Type 2 Diabetes (Y-T2D) in Youth

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Disclosures

Dr. Nadeau has no Conflicts of Interest to Disclose

Dispelling Myths to Prevent CVD

Fact: Cardiovascular disease is the #1 killer people with diabetes

1. **Myths preventing reduction of CVD risk in Y-T2D:**
   - **Y-T2D should be thought of as an earlier version of adult-onset T2D**
   - **Interventions used in adult-onset T2D are too aggressive for Y-T2D**

Y-T2D Characteristics

N		699
Age		14.0 (12,16)
Duration of DM (months)		5 (4,9)
BMI Z-score		2.21 (1.89, 2.47)
Female		64.9%
Ethnicity	White	19.9%
	Hispanic	42.2%
	AA	31.6%
	AI	6.2%
FH diabetes		
	Nuclear	59.6%
	Nuclear + GP	89.4%
GDM		33.3%

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Clinical Trial to Maintain Glycemic Control in Youth with Type 2 Diabetes

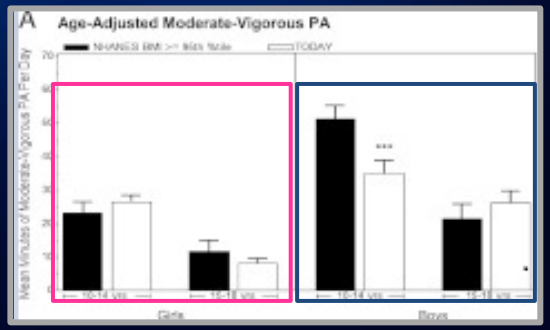
TODAY Study Group*

Female T2D Predominance in Youth, not Adults

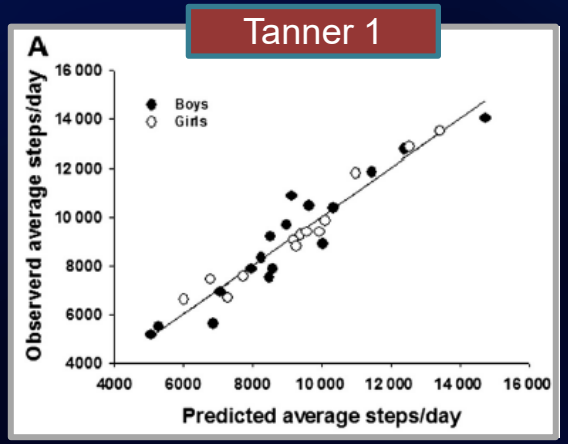
- Youth 35% male
- Adults 53% male

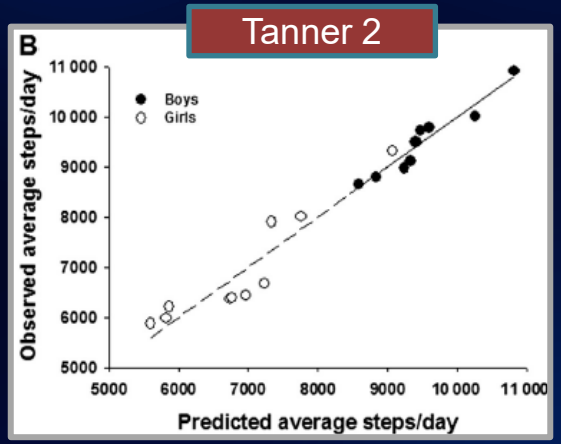
Why Female Y-T2D Predominance?
Girls Have Less Physical Activity (PA), Beginning Early in Puberty

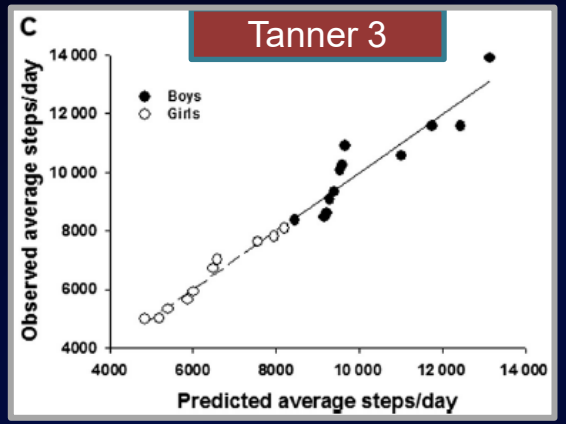
Girls with obesity or T2D have lower MVPA than boys which worsens in later teen years (NHANES and TODAY)



Kriska et al. Pediatrics 2013;131:e850-e856







Rudroff, J Pediatr 2013

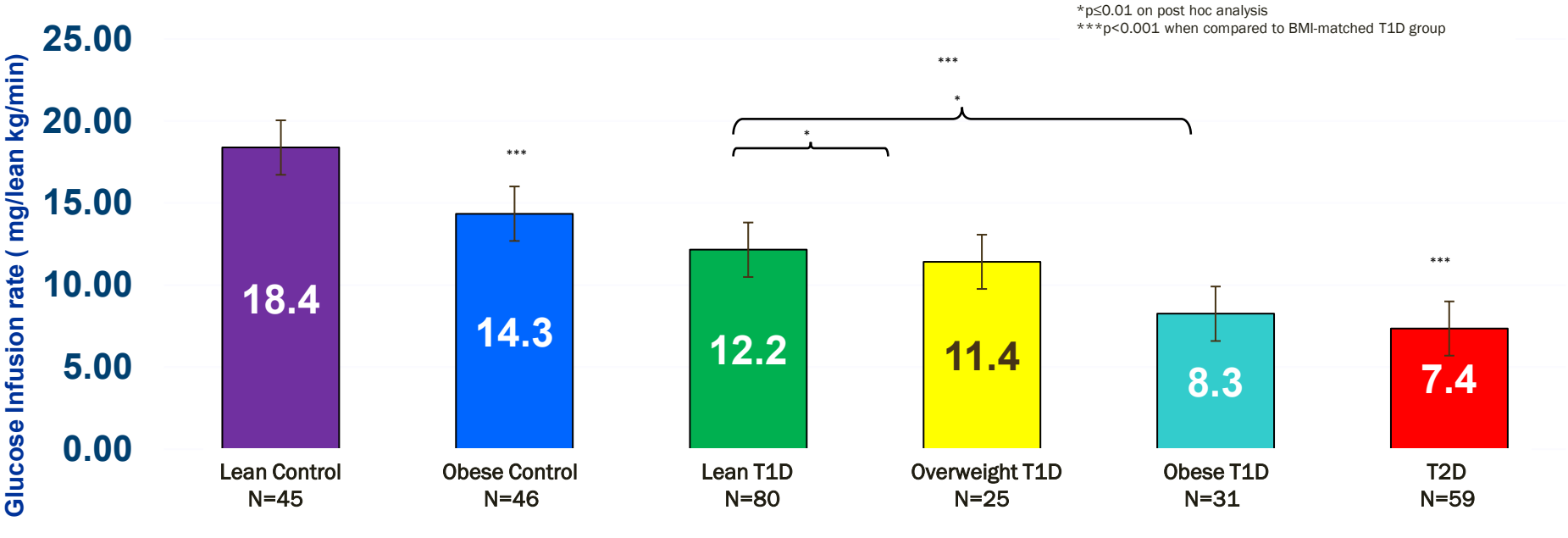
American Diabetes Association. Diabetes Care

Metabolic Syndrome is Prominent in YO-T2D

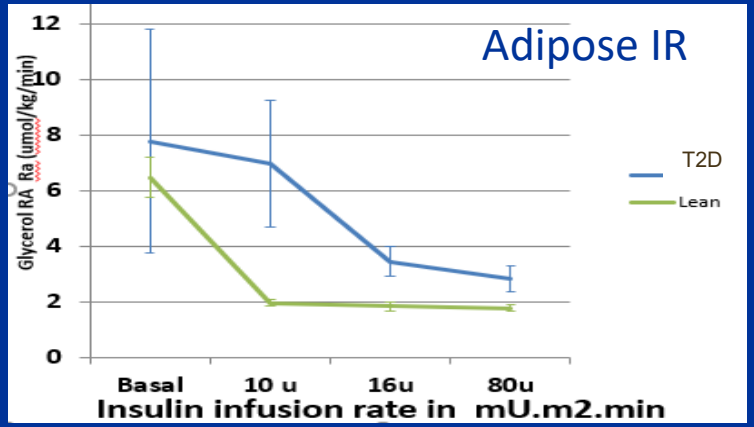
	Lean T1D	Obese T1D	T2D	p-value[a]
N	82	26	59	
AST (units/L)	20 (13,28)	27 (16, 35)	25 (15, 35)	0.351
ALT (units/L)	25 (16, 28)	26 (20, 36)	**32 (18, 58)**	**0.041**
Adiponectin (units/L)	11 (7.5, 14)	**7.6 (6.2, 12.0)**	**5.1 (3.5, 8.2)**	**0.044**
Leptin (units/L)	10 (3.3, 15)	**27 (18, 36)**	**28 (19, 39)**	0.898
hsCRP (units/L)	0.29 (0.15, 0.53)	**2.3 (0.9, 3.7)**	**3.3 (1.1, 6.2)**	0.175
TG (mg/dL)	74 (54, 95)	**90 (67, 115)**	**142 (86, 226)**	**0.005**
HDL (mg/dL)	46 (9.2)	**44±11**	**38±12**	**0.006**

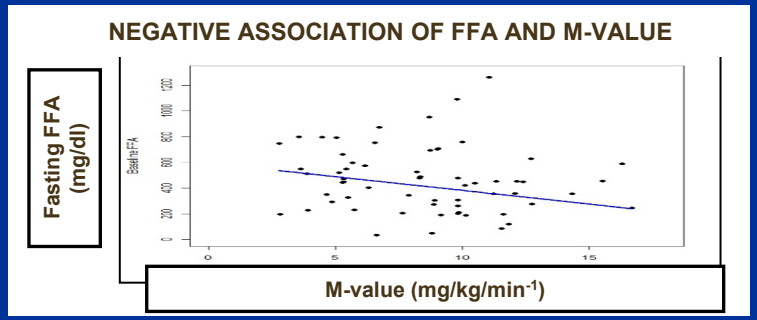
American Diabetes Association. Diabetes Care

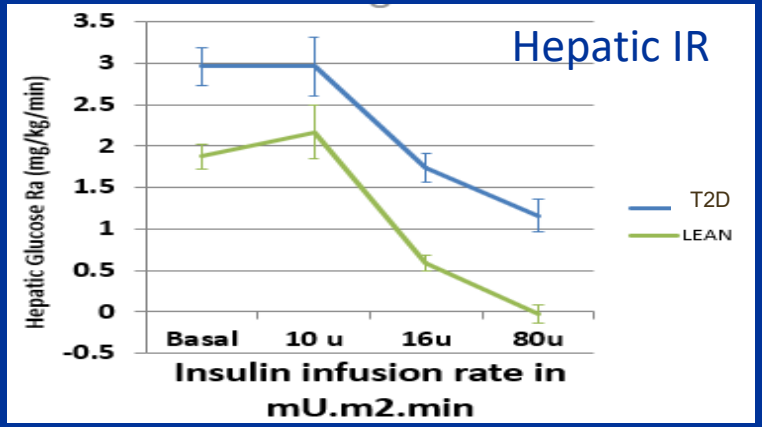
Insulin Resistance (IR) is Prominent in YO-T2D

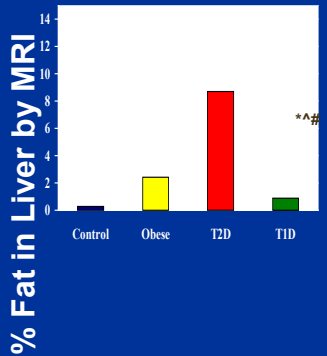


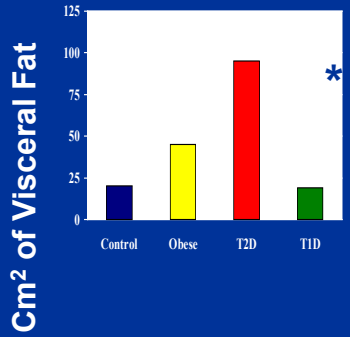
Adipose Hepatic IR is Prominent in YO-T2D and Correlate with Muscle IR and with Hepatic and Visceral Fat



