

SUPPLEMENTARY DATA

Type 1 Diabetes TrialNet Study Group

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Cara; Downey, CA: S. Shaw; Drayton, SC: W. Price; Dubuque, IA: R. Iverson; Duluth, MN: M. Slag; Durango, CO: J. Hutt; Eau Claire, WI: N. McLean, WI: R. Moore; El Paso, TX: R. Christenson; Elgin, IL: K. Valika; Englewood, CO: N. Nayak, C. A. Bloch; Englewood, NJ: L. Strom; Escondido, CA: T. S. Bailey, C. P. Varma; Eugene, OR: D. Calder, M. Bilger; Everett, WA: K. Larson, M. Papenhausen; Fairfield, CA: Y. Shlesinger; Fargo, ND: A. Kenien; Fayetteville, NC: E. Wright; Flint, MI: M. A. Jabbar; Flushing, NY: D. L. Lorber; Fort Dodge, IA: J. Berkett; Fort Smith, AR: R. P. Robinson; Fort Wayne, IN: A. Kadambi; Framingham, MA: W. Sullivan; Fremont, CA: E. Meyer; Fresno, CA: J. L. Bautista, P. C. Norwood; Ft. Lauderdale, FL: E. Biederman, S. Nassberg, L. Goscin, M. Mata, N. Thompson, R. M. Harrell, J. Cabral; Ft. Myers, FL: A. Pietri; Ft. Worth, TX: C. R. Scott, T. K. Flannery, D. B. Wilson; Gainesville, FL: B. Rogers; Glendale, CA: M. Campos, M. N. Montero; Gorham, NH: B. Beals; Grand Junction, CO: D. Mair, A. Long; Grand Rapids, MI: R. S. Rood; Green Bay, WI: J. Taylor; Greensboro, NC: R. Sevier; Greenville, NC: G. Harris, M. A. Pfeifer; Hackensack, NJ: M. Blechman, J. Giangola; Hermitage, TN: R. Creech; Hershey, PA: M. Lathrop, A. Dunaif; Hollywood, FL: G. Miceli, L. Lewy-Alterbaum, P. S. Jellinger, S. B. Novak, K. M. Gellman, S. Lerman; Honolulu, HI: S. Waxman; Houston, TX: D. J. Hamilton; Huntington, WV: H. Driscoll; Huntsville, AL: R. Schneier; Hutchinson, KS: J. L. Casey; Indianapolis, IN: P. Boyce, J. Meachum; Irving, TX: J. Milburn; Issaquah, WA: D. Pomeroy; Jackson, MS: G. Moll; Jacksonville, FL: K. Macyko, L. A. Fox, N. Mauras; Jersey City, NJ: P. Ledereich; Juneau, AK: D. Novotney; Kalispell, MT: C. Gill, B. Rossetto; Kingston, ON, R. Houlden; Klamath Falls, OR: P. Heck; La Crosse, WI: J. Korducki; La Habra, CA: J. Winston, MD, D. Geffner; La Jolla, CA: S. Edelman, MD: B. Henry; La Mesa, CA: D. Einhorn, R. Fink, E. Gold; Lake Charles, LA: R. W. (RW) Calhoun, MD; Lake Jackson, TX: J. Leidlein; Lancaster, CA: K. Arul; Lansing, MI: D. Henry; Las Vegas, NV: D. L. Donaldson; Lebanon, OR: K. Middlestadt; Lewiston, ID: L. Grande-Luke; Lincoln, NE: J. Guest, R. Wermers, B. Bells; Little Rock, AR: P. Frindik; Livingston, NJ: G. Gewirtz; Lompoc, CA: C. Blyfeld; Long Beach, CA: M. Brakin; Los Angeles, CA: D. Borut, D. Geffner, J. Winston, M. Geffner, M. Rodriguez, V. Gura, M. Rodriguez; Los Gatos, CA: C. Shough; Louisville, KY: H. Bays, H. Shenouda; Lubbock, TX: S. Varma, M. J. Bourgeois; Lufkin, TX: L. A. Sloan; Lynchburg, VA: C.E. Guthrow, Jr.; Lynwood, CA: S. Shaw; Manhattan Beach, CA: R. Ruby; Margate, FL: B. Motzkin-Kava; Marshalltown, IA: D. Jebsen; Marshfield, WI: I. Zador, S. Maby; McLean, VA: F. Crantz; Medford, OR: D. Zietlow; Miami Beach, FL: D. Kudzma; Miami, FL: E. Levy, E.T. Shapiro, J. Jacobi, J. Pita, W. Abelove, J. Perez-Rodriguez, L. Gonzalez-Mendoza, S. Richton, P. Weissman; Middletown, NY: N. Stein; Midland, TX: L. Sherman-Adcock; Milwaukee, WI: D. Fergeson, M. Jacobson, J. Sennett, R. Jain; Minneapolis, MN: D. Etzwiler, R. C. Ramsay; Minot, ND: M. Holland; Miramar, FL: S. Carrington; Missoula, MT: S. Seagraves; Modesto, CA: G. M. Yue, J. Downs-Colby; Montebello, CA: H. Flores; Montgomery, AL: S. Weinrib; Morgantwn, WV: E. Jones; Morristown, NJ: H. Starkman; Mount Vernon, WA: D. White; Mountain View, CA: L. Doberne, M. Greenfield; Muncie, IN: K. Alexander; Napa, CA: C. O'Sullivan; Naples, FL: R. Duncan; Naranja, FL: G. Barandiaran, J. Yunis, L. Nunez, V. Ramos; Nashua, NH: E. Holland; Natrona Heights, PA: W. R. Balash; Neptune, NJ: J. Sher; New Brunswick, NJ: R. Agrin; New Orleans, LA: J. Frentz; New York, NY: I. Fennoy; Newhall, CA: S. Baron; Nipomo, CA: J. Door; Norfolk, VA: A. Vinik; North Las Vegas, NV: F. Savery; Oakland, CA: F. Gareis, R. Mack, D. Devoe, Y. Fan; Oklahoma City, OK: D. Domek; Olympia, WA: D. Kelley; Onalaska, WI: T. Roberts; O'Neill, NE: B. Gutshall; Orange, CA: I. Madu, R. Poucher; Orlando, FL: M. Mengel, P. Desrosiers, R. A. Banks, B. Kopp; Pacific Grove, CA: I. Fishman; Pacific Palisades, CA: D. Geller, W. Smith; Palm Bay, FL: J. A. Duncan; Palm Beach Gardens, FL: O. Nyman, M. Vaccarello-Cruz; Parkersburg, WV: F. L. Schwartz; Pasadena, CA: O. Olambiwonnu; Paso Robles, CA: M. Ortiz; Pembroke Pines, FL: S. Freedman; Pendleton, OR: S. Merrill; Peoria, IL: J. Wise; Philadelphia, PA: I. Rezvani, D. Doyle, P. Hale, C. Singer-Granick, W. Fore; Phoenix, AZ: A. Perelman, R. Clemmons, R. Johnsonbaugh; Pittsburgh, PA: A. R. Gonzalez;

