CENTER FOR INDIGENOUS HEALTH

UW

The Impact of Familial and Adolescent Depressive Symptoms and Resilience on Glycemic Trends in Adolescents:

The Strong Heart Family Study

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Acknowledgements

We are broadcasting from Seattle, WA, the ancestral lands of Coast Salish Nations, whose people still steward this land today.

Objectives

1. Identify at least two key risk factors and trends of dysglycemia among American Indian adolescents.
2. Implement evidence-based strategies for managing dysglycemia in pediatric populations.
3. Examine how depressive symptoms can impact glycemic control over time, including mechanisms or clinical implications.

A Brief Review of Type 2 Diabetes in Adolescents

Type 2 Diabetes in Adolescents

- Similar to adults: physiology of type 2 diabetes (T2D) insulin resistance (liver, adipose, skeletal muscle), impaired insulin secretion
- Typically occurs after puberty (sex-hormone related insulin resistance)
- **However in indigenous populations,** adolescents should be screened before puberty if elevated BMI and there are risk factors present

Shah, A. S., Zeitler, P. S., Wong, J., Pena, A. S., Wicklow, B., Arslanian, S., ... & Craig, M. E. (2022). ISPAD Clinical Practice Consensus Guidelines 2022: Type 2 diabetes in children and adolescents. *Pediatric diabetes*, *23*(7), 872-902.

Type 2 Diabetes in Adolescents

- In indigenous populations, adolescents should be screened before puberty if there is evidence of obesity, and risk factors are present

Risk factors:

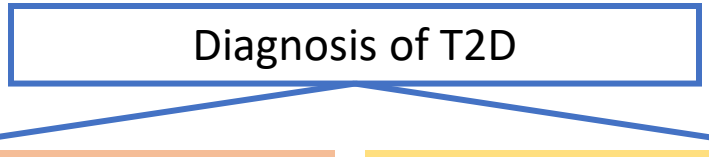
- Family Hx (1st,2nd degree),
- gestational DM,
- SGA / LGA,
- Race,
- other medical conditions associated with insulin resistance

Medical conditions associated with insulin resistance:

- acanthosis nigricans,
- fatty liver disease,
- hypertension,
- dyslipidemia,
- polycystic ovary syndrome [PCOS])

Shah, A. S., Zeitler, P. S., Wong, J., Pena, A. S., Wicklow, B., Arslanian, S., ... & Craig, M. E. (2022). ISPAD Clinical Practice Consensus Guidelines 2022: Type 2 diabetes in children and adolescents. *Pediatric diabetes*, *23*(7), 872-902.

Diagnosis of T2D in Adolescents



Symptoms of hyperglycemia

At least **one** of the following

- HbA1c ≥6.5% (48 mmol/mol)
- FPG ≥126 mg/dL (7.0 mmoL/L)
- Random plasma glucose ≥200 mg/dL (11.1 mmol/L)
- 2-h plasma glucose on an OGTT ≥200 mg/dL (11.1 mmoL/L).

No symptoms of hyperglycemia

At least **two** of the following

- BMI ≥85th percentile
- Signs of insulin resistance(dyslipidemia, MASLD, hypertension, PCOS)
- Family history of T2D
- Negative (absent) pancreatic autoantibodies.

Initial Management of T2D

Initially Management

- % HbA1C < 8.5 – initiate metformin and lifestyle changes
- % HbA1C > 8.5 – initiate basal insulin and metformin therapy

At follow up:

- % HbA1C < 6.5 – Continue metformin, wean insulin or additional meds if applicable
- % HbA1C > 6.5 – Review adherence, maximize or add medications

Exploring Depressive Symptoms and Glycemic Trends in American Indian Adolescents: the Strong Heart Family Study

Depression and Diabetes in American Indian Adolescents

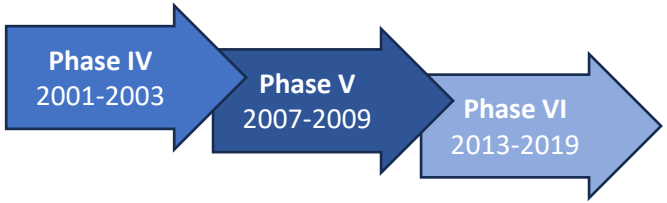
- American Indian (AI) adolescents have higher rates of and T2D than other racial or ethnic groups.
- AI adolescents also exhibit higher rates of depression and suicide as compared to other ethnic and racial groups.
- Cross-sectional studies in adults have associated higher depressive symptoms to higher %HbA1C.
- The impact of depression and family dynamics on glycemic measures in AI youth is not well understood.

Perng W, Conway R, Mayer-Davis E, Dabelea D. Youth-Onset Type 2 Diabetes: The Epidemiology of an Awakening Epidemic. Diabetes Care. 2023 Mar 1;46(3):490-499. doi: 10.2337/dci22-0046. PMID: 36812420; PMCID: PMC10090267.