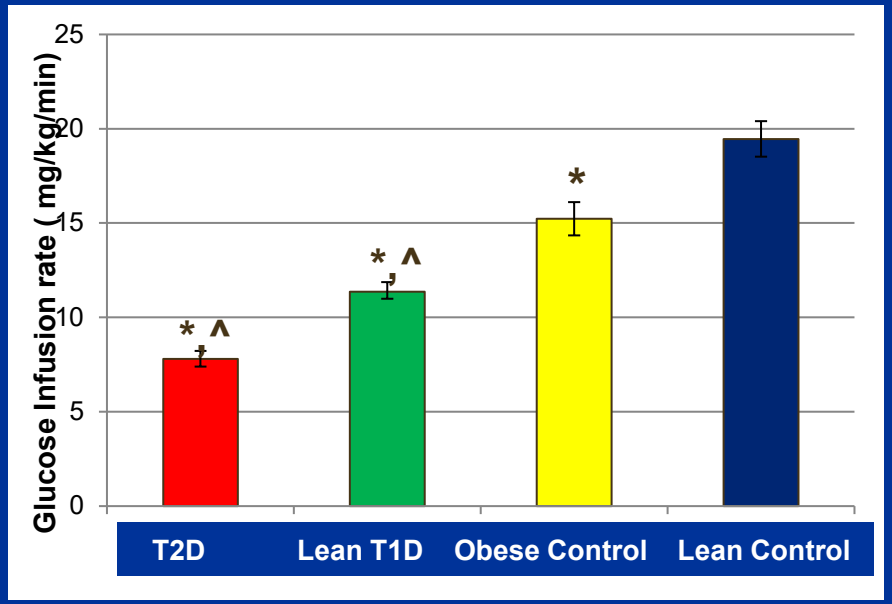




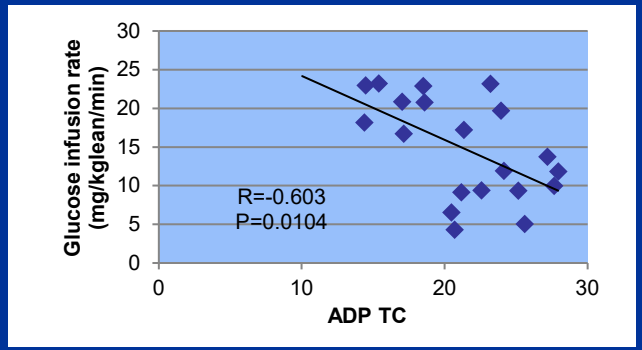




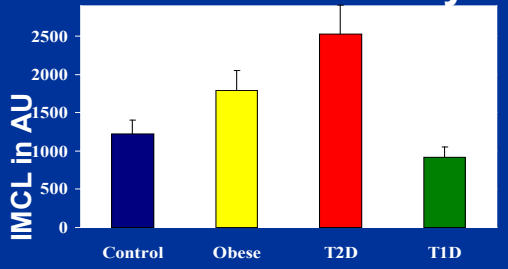
Muscle IR in YO-T2D also Correlates with Mitochondrial Function and Intramyocellular Lipid (IMCL)



Calf Mitochondrial Function by ^{31}P MRS



Soleus IMCL by ^{1}H MRS

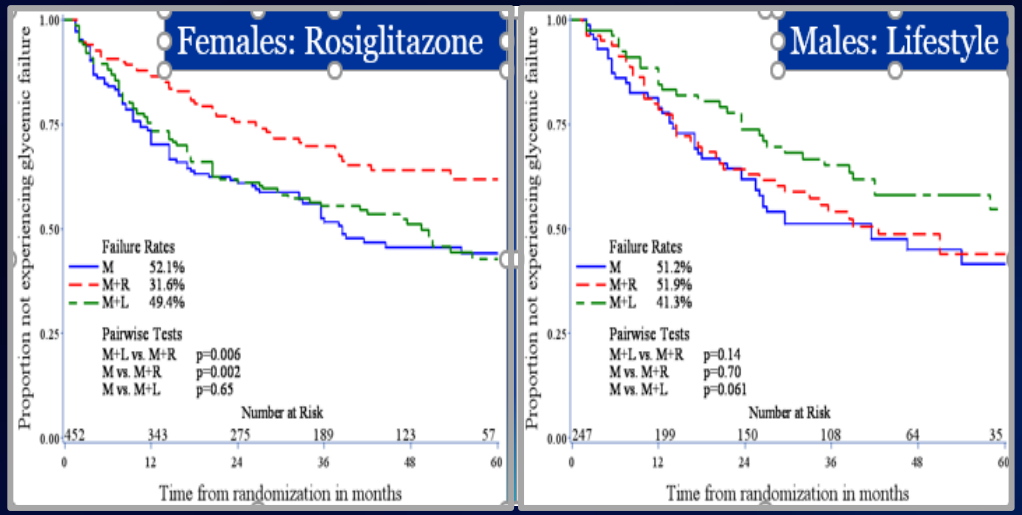


Lean Control Obese Control T2D Lean T1D

Nadeau *et al* JCEM 2010, Nadeau *et al* JCEM 2009, Green and Nadeau Diabetes 2016

More Y-T2D in TODAY Failed Metformin Rx than Adults, and Girls Responded Differently than Boys to Diabetes Treatments

Treatment Arm	Failure Rate	Median Time to Failure
Metformin + Rosiglitazone	38.6%	10.3 months
Metformin + Lifestyle	46.6%	12.0 months
Metformin alone	51.7%*	11.8 months



*52% of Y-T2D experienced treatment failure vs. 12% of adults in ADOPT with same duration of metformin treatment

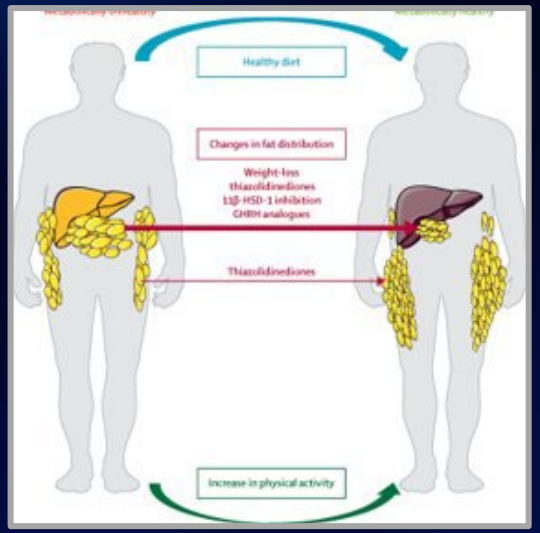
TODAY Study Group: N Engl J Med 366:2247-2256; 2012

ADOPT data Adapted from Kahn SE et al: N Engl J Med 355:2427-2443; 2006

Unlike Adults, Y-T2D do not Decrease Visceral to Subcutaneous Adipose Tissue Ratio (VAT:SAT) with Rosiglitazone

Adults

- Traditionally TZD's improve glycemia by decreasing visceral adiposity and improving insulin sensitivity[1,2,3]



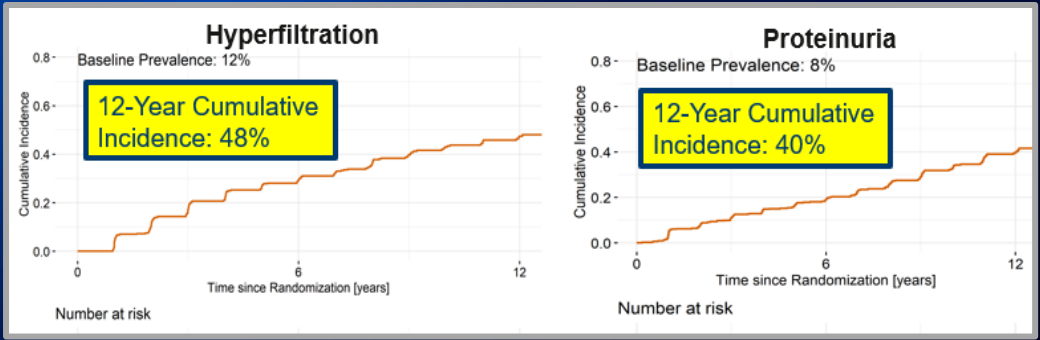
Youth

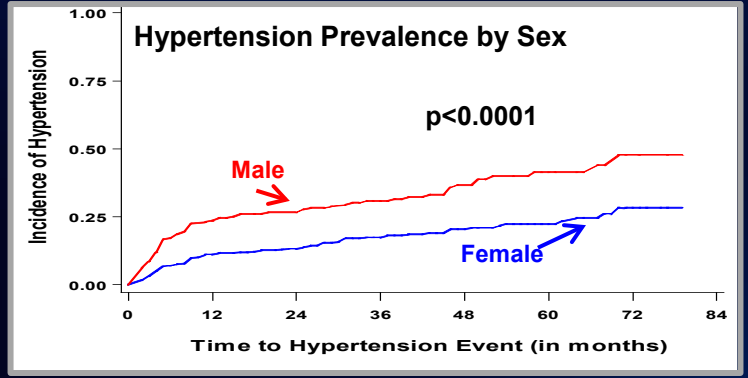
- In TODAY[4], improvements in glycemia with rosiglitazone not mediated by VAT decreases (both SAT and VAT increased with rosiglitazone, and more vs. MET or MET plus lifestyle)
- Argues for separate studies in youth

1. Carey et al Obesity Research 2002
2. Iozzo et al Diabetes Care 2003
3. Virtanen Diabetes 2003

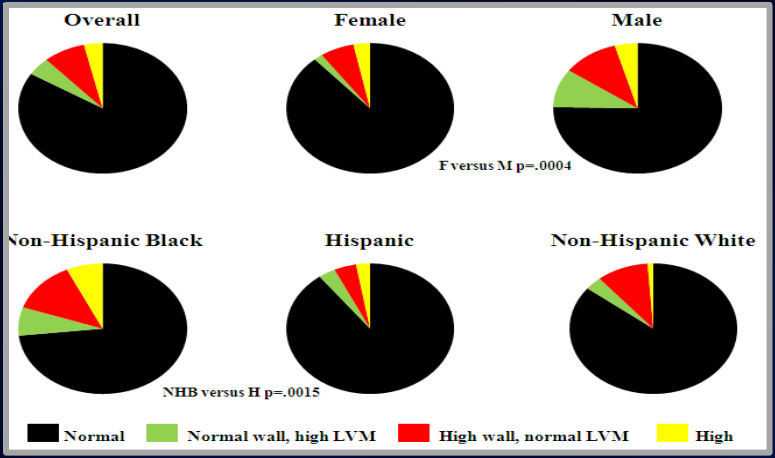
TODAY Study Group. Diabetes Care, Aug 2019 11

Frequent Diabetes Complications in TODAY Despite Short T2D Duration





Cardiac Hypertrophy



Multigenerational Consequences of Pregnancy

- Despite frequent contraception education and provision, 10% pregnant, 30% again
- 22% LGA, 6% SGA, 23% pre-term, similar to adults with T1D or T2D (4x general population)
- 21% (50% cardiac) major congenital anomalies, 4x the 4.6% reported in adult T2D.

