal	2.77	1.70 – 4.51	0.002	2.83	2.09 – 3.85	<0.001
	Diabetes range§ vs. Normal	3.81	1.19 – 12.17	0.024	4.86	1.52 – 15.57	0.008

* Hazard ratios > 1 indicate higher risk of being diagnosed with clinical type 1 diabetes.
† HLA-DQB1*0602
‡ Measured at time of detected multiple-autoantibody positivity
§ refers to participants who had a single OGTT in the diabetic reference range but subsequent tests reverted to the abnormal or normal glucose tolerance.

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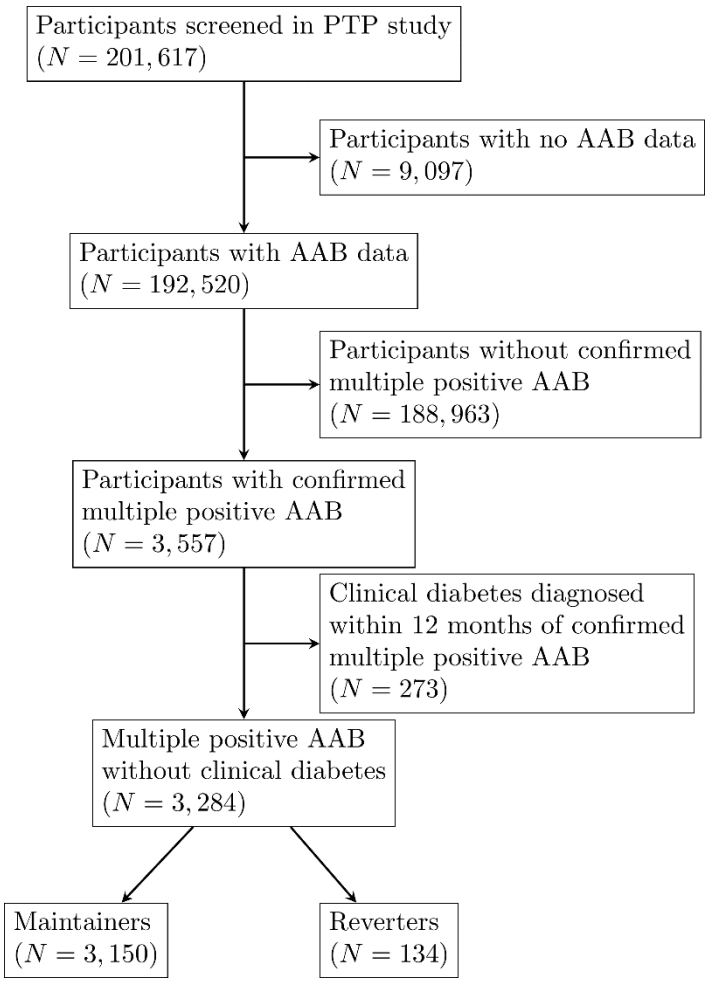
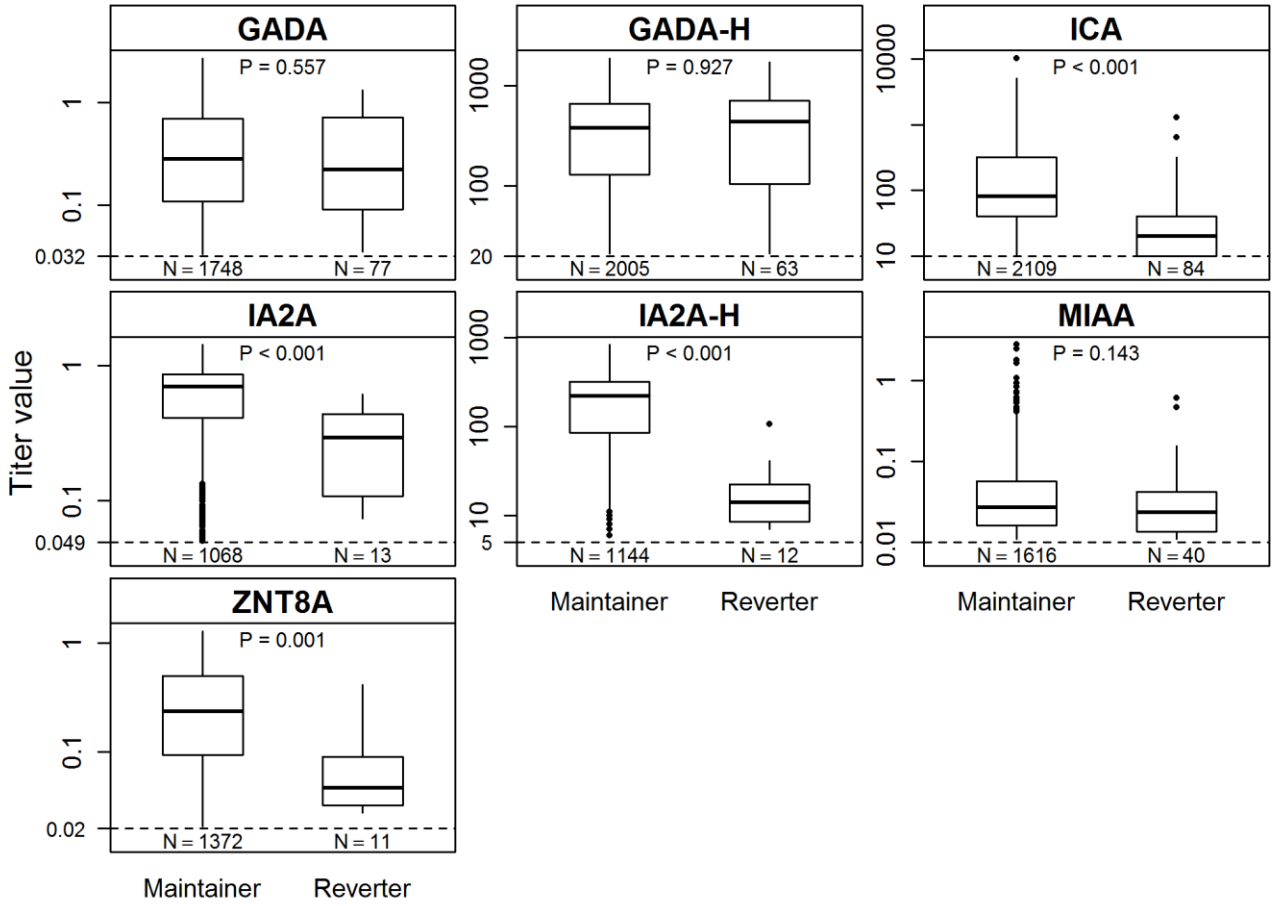
Supplementary Figure 1. CONSORT plot of PTP study participant disposition and analysis. PTP, Pathway to Prevention; AAB, autoantibody.