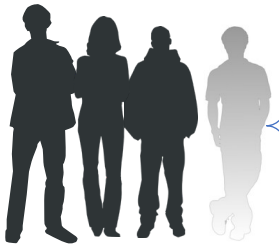
Methods

Strong Heart Family Study

Longitudinal data collection study of **American Indians** across multiple reservations



Center for Epidemiologic Studies Depression Scale (CESD), laboratory data, medications



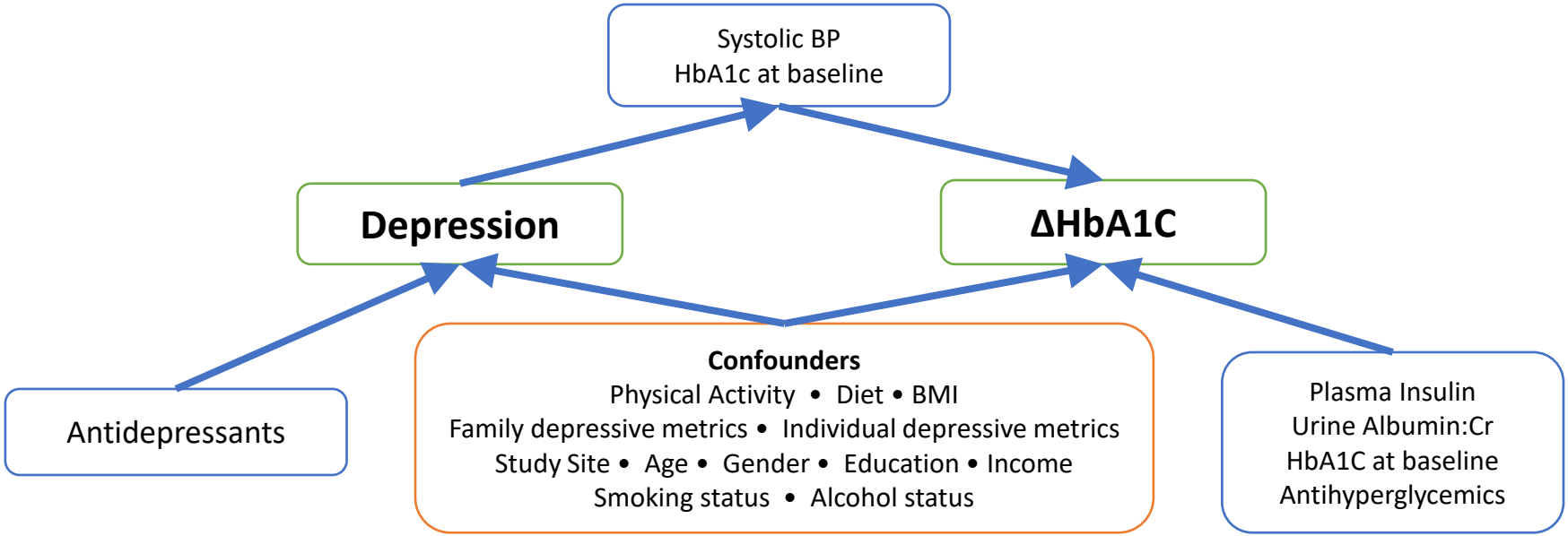
Phase IV: 2754 participants

- 674 adolescents aged 14-25 years
- Laboratory data and outcomes followed across 20-year span

? How do depressive scores impact adolescent glycemic trends **?**

Familial Self *Parental*

Methods: Generalized Linear Models



$$\Delta HbA1C = \beta_0 + \beta_a CESD + \beta_b Demographics + etc$$

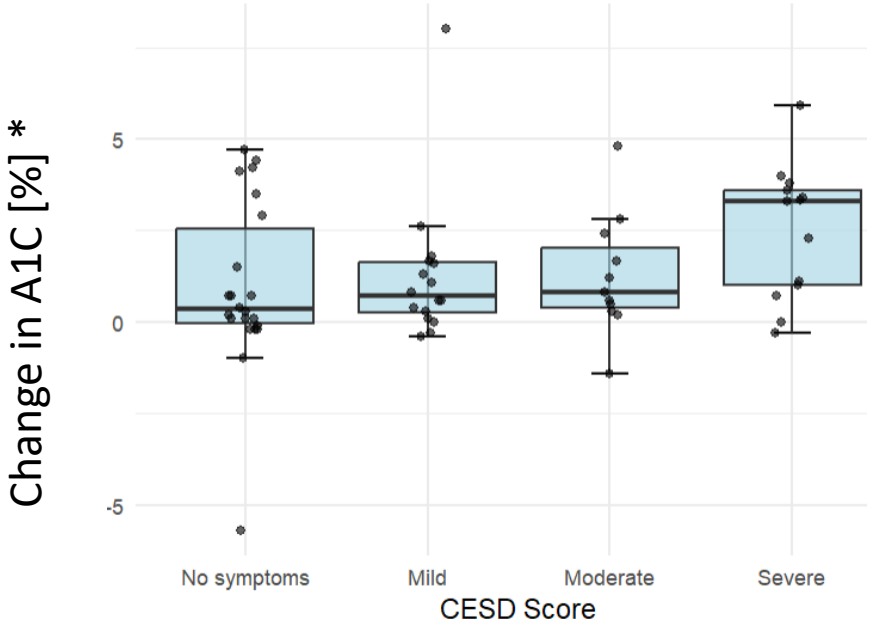
Almost 1/3 of Adolescents had Depressive Symptoms