TODAY Study group Diabetes Care 36:1735, 2013

American Diabetes Association. Diabetes Care

Stopping GDM

Stopping GDM Toolkits

General Toolkit
This link provides nation-wide resources to support Stopping GDM behaviors

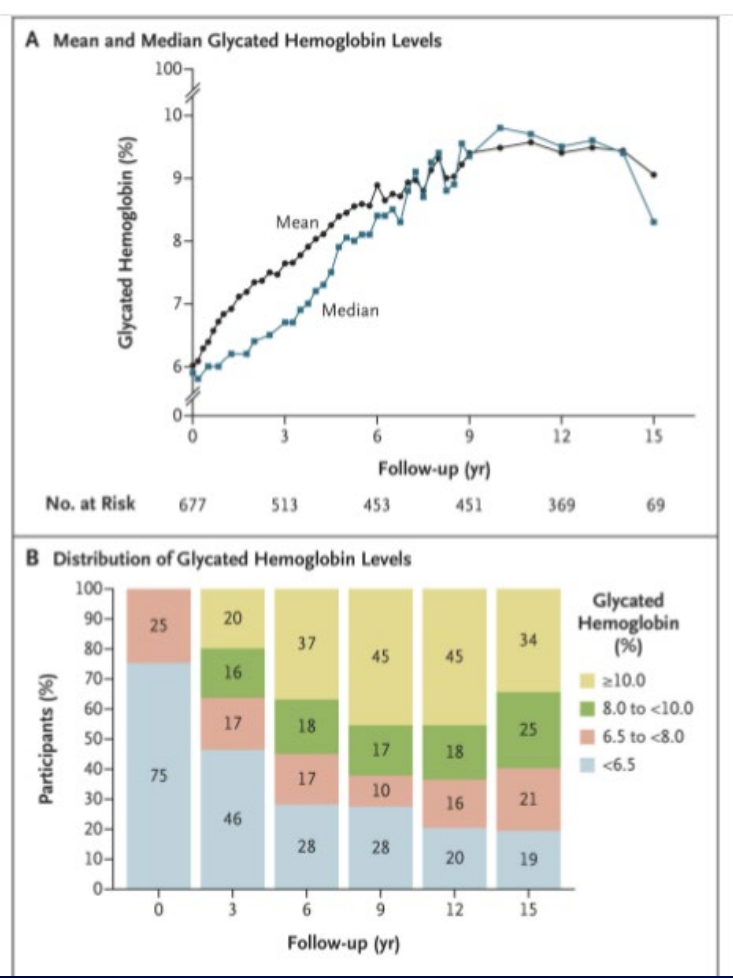
Shiprock Toolkit
This link provides Shiprock, NM-specific resources to support Stopping GDM behaviors

St. Regis Mohawk Toolkit
This link provides St Regis, NY-specific resources to support Stopping GDM behaviors

Tulsa and University of Oklahoma Toolkit
This link provides Tulsa, OK-specific resources to support Stopping GDM behaviors

Portland toolkit (Coming Soon)
This link provides Portland, OR-specific resources to support Stopping GDM behaviors

Stopping GDM https://www.stoppinggdm.com/



ORIGINAL ARTICLE

Long-Term Complications in Youth-Onset Type 2 Diabetes

TODAY Study Group*

Article Figures/Media Metrics

33 References

July 29, 2021
N Engl J Med 2021; 385:416-426
DOI: 10.1056/NEJMoa2100165
Chinese Translation 中文翻译

At the study-end, mean (±SD) age of the 500 participants who were assessed from March 2014 through January 2020 and included in the analyses was 26.4±2.8 years, and mean time since the T2D diagnosis was 13.3±1.8 years.

Risk factors for the development of complications included minority race/ethnicity hyperglycemia, insulin resistance, hypertension and dyslipidemia.

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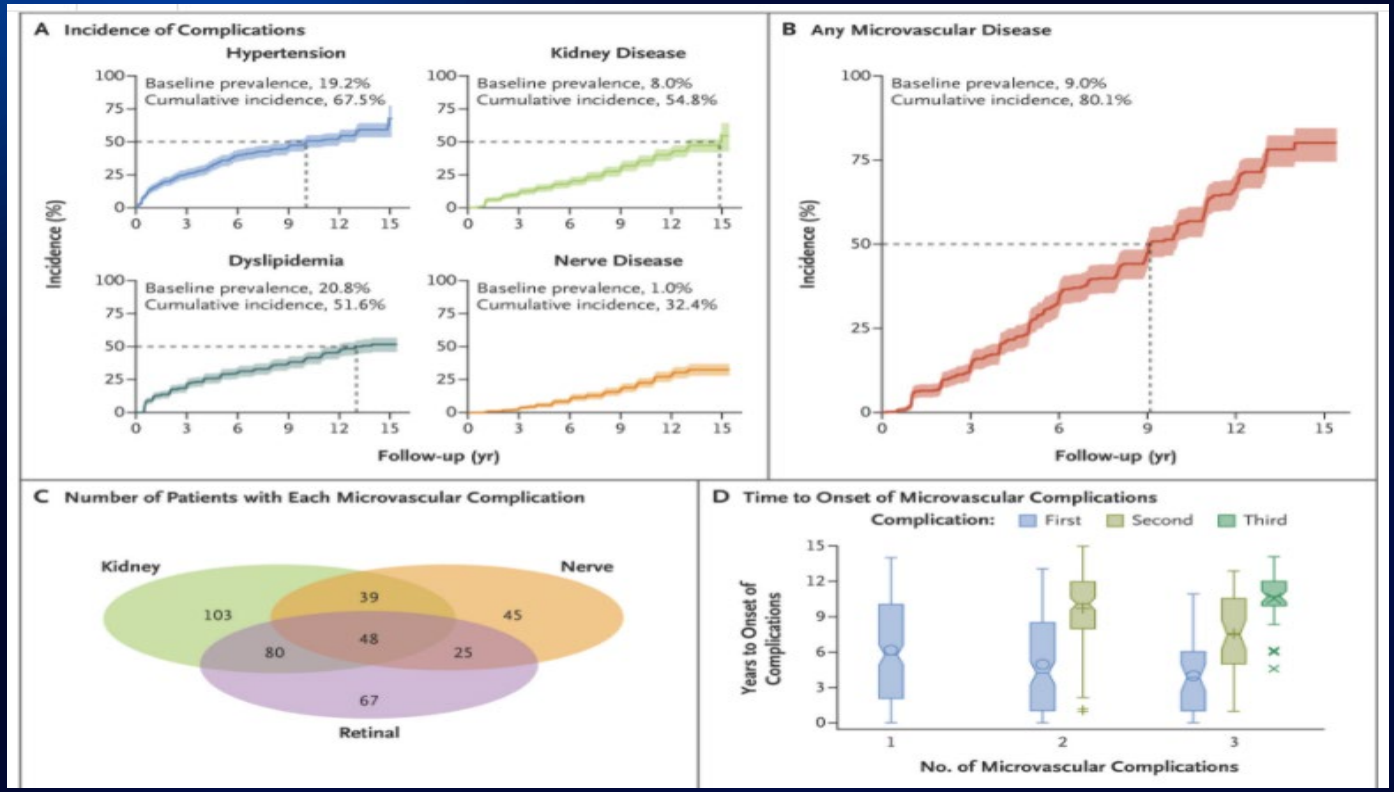


-Prevalence of retinal disease 13.7% in 2010-2011; 51.0% in 2017-2018.

-17 serious CV events (4 MI, 6 CHF, 3 CAD events and 4 strokes

-6 deaths (1 MI, kidney failure, drug overdose, sepsis; 2 sepsis with multiorgan failure).

Is it possible to intervene to preserve or improve β-cell function in youth and adults with IGT or early T2D?

Funding: NIDDK, ADA, Department of Veterans Affairs, and Kaiser Permanente Southern California. Additional financial material support from Abbott Laboratories, Allergan, Apollo Endosurgery and Novo Nordisk A/S.

RISE Medication Protocols: Study Phases and Key Time Points

The RISE Consortium: Diabetes Care 37:780-788; 2014

Youth in RISE: Female and Underrepresented Minority Race/Ethnicity Predominance

	Glargine Followed by Metformin		Metformin Alone	
	Adult	Youth	Adult	Youth
N	67	44	65	47
Age (years)*	54 ± 9	15 ± 2	55 ± 8	14 ± 2
Female, n (%)*	23 (34%)	27 (61%)	37 (57%)	38 (81%)
Race/Ethnicity, n (%)*				
White	37 (55%)	13 (30%)	34 (52%)	12 (26%)
Black	21 (31%)	14 (32%)	19 (29%)	9 (19%)
Hispanic (any)	5 (8%)	14 (32%)	6 (9%)	20 (43%)
Other	4 (6%)	3 (7%)	6 (9%)	6 (13%)
Weight (kg)	104 ± 20	102 ± 26	98 ± 19	98 ± 23
BMI (kg/m^2)	35 ± 6	37 ± 6	35 ± 5	37 ± 6

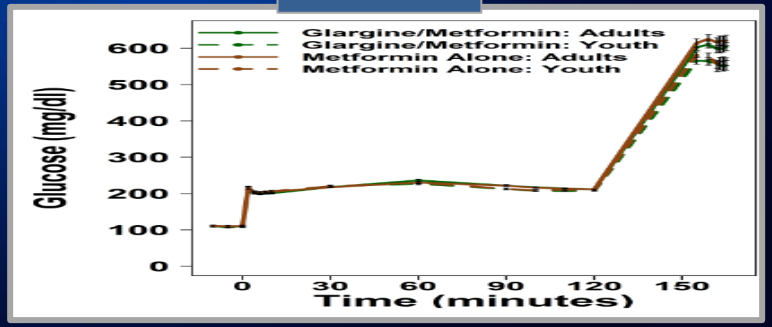
* $p<0.001$ for treatment group difference

The RISE Consortium: Diabetes Care, 2019.

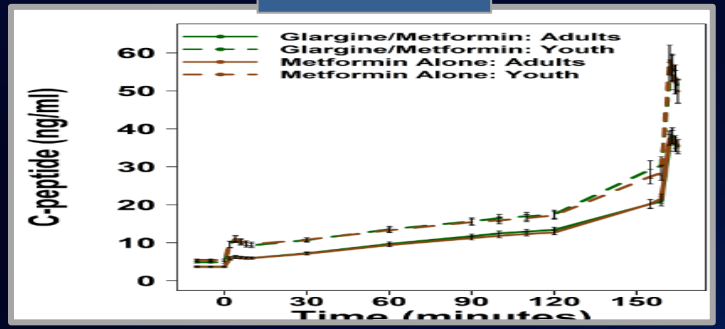
American Diabetes Association. Diabetes Care

Youth Make More C-Peptide and Insulin in Response to Similar Glycemic Stimuli than Adults

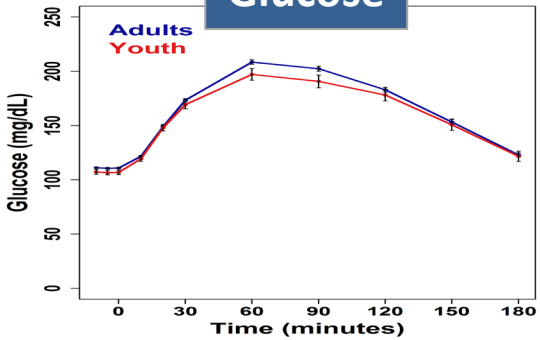
Glucose



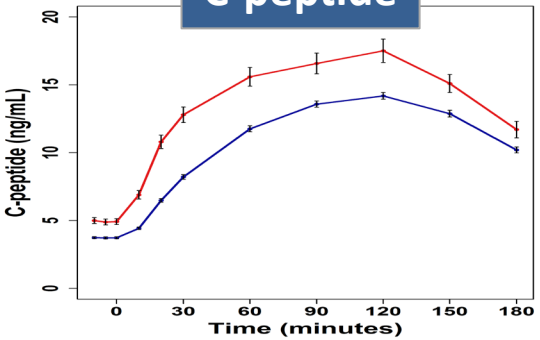
C-peptide



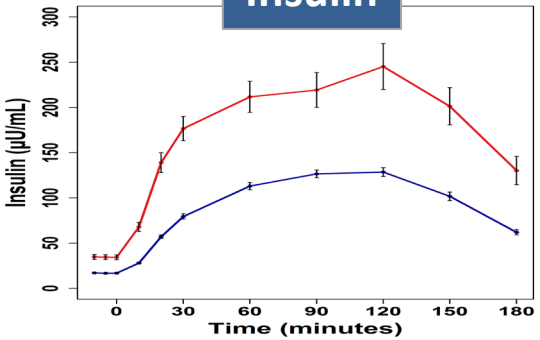
Glucose



C-peptide



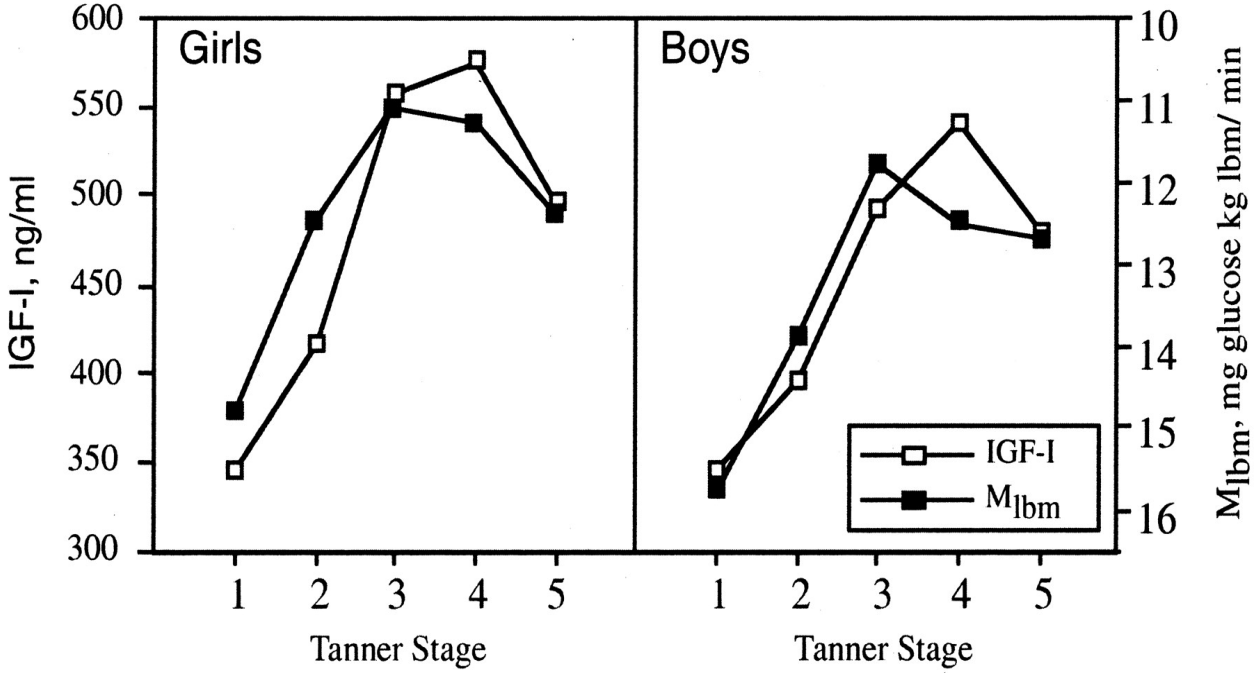
Insulin



The RISE Consortium: Diabetes Care, 2019.

