OGTT Glucose-Response-Curves, Insulin Sensitivity and β-cell Function in RISE: Comparison Between Youth and Adults at Randomization and in Response to Interventions to Preserve β-cell Function

Supplemental Materials

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Supplemental Table 1. Change in OGTT Glucose-Response-Curves from Randomization to Month 12 in Youth and Adult RISE Participants by Treatment Group*

Change in OGTT-Glucose-Response-Curves	Youth (n=76)		Chi-square P-value	Adults (n=145)		Chi-square P-value
	Glargine ➔ Metformin (n=37)	Metformin Alone (n=39)		Glargine ➔ Metformin (n=61)	Metformin Alone (n=84)	
Improvement	4 (10.8%)	7 (17.9%)	0.671	9 (14.7%)	19 (22.6%)	0.487
Worsening	8 (21.6%)	8 (20.5%)		13 (21.3%)	16 (19.0%)	
No Change	25 (67.6%)	24 (61.5%)		39 (63.9%)	49 (58.3%)	

* P-value from Chi-square test evaluating differences in the change in OGTT glucose-response-curves from baseline to month 12 between treatment groups within each age group. From among the 85 youth in the baseline analysis, 9 were excluded because of missing or incomplete OGTT data at month 12. Adults in the longitudinal analysis included those treated with metformin alone in the Medication Study (n=65) and Surgery BetaFat Study (n=43), plus those treated with glargine followed by metformin (n=67), total n=175. From among those, 30 were excluded due to missing or incomplete OGTT data at month 12.

Supplemental Table 2. Month 12 HbA1c, Insulin Sensitivity and β-cell Function Parameters and the Change in Them from Randomization to Month 12 in the Longitudinal Cohort of Youth and Adults Combined, Categorized by Baseline Glucose-Response-Curves*

Characteristics at month 12 and change from baseline	**Youth (n=76) and Adults (n=145) Combined (N=221)**			**P value for GRC differences**
	Biphasic (N=23)	**Monophasic (N=169)**	**Incessant increase (N=29)**	
Month 12 HbA1c (mmol/mol)	38.0 ± 4.1	38.9 ± 6.4	41.7 ± 9.9	0.078
Δ 0-12 change	-1.2 ± 3.4	-0.7 ± 4.6	+0.7 ± 7.2	0.245
Month 12 M/I ($x10^{-5}$ mmol/kg/min/pmol/L)	2.7 [1.6, 5.8]	3.2 [1.6, 5.2]	3.3 [1.7, 6.2]	0.931
Δ 0-12 change	+1.2 ± 2.3	+0.8 ± 3.0	+1.1 ± 2.6	0.694
Month 12 ACPRg (nmol/L)	1.1 [0.6, 2.5]	0.8 [0.4, 1.3]	0.8 [0.2, 1.3]	0.008[a]
Δ 0-12 change	+0.1 ± 0.8	0.0 ± 0.5	+0.2 ± 0.3	0.260
Month 12 ACPRmax (nmol/L)	5.4 [3.2, 8.1]	5.4 [3.9, 7.1]	4.0 [3.2, 5.5]	0.012[b]
Δ 0-12 change	-1.3 ± 1.4	-0.6 ± 1.7	-0.4 ± 1.2	0.172
Month 12 Steady-state C-peptide (nmol/L)	4.8 [2.9, 5.7]	4.2 [3.0, 5.4]	3.2 [2.2, 4.3]	0.027[c]
Δ 0-12 change	-0.3 ± 1.0	-0.4 ± 1.2	0.0 ± 0.6	0.919