Adolescent population

- 674 participants aged 14-25
- 53.7% F
- Average %HbA1C 5.37±1.12%
- Average BMI 28.7±7.9

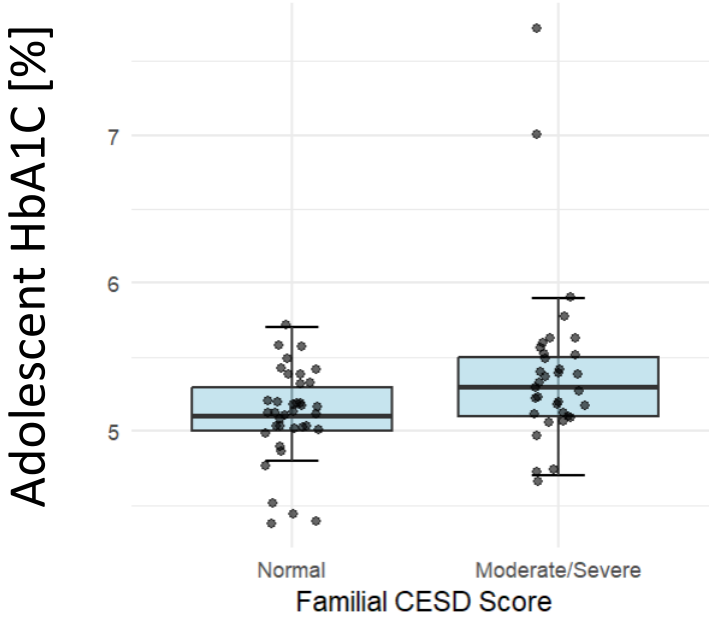
- **15.4%** prevalence of dysglycemia
- **31.5%** prevalence of moderate (CESD≥16) or severe (CESD≥25) depressive symptoms.

Higher Adolescent Depressive Symptoms Worsens %HbA1c



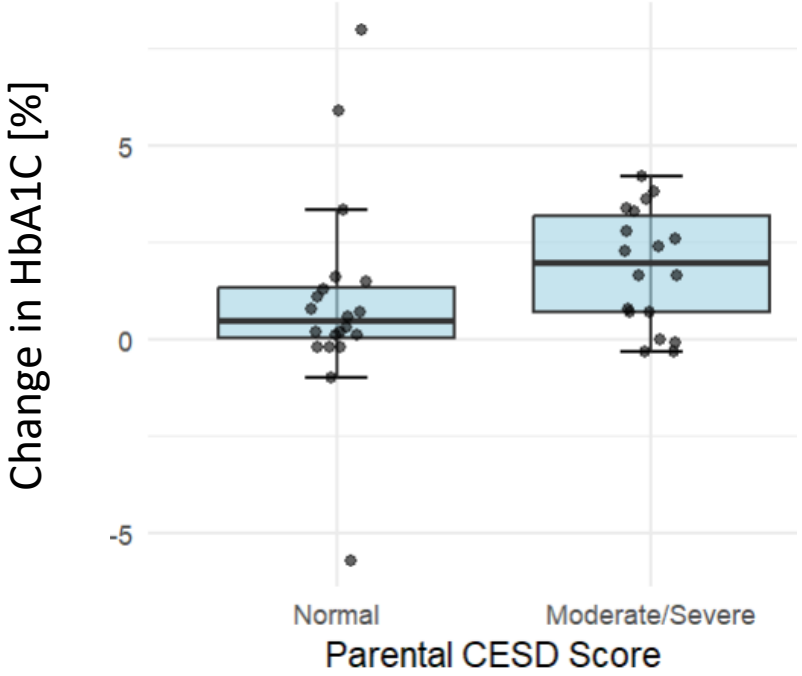
- Severe CESD scores imparted higher increases in %HbA1C upon 5-20 year follow-up as compared to adolescents with no depressive symptoms (CESD≤10) (2.47% vs 0.97%, P<0.05).

Familial Depressive Symptoms Associate to Higher %HbA1c in Adolescents



- At-least Moderate familial CESD scores associated to higher adolescent %HbA1C (5.4% vs 5.1%, P<0.05) as compared to families with no depressive symptoms.

Parental Depressive Symptoms Associate to Worsening Adolescent %HbA1c



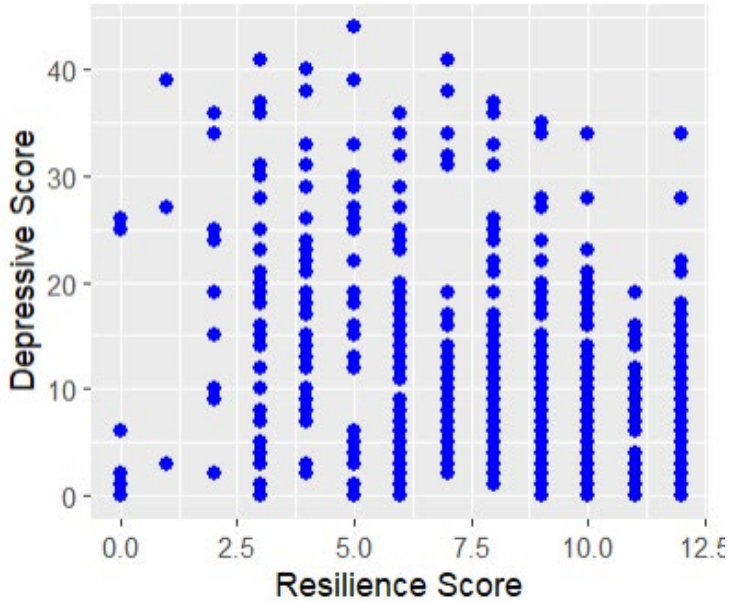
At-least moderate parental CESD scores were associated with nominally higher increases in %HbA1C upon 5-10 year follow-up (1.84% vs 0.92%, p = 0.19) as compared to parents with no depressive symptoms.