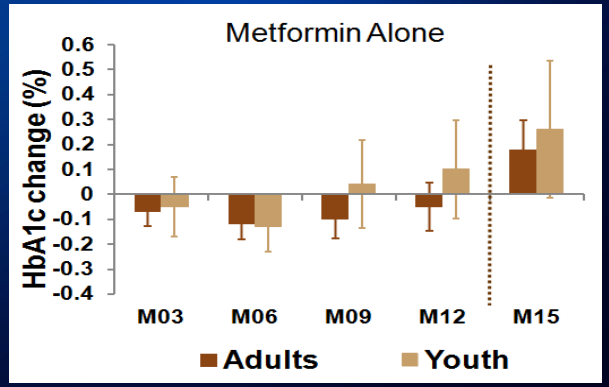
American Diabetes Association. Diabetes Care

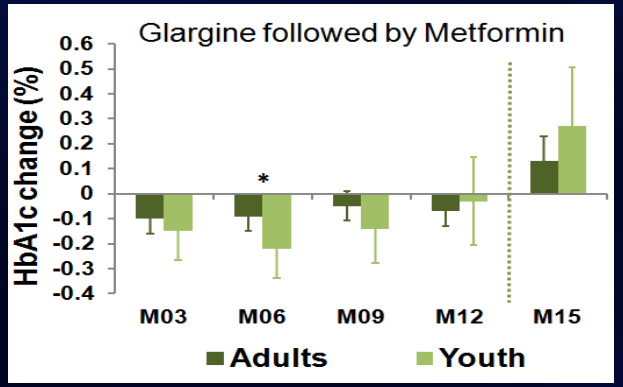
Why are Adolescents more Insulin Resistant than Adults?

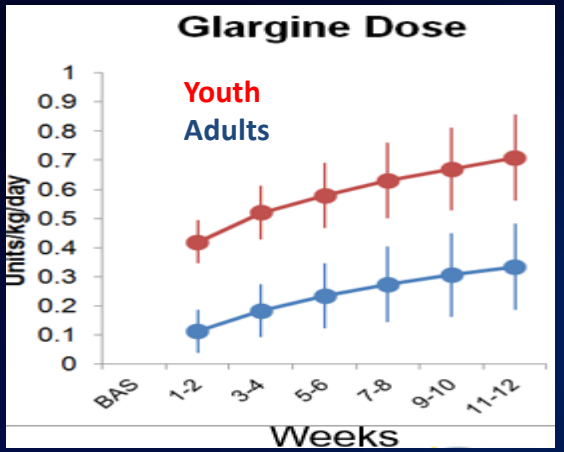


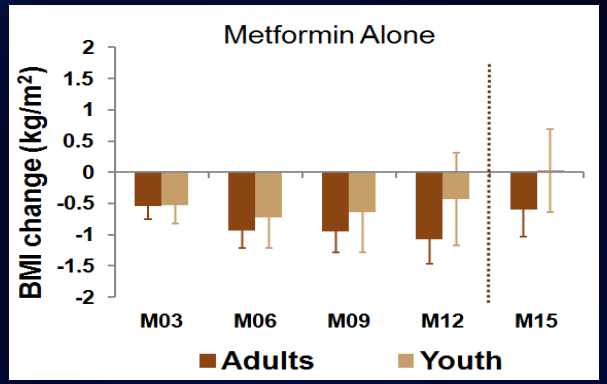
Moran et al J Clin Endocrinol Metab 87:4817, 2002

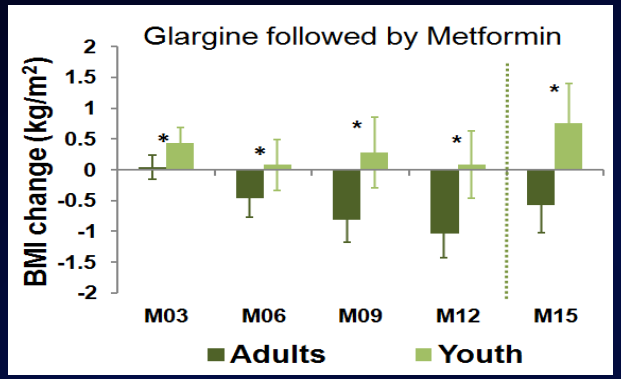
Glucose Control in Youth Requires More Insulin and is Associated with More Weight Gain







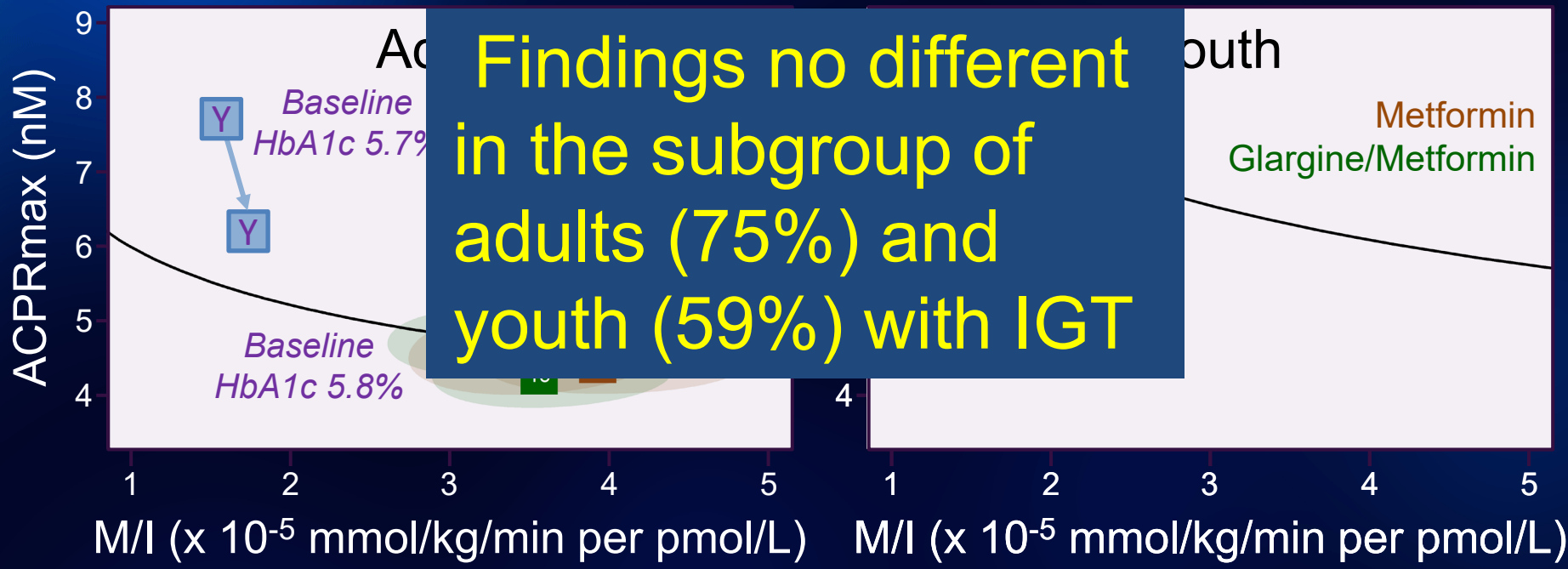




The RISE Consortium: Diabetes Care, 2019.

American Diabetes Association. Diabetes Care

Treatment Effects on Insulin Sensitivity and β-cell Function in Adults and Youth

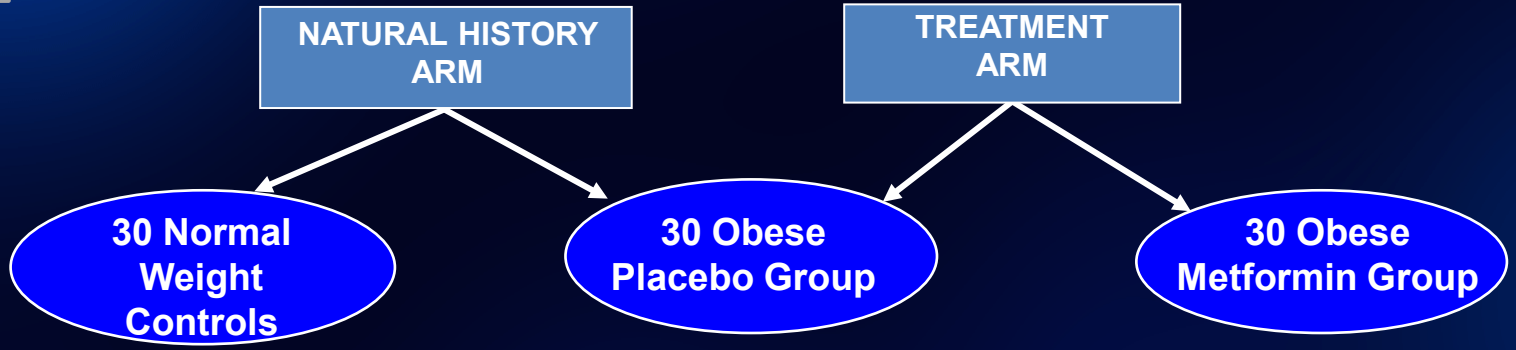


Findings no different in the subgroup of adults (75%) and youth (59%) with IGT

The RISE Consortium: Diabetes 68:1670-1680; 2019

Health Influences of Puberty (HIP): Metformin Does Not Appear to Be Beneficial in Obese Normoglycemic Youth