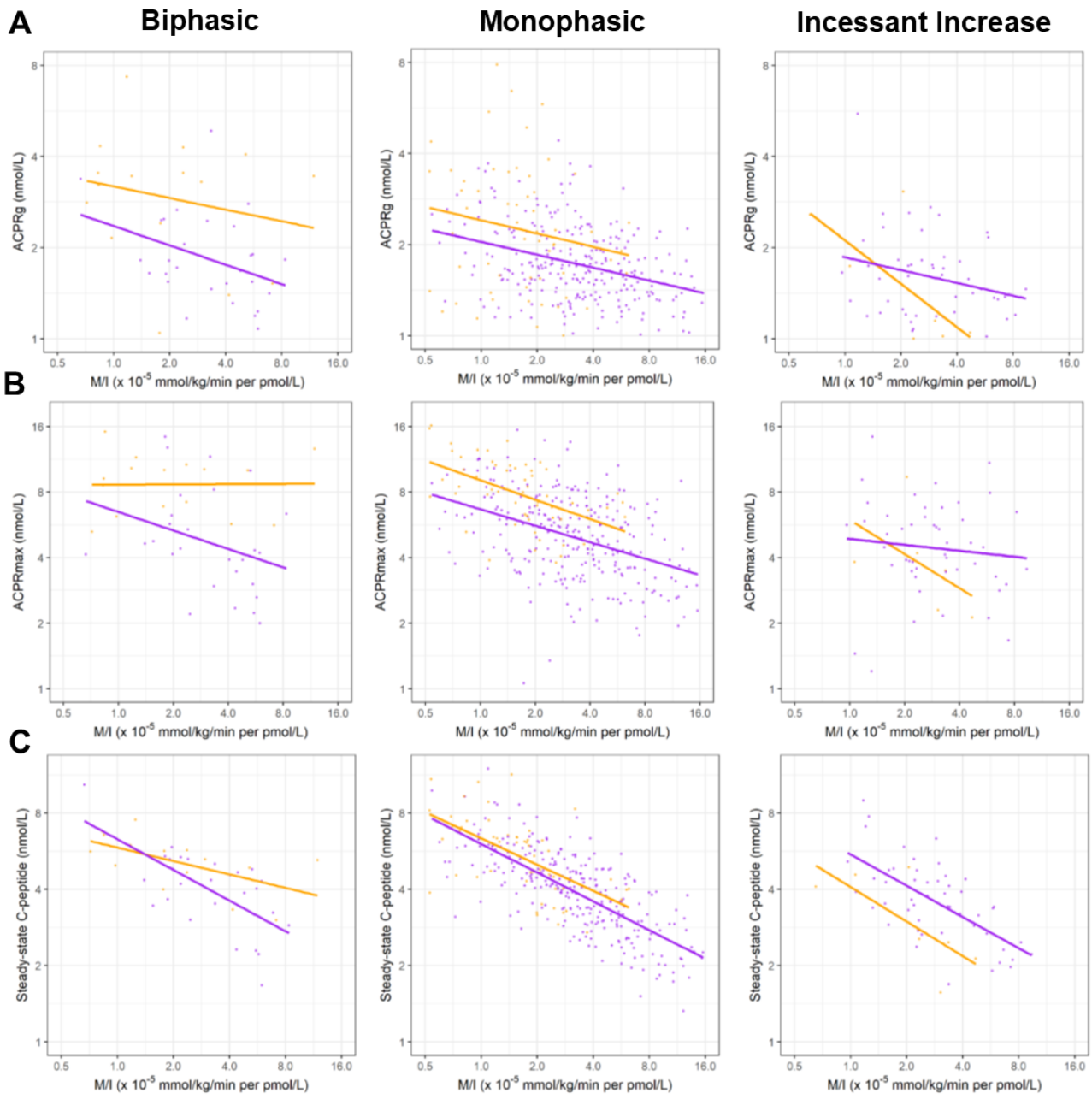
*Data are mean ± SD or median [25th-75th percentile] for skewed variables. P-values from unadjusted linear regression models. GRC: glucose-response-curve

[a] Biphasic different from the other 2 baseline curve types.

[b] Incessant increase different from monophasic.

[c] Incessant increase different from monophasic and biphasic.