Summary so far

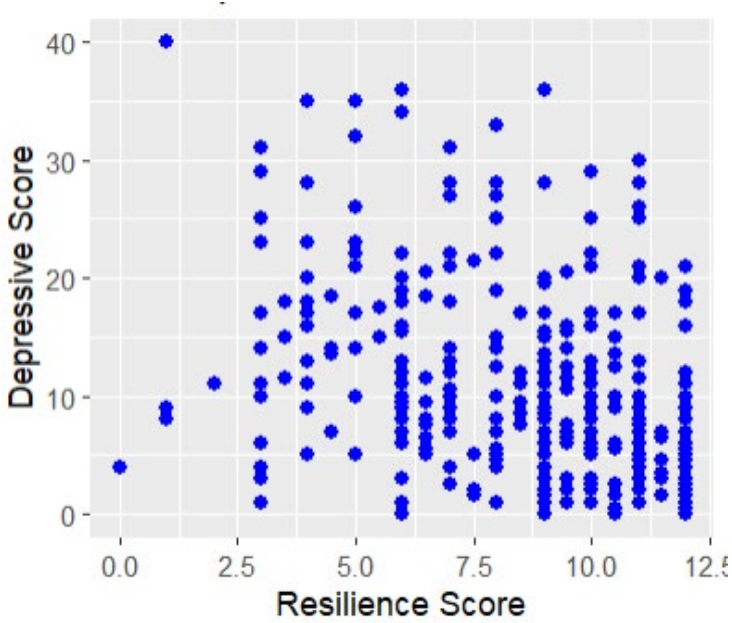
- Adolescents with severe depressive symptoms have significantly worse trends in %HbA1c over 20 years
- Where the adolescent starts in that journey, the baseline %HbA1c, is correlated to familial depressive symptoms