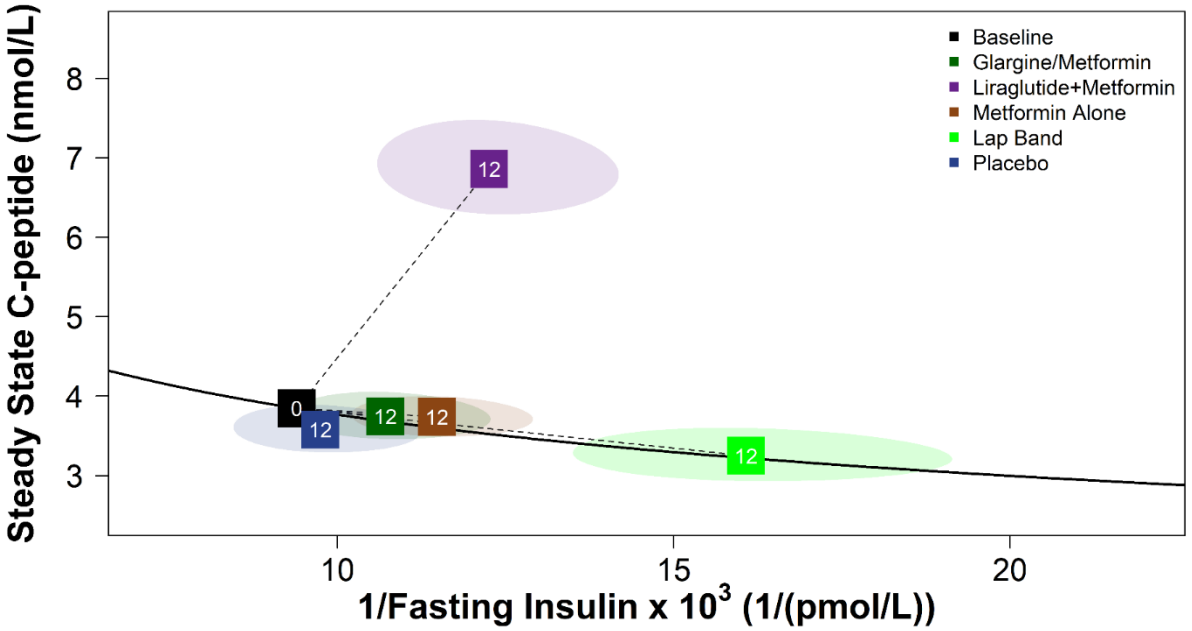
- Early Puberty (T2/T3)
- Age (9 years and up)
- Normoglycemic



1. Two years of metformin treatment in obese youth during puberty improved BMI and body fat, but not IR or β-cell function
2. High baseline Disposition Index (DI) predicted longitudinal decline in DI

Kelsey MM etc al, JCEM 2020 May

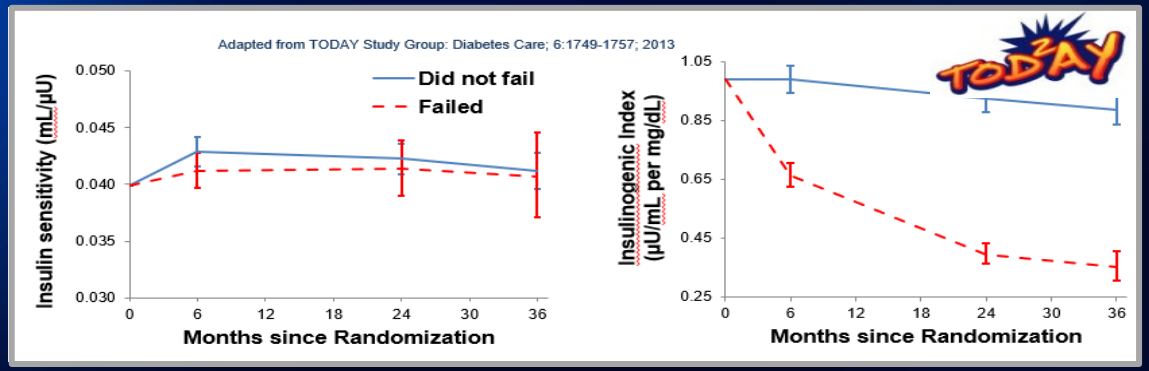
On Treatment Effect of Medication on β-Cell Function in Adults: Steady State C-peptide after 12 months Treatment



Baseline Combined

The RISE Consortium: Diabetes Care 42:1742, 2019.

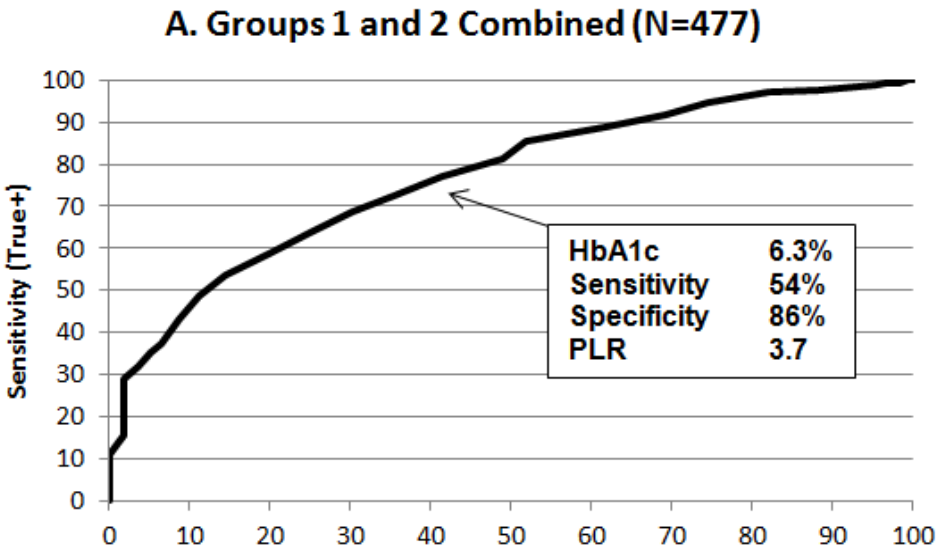
Baseline Predictors of Glycemic Worsening (GW) Differ in YO-T2D



- In RISE, GW occurred more in youth vs. adults (18% vs. 7.5% at M-12, 36% vs. 20% at M21)
- In all ages, lower β-cell responses: (clamp-derived at M12/M21, OGTT-derived M21)
- In youth, higher glycemia: (HbA1c and 2-h glucose at M12/M21; fasting glucose at M21)
- In adults, IR: (clamp and OGTT-derived at M12 and M21)

The RISE Consortium: Diabetes Care. June, 2021

HbA1c Predictive of Glycemic Failure in TODAY



- **A1c > 6.3% is a specific cut-off indicating likelihood to lose glycemic control**
- **A1c rising by more than 0.5% over any time period predicts loss of glycemic control**

Zeitler et al. Diabetes Care 2015

Insulin Clearance (IC) Lower in Youth, but Similar Baseline Predictors of Low IC as Adults

Insulin Clearance (IC) Measures	Adults	Youth
Fasting IC (x10^{-2} C-pep/Ins nmol/pmol)	1.08 (0.89-1.31)	0.72 (0.58-0.85)^
Molar Ratio 30mins (x10^{-2} iAUC$_{30}$ C-pep/iAUC$_{30}$ Ins nmol/pmol)	0.32 (0.27-0.39)	0.25 (0.22-0.29)^
Molar Ratio 3hr (x10^{-2} iAUC C-pep/iAUC Ins nmol/pmol)	0.46 (0.37-0.58)	0.31 (0.25-0.40)^
Fasting IC from Modeling (L min-1m-2)	1.34 (1.09-1.63)	0.94 (0.79-1.16)^
OGTT IC from Modeling (L min-1m-2)	0.82 (0.66-1.00)	0.60 (0.47-0.75)^

- Race/Ethnicity
  - Black < Hispanic < Caucasian
- IGT > T2D:
- Sex: No differences
- Treatment Group: No impact of metformin or lifestyle, but rosiglitazone decreases
- Insulin resistance: (metabolic syndrome characteristics, adiponectin)
- Obesity

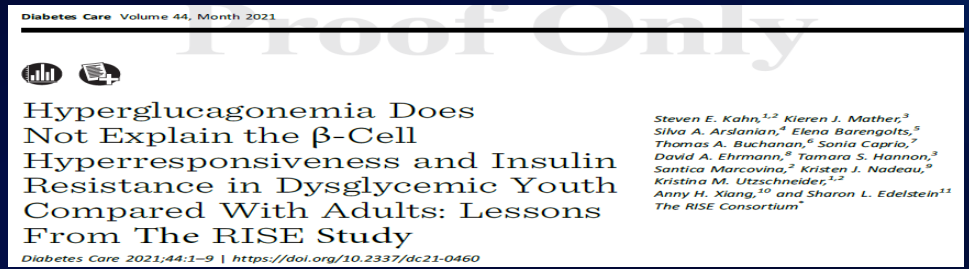
The RISE Consortium: Diabetes Care. ADA abstract, 2020

Could Glucagon Differences Explain the Initial Beta-Cell Hyper-responsiveness and Eventual Rapid Beta-Cell Failure in Youth?

Background: α-cell glucagon enhances β-cell insulin secretion, via glucagon and GLP-1 receptors on β-cell

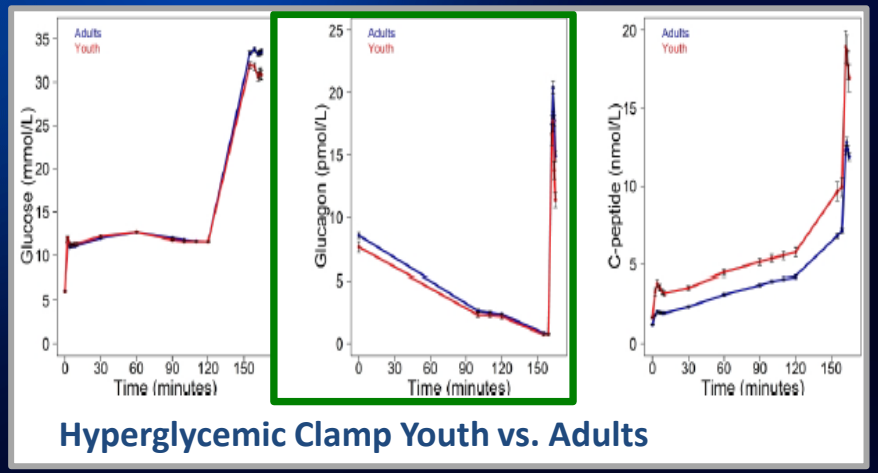
Hypotheses:

1) Hyperglucagonemia explains β-cell hyper-responsiveness seen in youth
2) Deterioration of α-cell function parallels the greater β-cell failure seen in youth

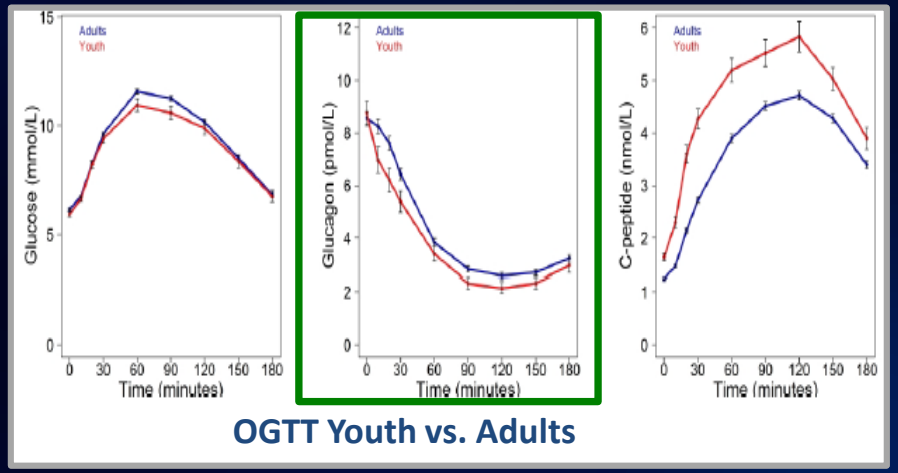


RISE Consortium: Diabetes Care. In Press, 2021

Glucagon Does Not Explain Youth vs. Adult Differences in Beta-Cell Function



Hyperglycemic Clamp Youth vs. Adults



OGTT Youth vs. Adults

1) We hypothesized that hyperglucagonemia might explain increased β-cell response in youth but it did not during the hyperglycemic clamp or OGTT (figures)
2) Longitudinally, rapid loss of β-cell function in youth in RISE is not paralleled by α-cell deterioration
3) No treatment group impact of MET or G►MET on glucagon

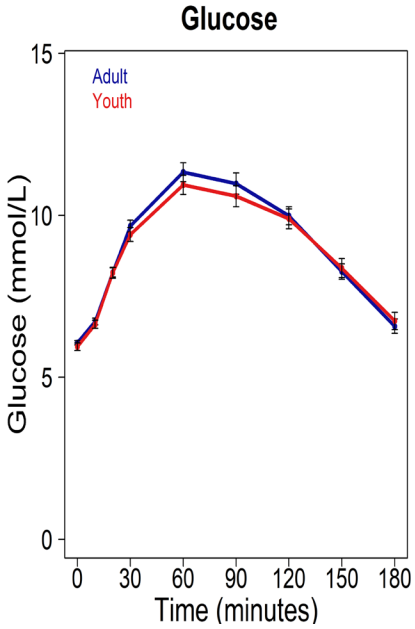
RISE Consortium: Diabetes Care. In Press, 2021