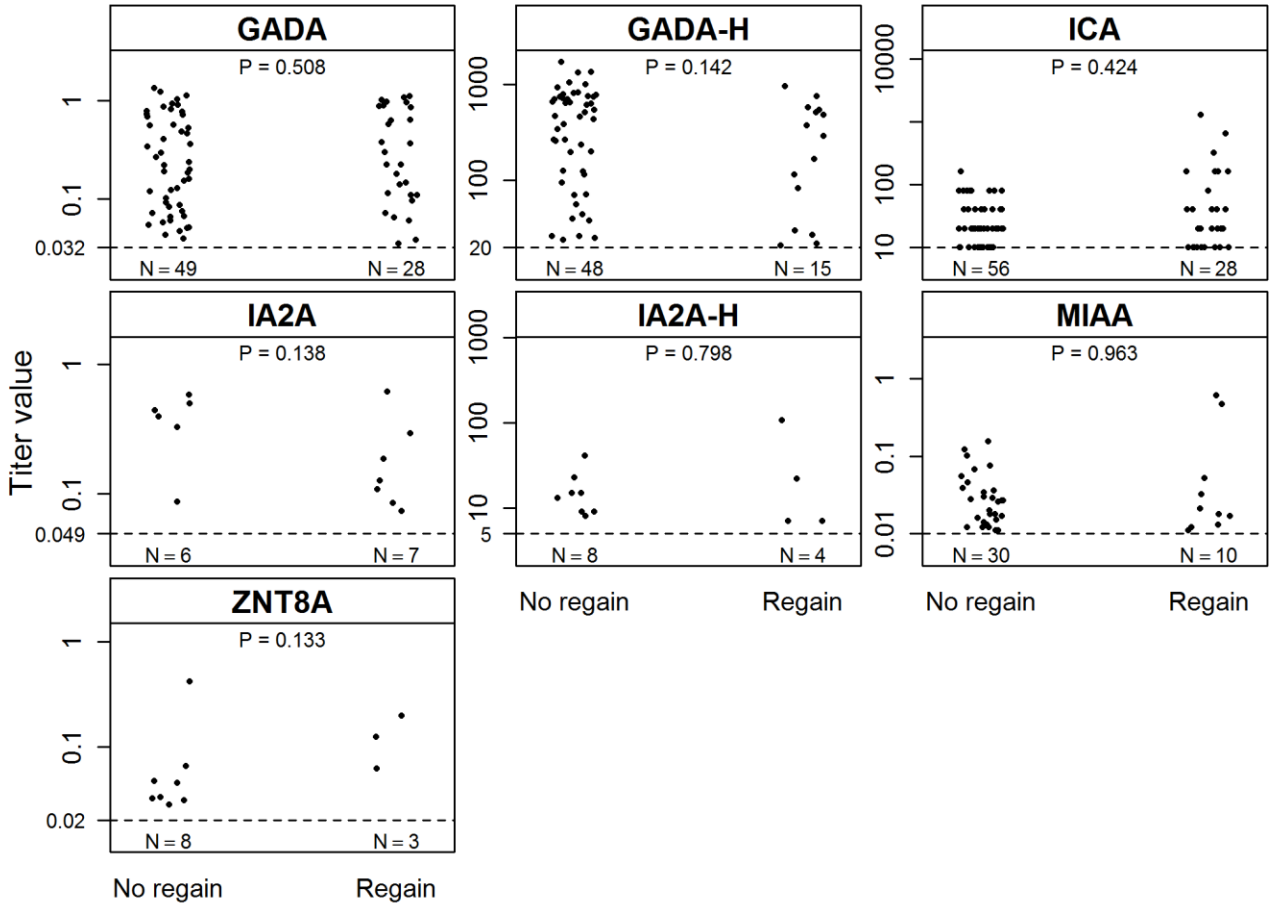


Supplementary Figure 2. Autoantibody (AAB) titer distribution for each AAB. Standard assays and harmonized assays (denoted with an H in the title) have been displayed separately where relevant. The titer cut-off for positivity is marked with a dashed line. All titer values are above the cut-off for positivity. Numbers of participants included in each plot are indicated. A: Maintainers and Reverters. Box plots show the distributions of titers. Horizontal box lines represent the lower quartile, median, and upper quartile. Whiskers extend to the largest/smallest datapoint within 1.5 IQR of the upper/lower quartile. B: Reverters who regain multiple AAB ("regain") and Reverters who do not regain multiple AAB ("no regain"). Strip charts show the distribution of titers with each point representing a participant.

A



B



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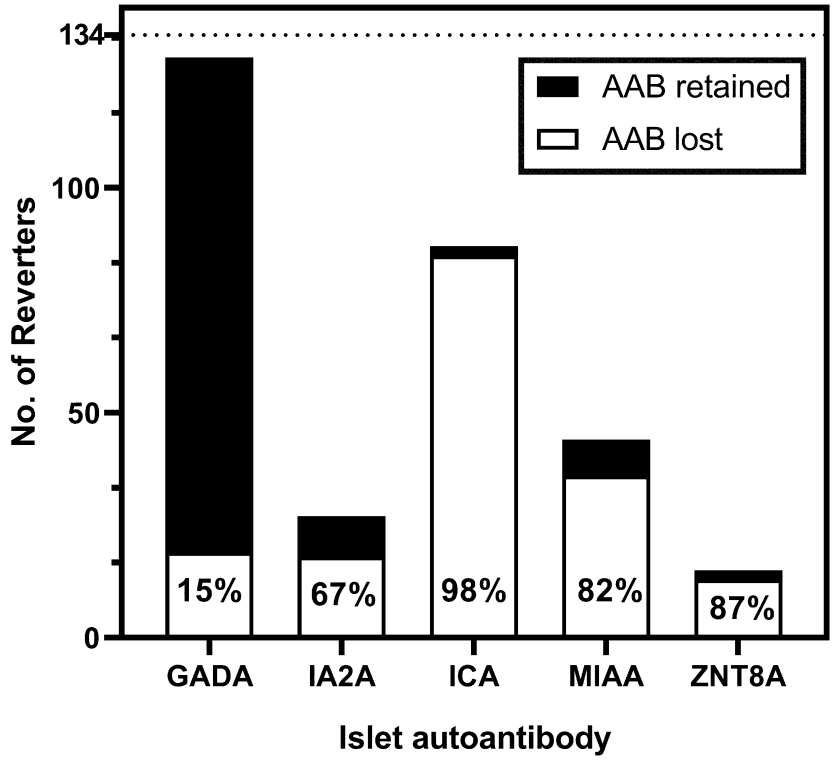