Supplemental Figure 1. Relationship of Log-transformed M/I and Log-transformed ACPRg (A), ACPRmax (B), and Steady-state (Second Phase) C-peptide (C) by OGTT Glucose-Response-Curves in Youth (in orange) and Adult (in purple) RISE Participants*



* The axes are logged with the values on each being natural numbers. Lines were fit by linear regression on the log-log scale. Within each OGTT-glucose-response-curve, the slopes relating the three β-cell response measures to M/I were all significant ($p<0.05$) in both age groups, except for the ACPRg and ACPRmax slopes within the biphasic group in both youth and adults and within the incessant increase group in adults. Age group differences were not significant except

for ACPRg and ACPRmax within the biphasic and monophasic group ($p<0.01$). The slopes for youth and adults did not differ (all $p>0.05$) except for the two ACPRmax slopes within the incessant increase curve type (interaction $p=0.04$). Statistical significance may be impacted by smaller numbers within the biphasic and incessant increase groups.

APPENDIX

RISE Consortium Investigators

University of Chicago Clinical Research Center and Jesse Brown VA Medical Center
(Chicago, IL)
David A. Ehrmann, MD*
Karla A. Temple, PhD, RD**
Abby Rue**
Elena Barengolts, MD
Babak Mokhlesi, MD, MSc
Eve Van Cauter, PhD
Susan Sam, MD, MSc
M. Annette Miller, RN

VA Puget Sound Health Care System and University of Washington
(Seattle, WA)
Steven E. Kahn, MB, ChB*
Karen M. Atkinson, RN**
Jerry P. Palmer, MD
Kristina M. Utzschneider, MD
Tsige Gebremedhin, BS
Abigail Kernan-Schloss, BA
Alexandra Kozedub, MSN, ARNP
Brenda K. Montgomery, RN, BSN, CDE
Emily J. Morse, BS

Indiana University School of Medicine and Richard L. Roudebush VA Medical Center
(Indianapolis, IN)
Kieren J. Mather, MD*
Tammy Garrett, RN**
Tamara S. Hannon, MD
Amale Lteif, MD
Aniket Patel MD
Robin Chisholm, RN
Karen Moore, RN
Vivian Pirics, RN
Linda Pratt, RN

University of Colorado Denver/Children's Hospital Colorado
(Denver, CO)
Kristen J. Nadeau, MD, MS*
Susan Gross, RD**
Philip S. Zeitler, MD, PhD
Jayne Williams, RN, MSN, CPNP
Melanie-Cree Green, MD, PhD
Yesenia Garcia Reyes, MS
Krista Vissat, RN, MSN, CPNP

* denotes Principal Investigator
** denotes Program Coordinator

Children's Hospital of Pittsburgh of UPMC
(Pittsburgh, PA)
Silva A. Arslanian, MD*
Kathleen Brown, RN, CDE**
Nancy Guerra, CRNP
Kristin Porter, RN, CDE

Yale University
(New Haven, CT)
Sonia Caprio, MD*
Mary Savoye, RD, CDE**
Bridget Pierpont, MS**

University of Southern California Keck School of Medicine/Kaiser Permanente Southern California
(Los Angeles, CA)
Thomas A. Buchanan, MD*
Anny H. Xiang, PhD*
Enrique Trigo, MD**
Elizabeth Beale, MD
Fadi N. Hendee, MD
Namir Katkhouda, MD
Krishan Nayak, PhD
Mayra Martinez, MPH
Cortney Montgomery, BS
Xinhui Wang, PhD

George Washington University Biostatistics Center
(RISE Coordinating Center; Rockville, MD)
Sharon L. Edelstein, ScM*
John M. Lachin, ScD
Ashley N. Hogan, MPH

Northwest Lipid Research Laboratories
(Central Biochemistry Laboratory; Seattle, WA)
Santica Marcovina, PhD*
Jessica Harting**
John Albers, PhD

Belmar Pharmacy
(Drug Distribution Center; Lakewood, CO)
Dave Hill

NIH/NIDDK
(Bethesda, MD)
Peter J. Savage, MD
Ellen W. Leschek, M