Depressive Symptoms and Resilience

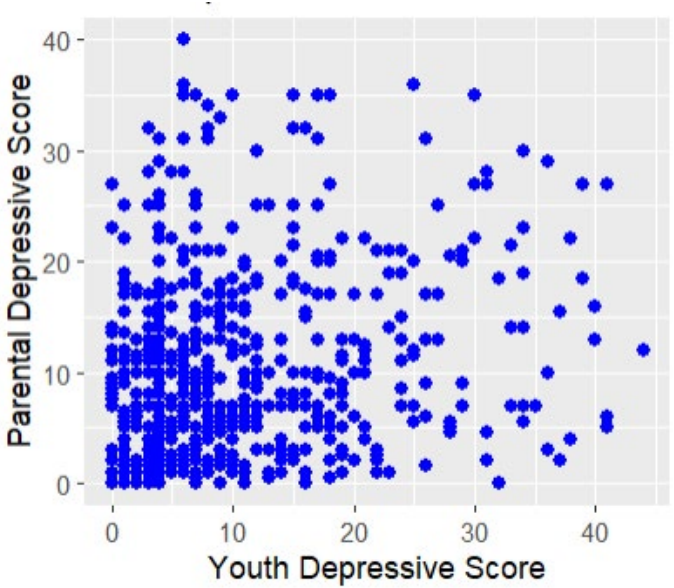
Adolescent CESD Score

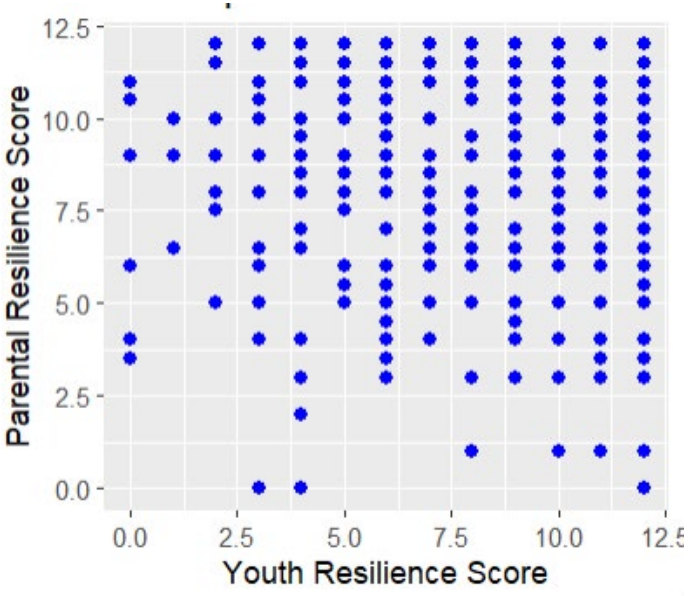


Parental CESD Scores

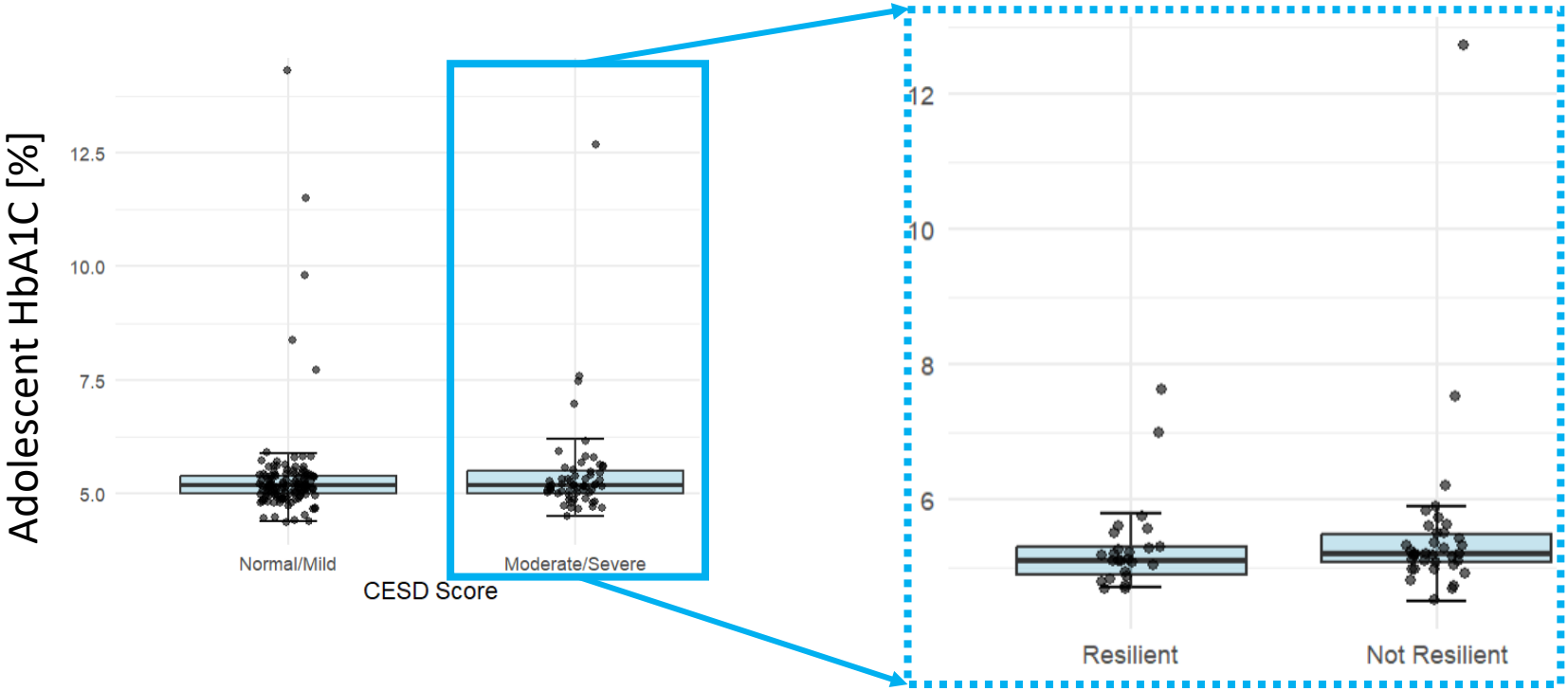


Adolescent Resilience and Parental Resilience





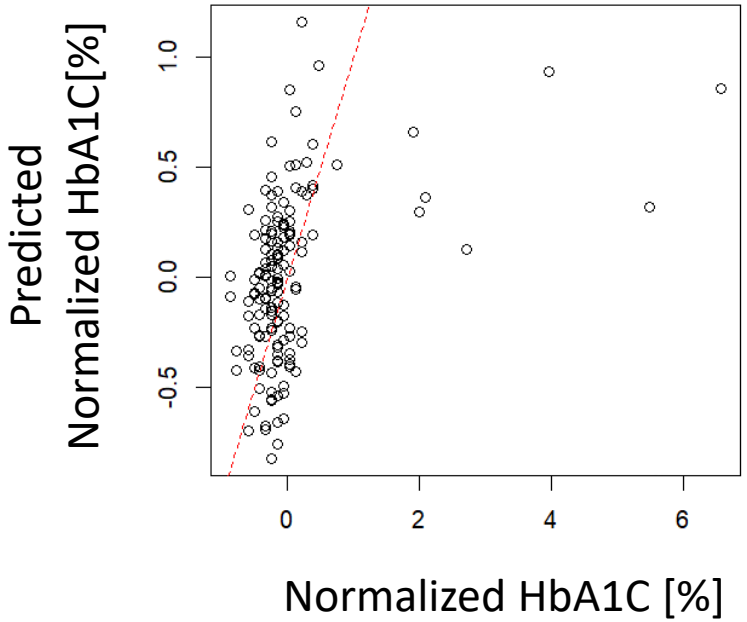
Results: Lower %HbA1c in Resilient Adolescents