Supplementary Figure 3. Reverters grouped according to autoantibody (AAB) present at multiple-autoantibody positivity. Reverters who lost the indicated AAB are represented in white. Reverters who retained the indicated AAB are represented in black. The dotted line indicates the total number of reverters. AAB, autoantibody; MIAA, insulin antibody; ICA, islet cell antibody; GADA, glutamic acid decarboxylase antibody; IA2A, insulinoma-associated antigen antibody, ZNT8A, zinc transporter 8 antibody.



	GADA	IA2A	ICA	MIAA	ZNT8A
AAB retained	110 (85%)	9 (33%)	2 (2%)	8 (18%)	2 (13%)
AAB lost	19 (15%)	18 (67%)	85 (98%)	36 (82%)	13 (87%)
Total	129	27	87	44	15

Supplementary Figure 4. Effects plot from the multivariable model of clinical type 1 diabetes risk demonstrating the interaction between age at positivity and autoantibody maintenance group. Estimates of clinical type 1 diabetes risk with increasing age are provided within the maintainer (n=3150) and reverter (n=134) groups, with the following variables held fixed at their baseline values: HLA (HLA DR-3, HLA DR-4, HLA*0602), gender, BMI (z-score), baseline OGTT. Shaded area displays the 95% CI for the HR. HR, hazard ratio; AAB, autoantibody.