SUPPLEMENTARY DATA

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Calculations of Risk Scores

ABRS (including ICA) =

$$\begin{aligned} & [0.819*(GADA\ Positivity)]+[53.433*(GADA\ Level)]+[-53.647*(GADA\ Positivity\ x\ GADA\ Level)] \\ & \quad + \\ & [-0.132*(IA-2A\ Positivity)]+[-1.005*(IA-2A\ Level)]+[2.475*(IA-2A\ Positivity\ x\ IA-2A\ Level)] \\ & \quad + \\ & [0.818*(mIAA\ Positivity)]+[108.186*(mIAA\ Level)]+[-107.559*(mIAA\ Positivity\ x\ mIAA\ Level)] \\ & \quad + \\ & [0.670*(ZnT8A\ Positivity)]+[-30.247*(ZnT8A\ Level)]+[30.187*(ZnT8A\ Positivity\ x\ ZnT8A\ Level)] \\ & \quad + \\ & [0.167*(ICA\ Positivity)]+[-0.024*(ICA\ Level)]+[0.024*(ICA\ Positivity\ x\ ICA\ Level)] \end{aligned}$$

SUPPLEMENTARY DATA

ABRS (excluding ICA) =

$$\begin{aligned} & [0.837*(\text{GADA Positivity})]+[53.244*(\text{GADA Level})]+[-53.396*(\text{GADA Positivity} \times \text{GADA Level})] \\ & \quad + \\ & [-0.139*(\text{IA-2A Positivity})]+[-0.433*(\text{IA-2A Level})]+[1.982*(\text{IA-2A Positivity} \times \text{IA-2A Level})] \\ & \quad + \\ & [0.840*(\text{mIAA Positivity})]+[113.151*(\text{mIAA Level})]+[-112.496*(\text{mIAA Positivity} \times \text{mIAA Level})] \\ & \quad + \\ & [0.711*(\text{ZnT8A Positivity})]+[-32.821*(\text{ZnT8A Level})]+[32.817*(\text{ZnT8A Positivity} \times \text{ZnT8A Level})] \end{aligned}$$