Results: Familial Resilience Associates to Lower Baseline %HbA1c

%HbA1C = β_0 + β_1**Depression** + β_2**Resilience** + β_3**Familial Depression** + β_4**Familial Resilience** + β_5BMI + β_6Age + β_7Gender + β_8Income + β_9Education + β_{10}Alcohol + β_{11}Diet + β_{12}Activity

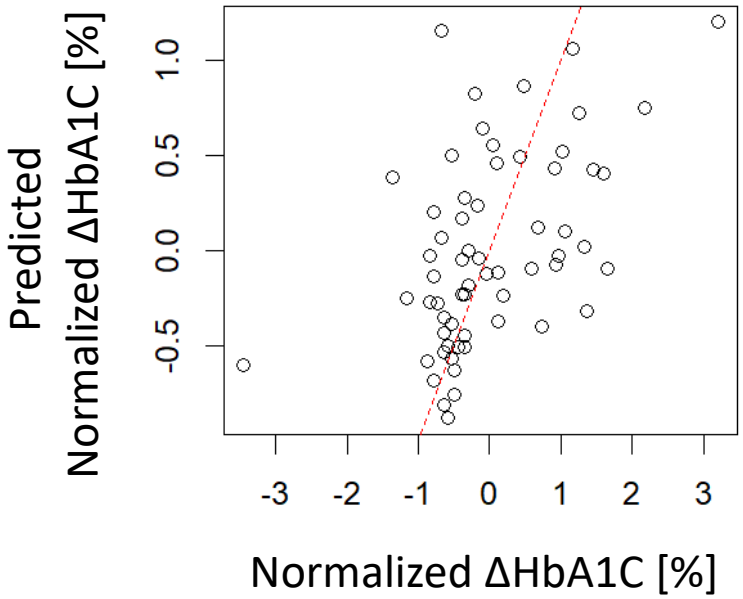
```
Coefficients:
                  Estimate
(Intercept)       0.255764
S4CESD_SAD_SUM    0.012610
S4CESD_RES_SUM   -0.053198
S4CESD_FAMSADSUM -0.413119
S4CESD_FAMRESSUM -0.623494*
S4BMI             0.235817*
S4AGE             0.008135
GENDER            0.193649
S4INCNEED        -0.203954
S4ETOHY          -0.178758
S4EDUg12         -0.073326
AHEI             -0.067660
S47DACT           0.069572
```



Results: Generalized linear model of adolescent trends in %HbA1c over 20 years

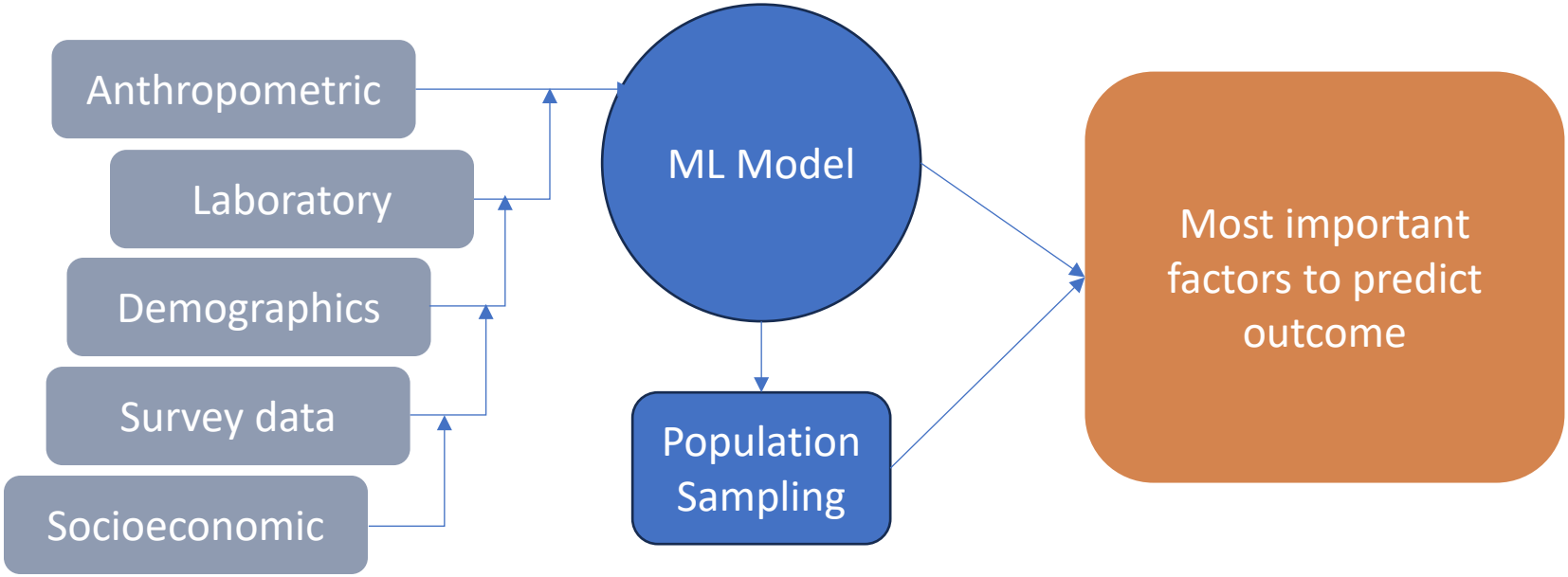
Δ%HbA1C = β_0 + β_1**Depression** + β_2**Resilience** + β_3BMI + β_4Age + β_5Gender + β_6Income + β_7Education + β_8Alcohol + β_9Diet + β_{10}Activity + β_{11}HbA1c

```
Coefficients:
                Estimate
(Intercept)      0.56033
S4CESD_SAD_SUM   0.20278
S4CESD_RES_SUM  -0.11466
S4BMI           -0.12773
S4AGE            0.03890
GENDER           0.33367
S4INCNEED       -0.56717
S4ETOHY         -0.01122
S4EDUg12        -0.33167
AHEI             0.18265
S47DACT          0.02766
S4HBA1C         -0.20474*
```