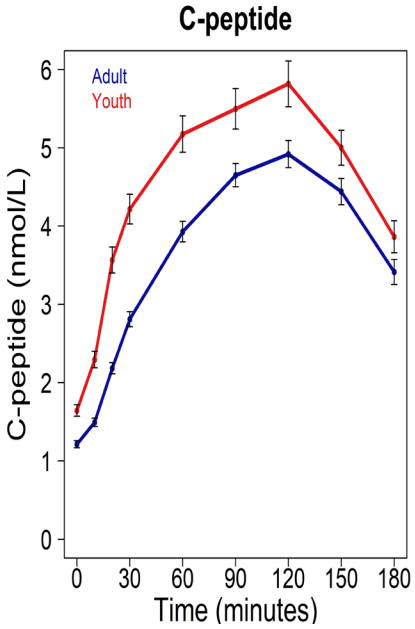
GLP-1 Relationships Differ in Youth vs. Adults

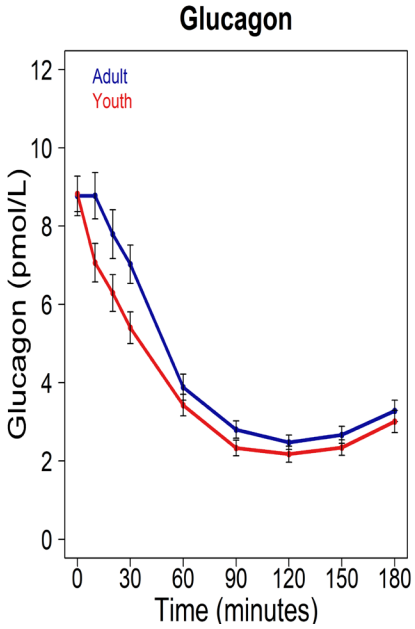
1) Glucagon-like peptide 1 (GLP-1) increases C-peptide release and decreases glucagon release
2) We hypothesized youth might have higher GLP-1 to explain their higher C-peptide and lower glucagon
1) We measured GLP-1 during a 3-hr OGTT in RISE

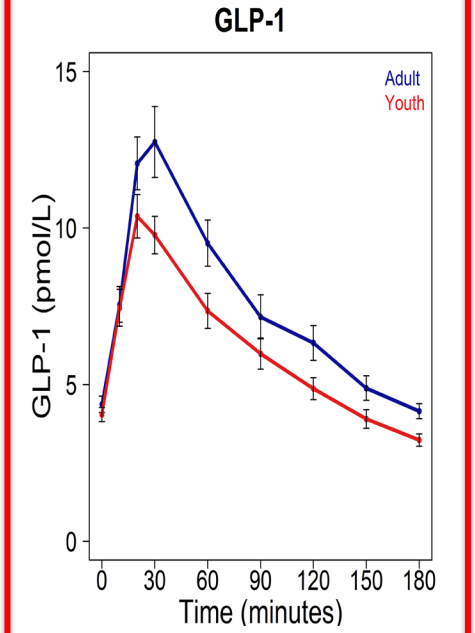
RISE Consortium: ADA Abstract 2022

RISE OGTT GLP-1 Profiles in Youth vs. Adults









Treatment implications of pathophysiology

- Youth have more severe IR than equally obese adults
- While 90% of youth will attain initial glycemic control with metformin alone, ~50% will not have a sustained response
  - HbA1c > 6.3% after initial metformin treatment predicts failure of monotherapy
  - HbA1c rising by more than 0.5% over any time period predicts loss of glycemic control
- β-cell dysfunction in youth is unresponsive to metformin or glargine
- Compared to adults, β-cells in youth are hyperresponsive; Poorer outcome in youth may be related to higher β-cell secretory burden
- Treatment of youth requires more aggressive efforts to improve insulin resistance and arrest the progressive loss of β-cell function than adults

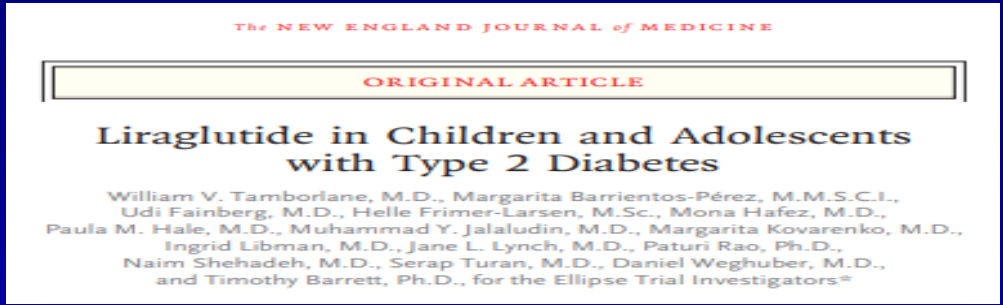
Thiazolidinediones in TODAY

- Oral once daily
- Lower A1c by ~0.8-1%
- Decreases inflammation, promote healthy fat storage?, improves peripheral and hepatic insulin sensitivity, reduces hepatic inflammation, increases adiponectin, increases insulin clearance
- Reduced loss of glycemic control by 23% in TODAY – mostly driven by benefit to girls
- Side effects
  - Weight gain
  - Fluid retention: worse with insulin and in patients with pre-existing CV disease
  - Decrease bone density and increase fracture risk in older patients – decreased BMD seen in TODAY.
  - Macular edema – not seen in TODAY
  - Possible increased risk for bladder cancer
- CV Risk
  - No evidence for CV risk reduction
  - Rosiglitazone initially associated with CV mortality in meta-analysis, not confirmed
  - No abnormalities noted on echocardiograms in TODAY

Glycemic Control Post-Insulin Initiation in TODAY

- No difference in A1c 1 year after starting insulin
  - At failure: 9.7 ± 1.7%
  - 1 year later: 9.5 ± 2.0%
- Therefore:
  1. Starting insulin following failure of oral therapy +/-intensive lifestyle does not correct glycemic or non-glycemic abnormalities
  2. There are barriers to successful insulin therapy in this demographic
  3. The best approach to add-on therapy in youth-onset T2D remains unclear

Levitt-Katz et al J Pediatr 2018



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Liraglutide in Children and Adolescents with Type 2 Diabetes

William V. Tamborlane, M.D., Margarita Barrientos-Pérez, M.M.S.C.I., Udi Fainberg, M.D., Helle Frimer-Larsen, M.Sc., Mona Hafez, M.D., Paula M. Hale, M.D., Muhammad Y. Jalaludin, M.D., Margarita Kovarenko, M.D., Ingrid Libman, M.D., Jane L. Lynch, M.D., Paturi Rao, Ph.D., Naim Shehadeh, M.D., Serap Turan, M.D., Daniel Weghuber, M.D., and Timothy Barrett, Ph.D., for the Ellipse Trial Investigators*

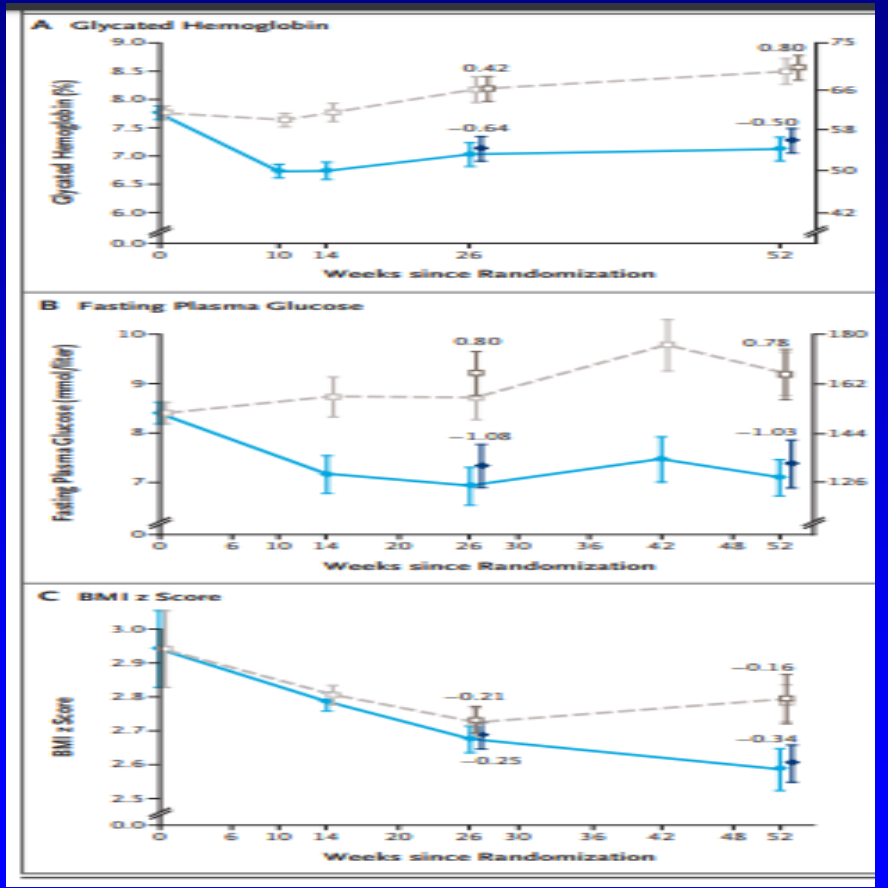
- **ELIPSE: 11-to-12-week run-in: 3-4 weeks of metformin titration to max tolerated (1000-2000 mg/day) (or metformin continued if already on it).**
- **Eligibility: fasting glucose 126-220 mg/dL and ≥ 8 weeks of stable metformin**
- **Randomized 1:1, to liraglutide/placebo injection x 26 weeks plus metformin, +/- basal insulin. Liraglutide/placebo initiated at 0.6 mg/day, escalated by 0.6 mg/week to max 1.8 mg/day based on side effects and average of 3 consecutive fasting glucose >110 mg/dL**
- **Overall rates of GI adverse events higher with liraglutide**
- **No significant hypoglycemia**

ELIPSE Outcomes

Table 1. Baseline Characteristics of the Patients.*

Characteristic	Liraglutide (N=66)	Placebo (N=68)	Total (N=134)
Age — yr	14.6±1.7	14.6±1.7	14.6±1.7
Female sex — %	62.1	61.8	61.9
Age of 10 to 14 yr at end of trial — no. (%)	21 (31.8)	19 (27.9)	40 (29.9)
Region — no. (%)			
Asia	6 (9.1)	6 (8.8)	12 (9.0)
Europe	24 (36.4)	21 (30.9)	45 (33.6)
North America	28 (42.4)	35 (51.5)	63 (47.0)
Rest of the world	8 (12.1)	6 (8.8)	14 (10.4)
Race or ethnic group — no. (%)†			
White	42 (63.6)	45 (66.2)	87 (64.9)
Black	9 (13.6)	7 (10.3)	16 (11.9)
Asian	10 (15.2)	8 (11.8)	18 (13.4)
American Indian or Alaska Native	2 (3.0)	1 (1.5)	3 (2.2)
Native Hawaiian or Other Pacific Islander	0	0	0
Other	3 (4.5)	7 (10.3)	10 (7.5)
Hispanic or Latino ethnic group — no. (%)†			
Yes	16 (24.2)	23 (33.8)	39 (29.1)
No	50 (75.8)	45 (66.2)	95 (70.9)
Duration of diabetes — yr	1.9±1.7	1.9±1.3	1.9±1.5
Body weight — kg	93.3±31.0	89.8±22.1	91.5±26.8
BMI‡	34.55±10.87	33.27±7.36	33.90±9.25
BMI z score	3.03±1.47	2.86±1.11	2.94±1.30
Glycated hemoglobin — %	7.87±1.35	7.69±1.34	7.78±1.34
Fasting plasma glucose — mg/dl	156.8±52.2	146.8±38.3	151.7±45.8
Blood pressure — mm Hg			
Systolic	118.4±11.4	115.3±12.0	116.8±11.8
Diastolic	73.2±8.5	71.2±7.6	72.2±8.1
Metformin dose at baseline — mg	1912±286	1877±384	1894±339
Basal insulin use at baseline			
No. (%) of patients	15 (22.7)	10 (14.7)	25 (18.7)
Mean dose — U	29.6±19.5	29.6±17.7	29.6±18.4

* There were no significant differences between the groups in the characteristics listed. Percentages may not total 100 because of rounding. To convert the values for plasma glucose to millimoles per liter, multiply by 0.05551.
† Race and ethnic group were reported by the patient or the patient's guardian.
‡ The body-mass index (BMI) is the weight in kilograms divided by the square of the height in meters.