DPTRS =

$$\begin{aligned} & +1.569*[\log\text{-BMI (kg/m}^2)] \\ & -0.056*[\text{Age (years)}] \\ & +0.813*[\text{Total Glucose (mg/dl)/100}] \\ & +0.476*[\log\text{-Fasting C-peptide (ng/ml)}] \\ & -0.848*[\text{Total C-peptide (ng/ml)/10}] \\ & (\text{Totals do not include fasting values.}) \end{aligned}$$

$$\text{Combined Risk Score (including ICA)} = [0.906*(\text{DPTRS})]+[0.569*(\text{ABRS})]$$

$$\text{Combined Risk Score (excluding ICA)} = [0.906*(\text{DPTRS})]+[0.571*(\text{ABRS})]$$

Conversion of Risk Scores to Risk Estimates

The risk scores can be converted to risk estimates of T1D by the following equation.

$$\text{Risk} = 1 - (\text{proportion without disease over the defined period})^{\exp(\text{risk score} - \text{mean risk score of cohort})}$$

The equations for the 3-year risk calculations of the autoantibody risk scores and an example are shown below.

ABRS (including ICA)

Mean Risk Score = 1.52

Proportion without disease at 3 years = 0.83

$$\text{Risk} = 1 - (0.83)^{\exp(\text{risk score} - 1.52)}$$

ABRS (excluding ICA)

Mean risk score = 1.53

Proportion without disease at 3 years = 0.83

$$\text{Risk} = 1 - (0.83)^{\exp(\text{risk score} - 1.53)}$$

Combined Risk Score (including ICA)

Mean risk score = 6.45

Proportion without disease at 3 years = 0.83

$$\text{Risk} = 1 - (0.83)^{\exp(\text{risk score} - 6.45)}$$

Combined Risk Score (excluding ICA)

Mean risk score = 6.46

Proportion without disease at 3 years = 0.83

$$\text{Risk} = 1 - (0.83)^{\exp(\text{risk score} - 6.46)}$$

SUPPLEMENTARY DATA

Example: An individual with a calculated (see above) ABRS (including ICA) value of 2.00:

$$\text{Risk at 3 Years} = 1 - (0.83)^{\exp(2.00 - 1.52)} = 0.26$$

An individual with an ABRS (including ICA) value of 3.00:

$$\text{Risk at 3 Years} = 1 - (0.83)^{\exp(3.00 - 1.52)} = 0.56$$

Supplementary Table 1. Autoantibody levels of outliers excluded from analyses along with ranges of values after exclusion

	Outlier Level	Range without Outlier
MIAA Positives	2.47	0.011 to 0.838
MIAA Negatives	-0.023	-0.010 to 0.010
GADA Negatives	-0.077	-0.034 to 0.029
ICA Positives	10,240	10 to 2,560

Supplementary Table 2. Frequencies of negativity and positivity, and levels** of autoantibodies for the 784 TrialNet participants studied

	Negative		Positive	
	Total	Levels	Total	Levels
IA-2A	512 (65%)	0.005±0.13	272 (35%)	0.340±0.322
GAD65	180 (23%)	0.005±0.013	604 (77%)	0.564±0.331
mIAA	463 (59%)	0.001±0.003	321 (41%)	0.053±0.082
ZnT8A	523 (67%)	0.002±0.006	261 (33%)	0.314±0.241
ICA*	505 (64%)	0	179 (36%)	80 (20,160)

*Levels did not vary in the negative range for ICA.

**Mean±SD levels are shown with the exception of ICA for which median and quartile boundaries are shown.

Supplementary Table 3. Values (mean±SD) of the DPTRS components for the 704 TrialNet participants studied

DPTRS Components	Values
Age (Years)	18.96±13.60
Log BMI	3.05±0.28 (22.00±6.63)*
Log Fasting C-peptide	0.30±0.52 (1.54±0.79)*
C-peptide Sum/10	2.40±0.96
Glucose Sum/100	5.32±1.07

*Actual values are shown in parentheses