Comparing our Findings to Machine Learning

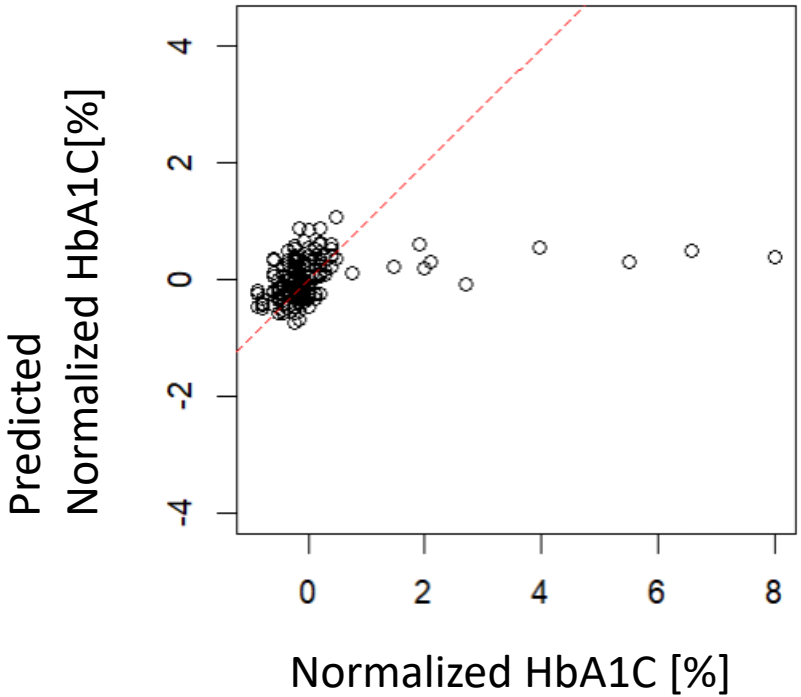
Machine Learning Identifies Factors



Familial resilience predicts baseline %HbA1c

Variables from the Epi model

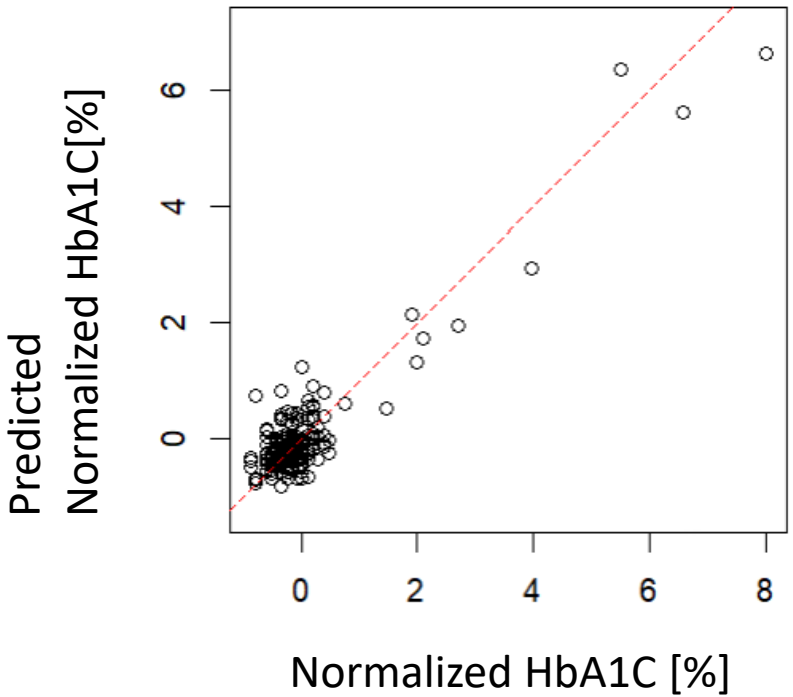
	Estimate	
(Intercept)	0.08611	
S4CESD_FAMRESSUM	-0.50443	*
S4BMI	0.23429	***
S4EDUg12	-0.21022	