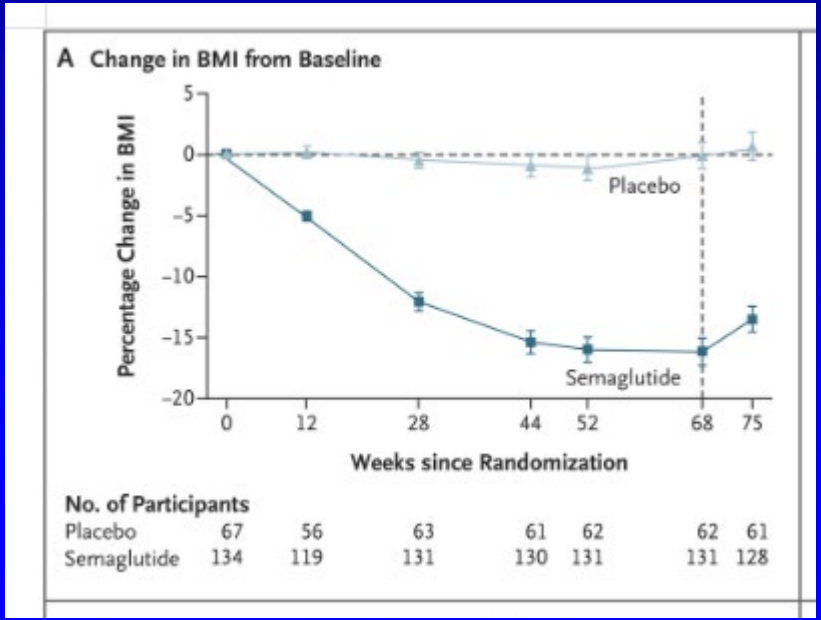


ORIGINAL ARTICLE

Once-Weekly Semaglutide in Adolescents with Obesity

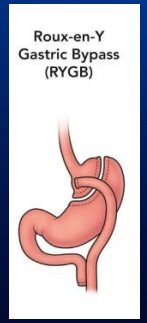
Daniel Weghuber, M.D., Timothy Barrett, Ph.D., Margarita Barrientos-Pérez, M.D., Inge Gies, Ph.D., Dan Hesse, Ph.D., Ole K. Jeppesen, M.Sc., Aaron S. Kelly, Ph.D., Lucy D. Mastrandrea, M.D., Rasmus Sørrig, Ph.D., and Silva Arslanian, M.D. for the STEP TEENS Investigators*

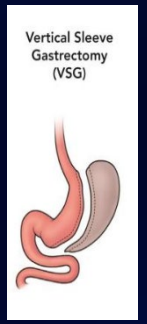
-Adolescents (12 to <18 years of age) with BMI 85th >/=85th%ile plus one or more weight-related coexisting condition
-Randomly assigned to once-weekly 2.4 mg SQ semaglutide or placebo for 68 weeks, plus lifestyle



Medical vs. Surgical Rx in Y-T2D: Youth from TODAY Chosen to Match the Youth with T2D from Teen-LABS

Teen-LABS: n=242 youth undergoing Metabolic Bariatric Surgery(MBS) age 13-19 yrs

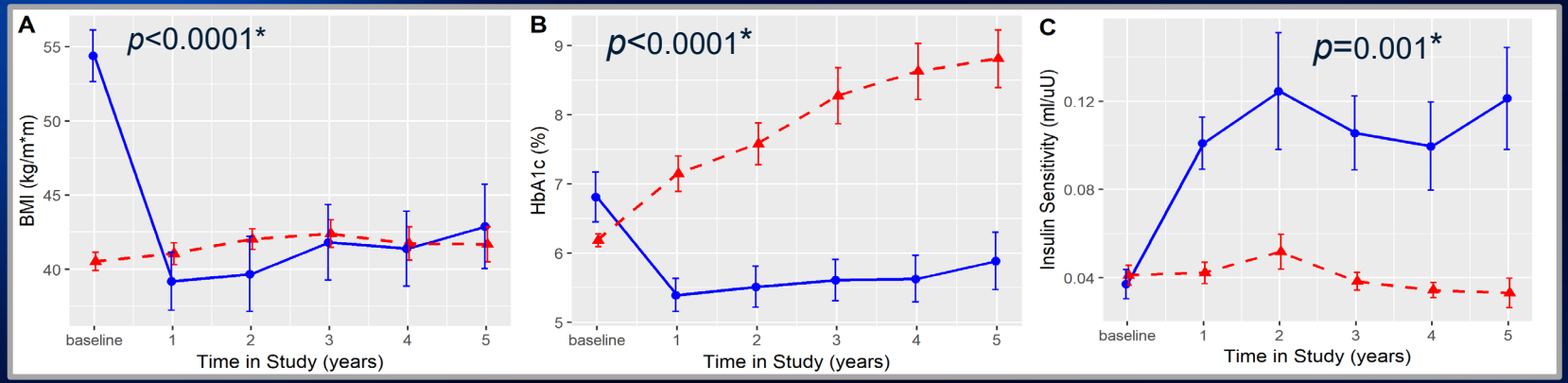




	Teen-LABS (n=30)	TODAY (n=63)	*p*-value
Age (years)	16.9 ± 1.3	15.4 ± 1.3	<0.0001
Sex (female, %)	70.0	55.6	0.18
Race/ethnicity (%)			
Black non-Hispanic	30.0	28.6	0.89
Hispanic	3.3	0	0.32
White non-Hispanic	60.0	71.4	0.27
Other	6.7	0	0.10
BMI (kg/m^2)	54.4 ± 9.5	40.5 ± 4.9	<0.0001
UACR (µg/mg)	11 (5-32)	10 (5-22)	0.66
eGFR – FAS (mL/min/1.73m^2)	118 ± 22	115 ± 15	0.53
HbA1c (%)	6.8 ± 1.9	6.2 ± 0.7	0.53
Insulin sensitivity (mL/µU)	0.04 ± 0.04	0.04 ± 0.04	0.14

Bjornstad et al. Diabetes Care 2019

Teen-LABS vs. TODAY: Superior Outcomes with MBS over 5 years

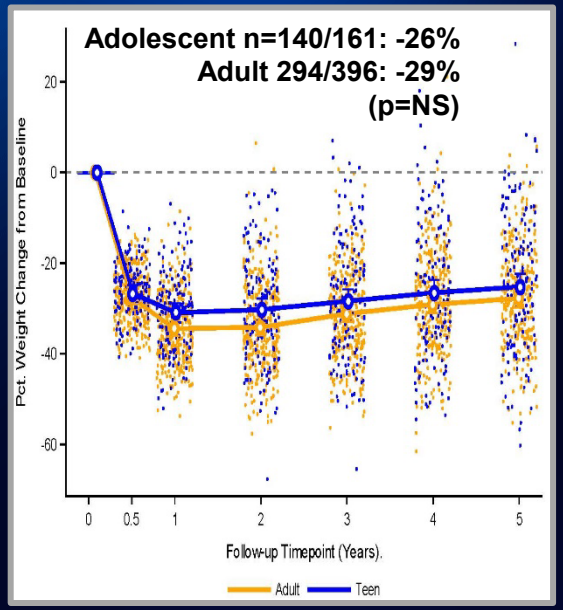


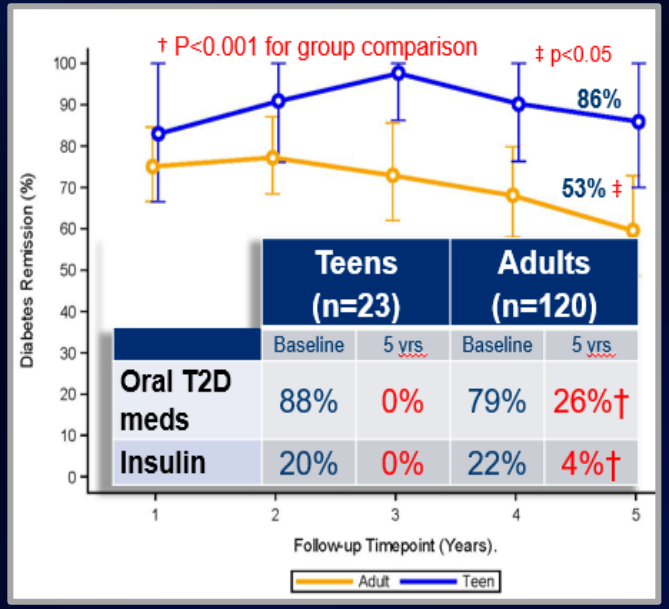
*Adjusted for baseline age, sex, HbA1c, insulin sensitivity, BMI and antihypertensive use

Bjornstad et al. Diabetes Care 2019

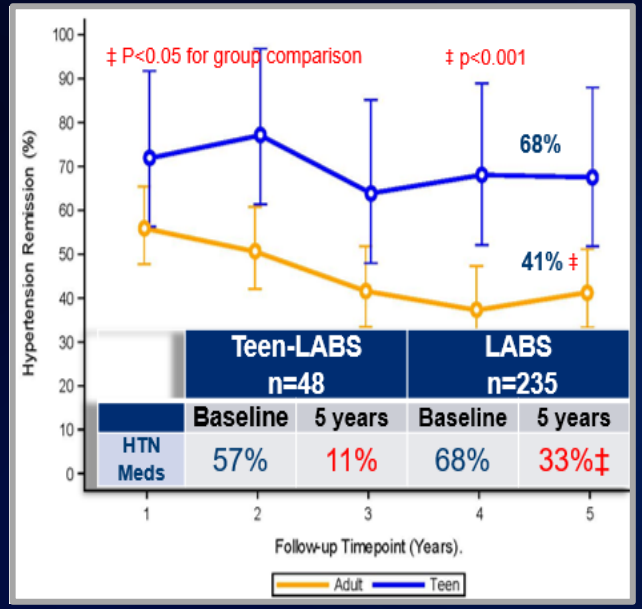
Teen-LABS vs. LABS: More T2D and Hypertension Remission in Youth with RYGB Despite Similar Weight Loss

LABS: adults (ages 25-60 yrs) MBS design coordinated to Teen-LABS





	Teens (n=23)		Adults (n=120)	
	Baseline	5 yrs	Baseline	5 yrs
Oral T2D meds	88%	0%	79%	26%†
Insulin	20%	0%	22%	4%†



	Teen-LABS n=48		LABS n=235	
	Baseline	5 years	Baseline	5 years
HTN Meds	57%	11%	68%	33%‡

Inge, Courcoulas, Jenkins, Michalsky, et.al.
NEJM 2019; 374:113-123

IMPROVE: VSG in T2D (n=11)

Table 1. Participant Demographics

Variable (units)	Baseline	3-Month Post Surgery
Age (years)	17±1.6	17.3±1.5
Sex (m/f)	6/5	-
Race/Ethnicity Hispanic Non-Hispanic	 8 3	 -
Height (cm)	170.1±7.3	170.1±7.6
Body Weight (kg)	131.9±18.6	108.4±15.7*
BMI (kg/m²)	45.6±5.7	37.5±5*
BMI (% of 95th %ile)	160.4±21	130±19.7*
# Diabetes Medications 0 1 2 3	 0 4 5 2	 10 1 0 0

Table 1. Baseline characteristics are presented as mean ± SD. *p<0.05.

