A. Youth and Adult Medication Protocols



B. Adult Surgery Protocol



Timeline of measurements and procedures in the three RISE protocols examining (A) the effect of medication interventions in youth and adults and (B) lap band surgery in adults.

Supplemental Figure 2A



Plasma glucose concentrations during the hyperglycemic clamp in youth in the RISE Pediatric Medication Study. (A) glargine followed by metformin and (B) metformin alone at baseline (red), after 12 months of intervention (blue) and after 3 months of intervention withdrawal (green). Data are displayed as mean \pm SEM.

Supplemental Figure 2B



Plasma C-peptide concentrations during the hyperglycemic clamp in youth in the RISE Pediatric Medication Study. (A) glargine followed by metformin and (B) metformin alone at baseline (red), after 12 months of intervention (blue) and after 3 months of intervention withdrawal (green). Data are displayed as mean ± SEM.





Box plots illustrating the effect of treatment and treatment withdrawal on the glucagon responses during the hyperglycemic clamp in youth in the RISE Pediatric Medication Study. (A) Fasting glucagon, (B) steady-state glucagon and (C) acute glucagon response at baseline (red), after 12 months of intervention (blue) and after 3 months of intervention withdrawal (green) for the two intervention arms, glargine followed by metformin (first row) and metformin alone (second row). Data displayed are the median, interquartile range and the mean shown as a diamond.

Supplemental Figure 4A



Plasma glucose concentrations during the oral glucose tolerance test in youth in the RISE Pediatric Medication Study. (A) glargine followed by metformin and (B) metformin alone at baseline (red), after 12 months of intervention (blue) and after 3 months of intervention withdrawal (green). Data are displayed as mean \pm SEM.

Supplemental Figure 4B



Plasma C-peptide concentrations during the oral glucose tolerance test in youth in the RISE Pediatric Medication Study. (A) glargine followed by metformin and (B) metformin alone at baseline (red), after 12 months of intervention (blue) and after 3 months of intervention withdrawal (green). Data are displayed as mean \pm SEM.



Plasma glucose concentrations during the hyperglycemic clamp in adults in the RISE Adult Medication Study. (A) glargine followed by metformin, (B) metformin alone, (C) liraglutide plus metformin and (D) placebo at baseline (red), after 12 months of intervention (blue) and after 3 months of intervention withdrawal (green). Data are displayed as mean ± SEM.



Plasma C-peptide concentrations during the hyperglycemic clamp in adults in the RISE Adult Medication Study. (A) glargine followed by metformin, (B) metformin alone, (C) liraglutide plus metformin and (D) placebo at baseline (red), after 12 months of intervention (blue) and after 3 months of intervention withdrawal (green). Data are displayed as mean ± SEM.

Supplemental Figure 6





Box plots illustrating the effect of treatment and treatment withdrawal on the glucagon responses during the hyperglycemic clamp in adults in the RISE Adult Medication Study. (A) Fasting glucagon, (B) steady-state glucagon and (C) acute glucagon response at baseline (red), after 12 months of intervention (blue) and after 3 months of intervention withdrawal (green) for the four intervention arms, glargine followed by metformin (first row), metformin alone (second row), liraglutide plus metformin (third row) and placebo (fourth row). Data displayed are the median, interquartile range and the mean shown by a diamond.



Plasma glucose concentrations during the oral glucose tolerance test in adults in the RISE Adult Medication Study. (A) glargine followed by metformin, (B) metformin alone, (C) liraglutide plus metformin and (D) placebo at baseline (red), after 12 months of intervention (blue) and after 3 months of intervention withdrawal (green). Data are displayed as mean ± SEM.



Plasma C-peptide concentrations during the oral glucose tolerance test in adults in the RISE Adult Medication Study. (A) glargine followed by metformin, (B) metformin alone, (C) liraglutide plus metformin and (D) placebo at baseline (red), after 12 months of intervention (blue) and after 3 months of intervention withdrawal (green). Data are displayed as mean ± SEM.

Supplemental Figure 8A



Plasma glucose concentrations during the hyperglycemic clamp in adults in the RISE Adult Surgery (BetaFat) Study. (A) lap band surgery and (B) metformin alone at baseline (red), after 12 months (blue) and 24 months of intervention (green). Data are displayed as mean ± SEM.

Supplemental Figure 8B



Plasma C-peptide concentrations during the hyperglycemic clamp in adults in the RISE Adult Surgery (BetaFat) Study. (A) lap band surgery and (B) metformin alone at baseline (red), after 12 months (blue) and 24 months of intervention (green). Data are displayed as mean ± SEM.

Supplemental Figure 9



Box plots illustrating the effect of treatment on the glucagon responses during the hyperglycemic clamp in adults in the RISE Adult Surgery (BetaFat) Study. (A) Fasting glucagon, (B) steady-state glucagon and (C) acute glucagon response at baseline (red), after 12 (blue) and 24 months of intervention (green) for the two intervention arms, lap band surgery (first row) and metformin alone (second row). Data displayed are the median, interquartile range and the and the mean shown as a diamond.

Supplemental Figure 10A



Plasma glucose concentrations during the oral glucose tolerance test in adults in the RISE Adult Surgery (BetaFat) Study. (A) lap band surgery and (B) metformin alone at baseline (red), after 12 months (blue) and 24 months of intervention (green). Data are displayed as mean ± SEM.

Supplemental Figure 10B



Plasma C-peptide concentrations during the oral glucose tolerance test in adults in the RISE Adult Surgery (BetaFat) Study. (A) lap band surgery and (B) metformin alone at baseline (red), after 12 months (blue) and 24 months of intervention (green). Data are displayed as mean \pm SEM.

APPENDIX 1

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