Figure 2. Glucose and insulin AUC during a MMTT

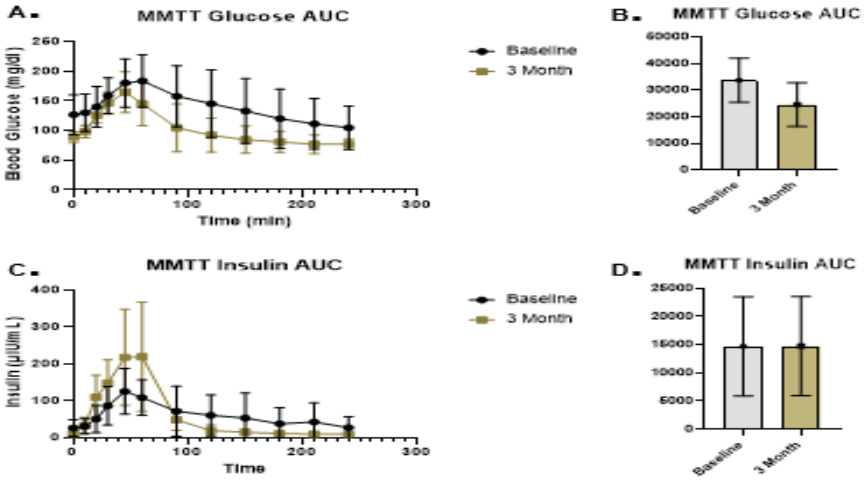
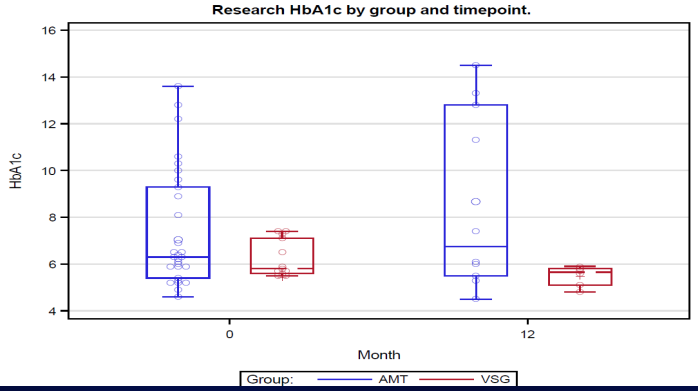
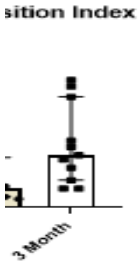
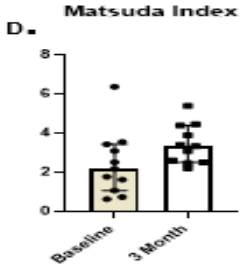


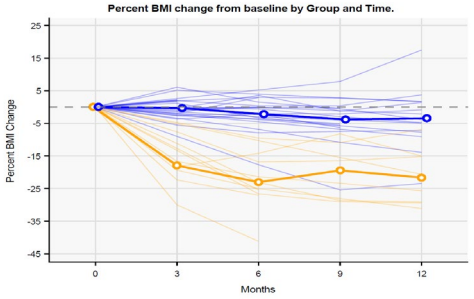
Figure 2. Glycemia



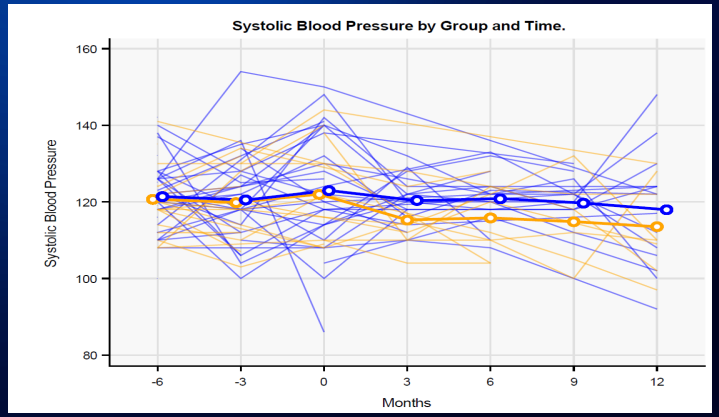
ecretion are improved after surgery

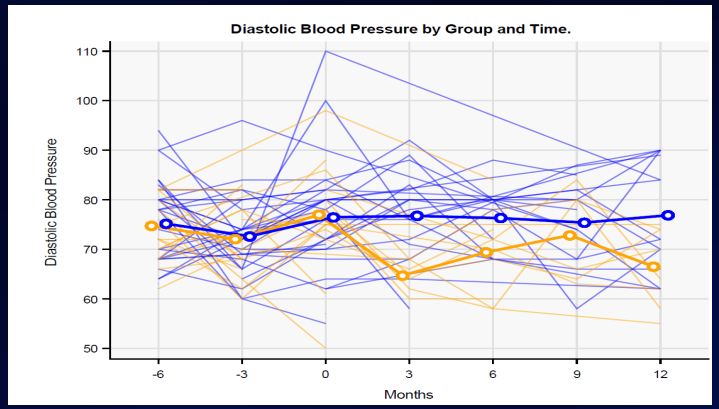


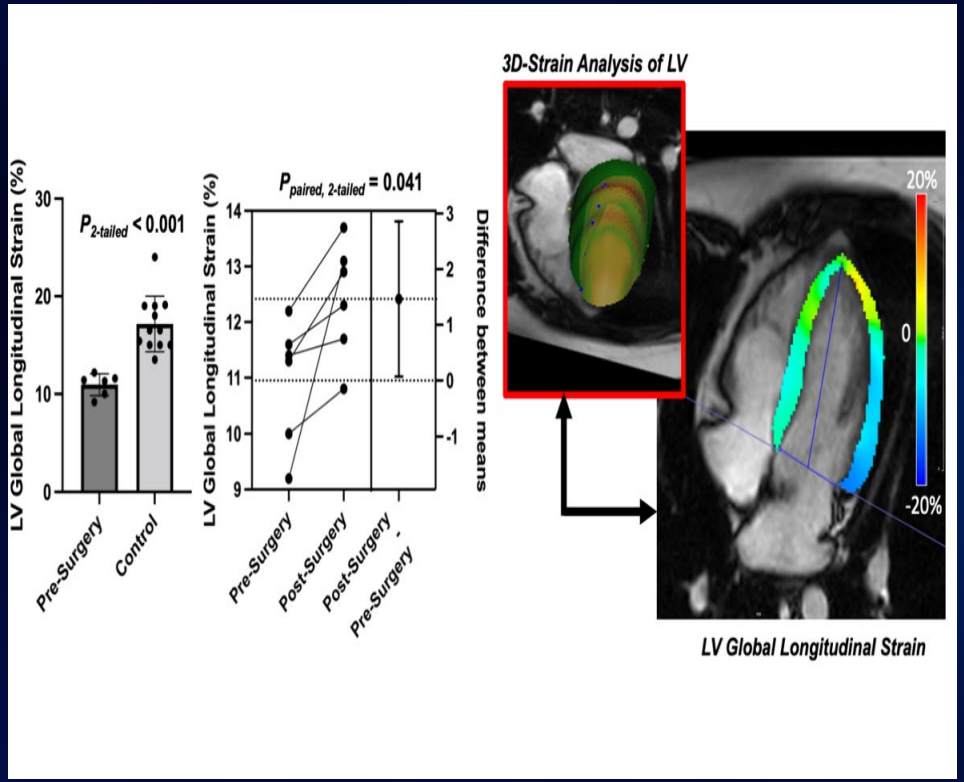


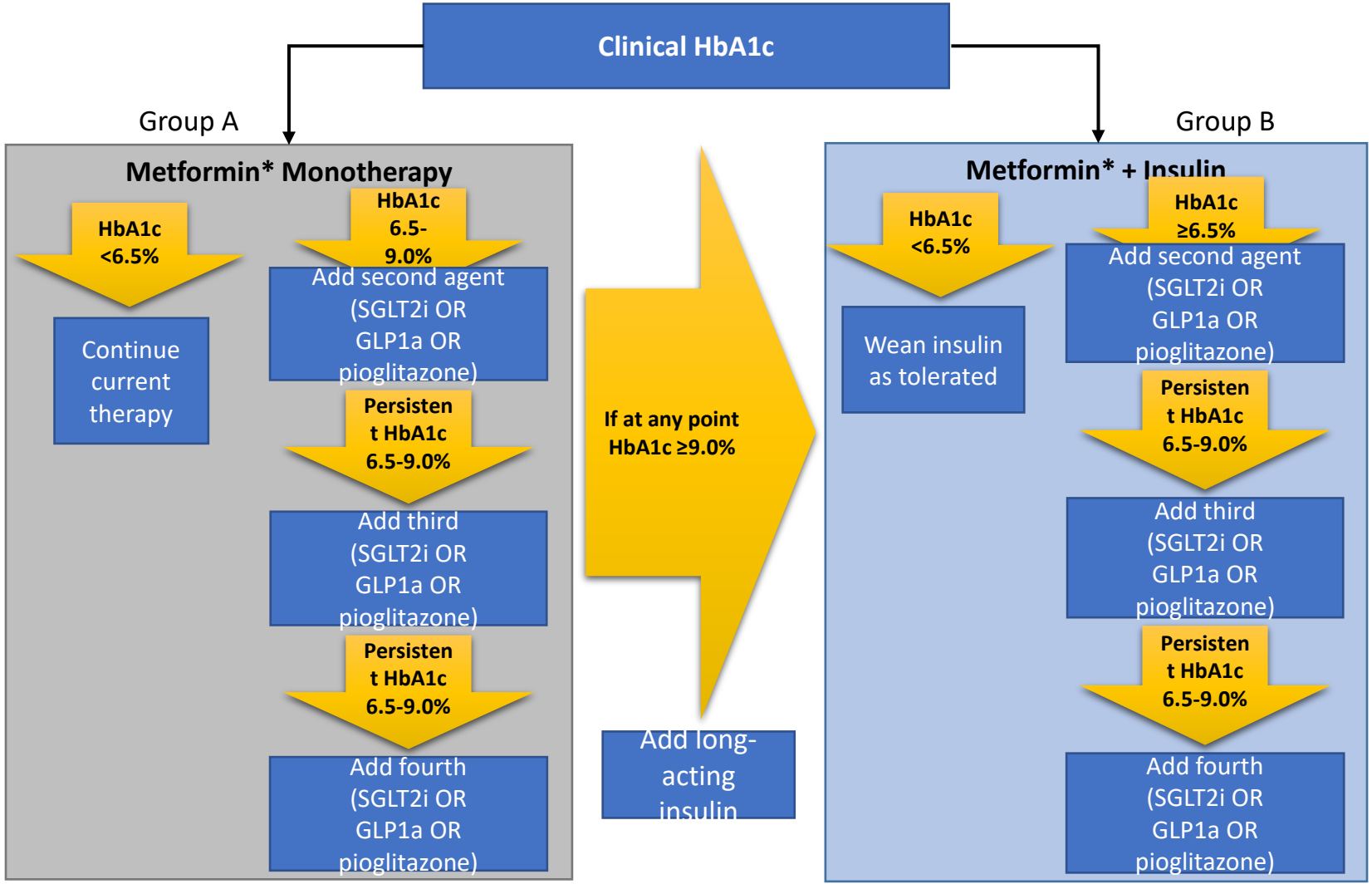


IMPROVE: CVD VSG in T2D Youth








Clinical HbA1c
Group A
Group B
Metformin* Monotherapy
HbA1c <6.5%
Continue current therapy
HbA1c 6.5-9.0%
Add second agent (SGLT2i OR GLP1a OR pioglitazone)
Persistent HbA1c 6.5-9.0%
Add third (SGLT2i OR GLP1a OR pioglitazone)
Persistent HbA1c 6.5-9.0%
Add fourth (SGLT2i OR GLP1a OR pioglitazone)
If at any point HbA1c ≥9.0%
Add long-acting insulin
Metformin* + Insulin
HbA1c <6.5%
Wean insulin as tolerated
HbA1c ≥6.5%
Add second agent (SGLT2i OR GLP1a OR pioglitazone)
Persistent HbA1c 6.5-9.0%
Add third (SGLT2i OR GLP1a OR pioglitazone)
Persistent HbA1c 6.5-9.0%
Add fourth (SGLT2i OR GLP1a OR pioglitazone)

Y-T2D Summary

- Youth-onset T2D differs from adults, is more aggressive and responds poorly to medications typically used in adult-onset T2D, requiring different approaches
- Studies of the long-term impact of GLP-1 analogues and SGLT-2 inhibitors in youth with beta-cell, CV, hepatic and renal outcomes are needed
- A better understanding of the early changes in puberty regarding insulin sensitivity, secretion and clearance are needed to determine in whom and how to intervene in high-risk youth: NIDDK U01
- Surgical data in adults and Teen-LABS data encouraging, but only 30 youth in Teen-LABS had T2D and almost all got RYGB, a surgery now almost completely replaced by the better-tolerated vertical sleeve gastrectomy: ST_2OMP R01

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malondo
paldies
grazzi
kiitos
dankie
nanni
nandri
dhanyavad
maururu
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gracias
хвала
asante
manana
obrigada
tenki
bedankt
bayarlalaa
gracje
hvala
köszönöm
aciū
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taiku
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rahmat
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merci