Familial resilience predicts baseline %HbA1c

Lab, anthropometric, physical exam, demographic, CESD data

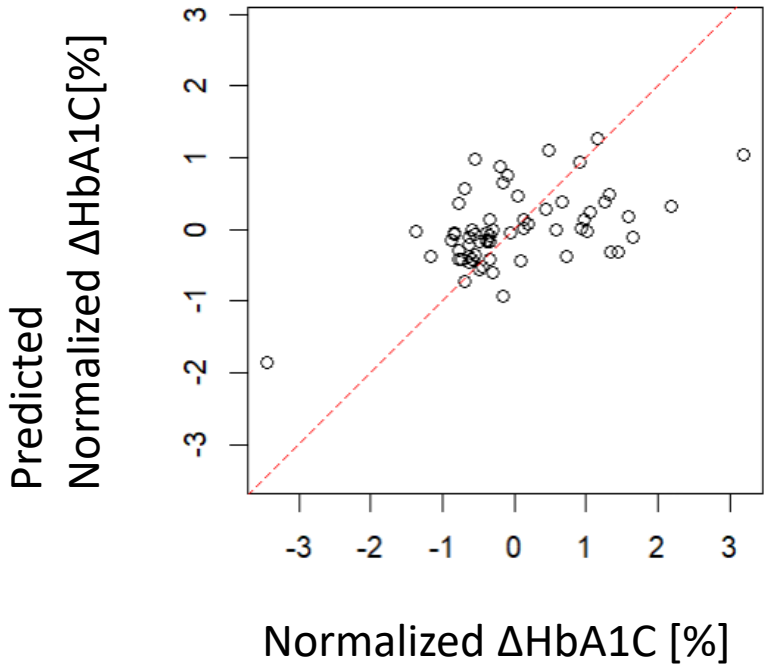
```
Coefficients:
                   Estimate
(Intercept)        -0.19779    ***
xS4CESD_FAMRESSUM  -0.22103    *
xS4INSU            -0.14607    ***
xS4U_ALB            0.21887    **
xS4G0               0.55309    ***
xS4ACANTH           0.22828    **
```



Adolescent depressive symptoms significantly predict glycemic trends

Variables from the Epi model

```
Coefficients:
                  Estimate
(Intercept)        0.63144    *
xS4CESD_SAD_SUM    0.25257    *
xS4HBA1C          -0.18909    *
xS4INCNEED        -0.78607    **
xAHEI              0.14845
xS47DACT          -0.02562
```

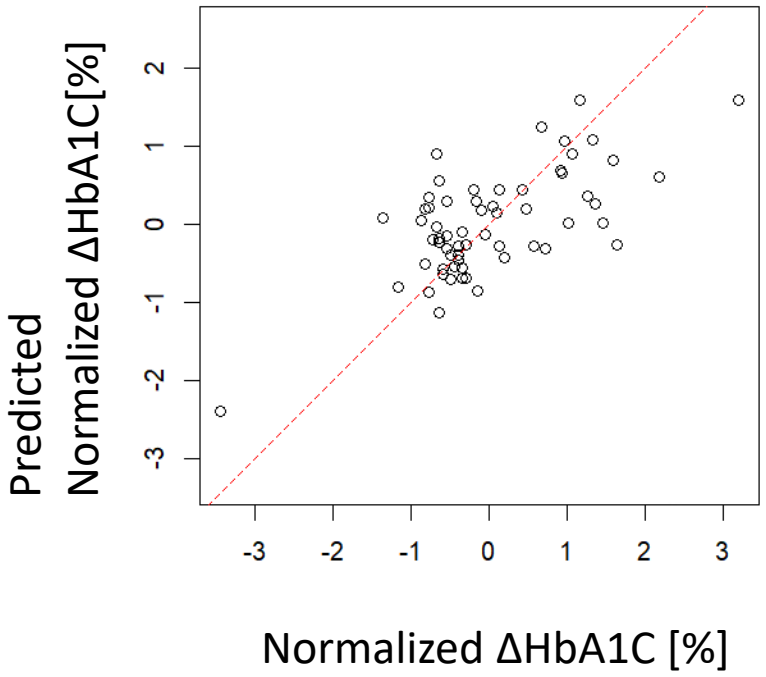


Adolescent depressive symptoms significantly predict glycemic trends

Lab, anthropometric, demographic, physical exam, CESD data

coefficients	
(Intercept)	1.0813743
S4INCNEED	-0.7969885
h(S4CESD_SAD_SUM-0.0395806)	0.4449487
h(AHEI-0.43366)	0.5176689
h(0.28966-S4U_CREA)	-0.4023272
h(0.995623-S4G0)	-0.5815530
h(S4G0-0.995623)	-0.1854184

		gcv	rss
S4CESD_SAD_SUM	5	100.0	100.0
S4INCNEED	5	86.2	96.6
S4U_CREA	3	86.2	81.5
S4G0	3	53.1	68.2
AHEI	2	43.7	55.0



In Summary

- For American Indian adolescents in the Strong Heart Family Study, there was a 31% prevalence of depressive symptoms and 15% prevalence of dysglycemia.
- Higher depressive symptoms correlated to worsening glycemic trends over 5-20 years, irrespective of a diagnosis of diabetes.
- Diabetes should initially be treated with metformin and insulin

In Summary

- **Should we expand our screening criteria?**

Risk factors:
- Family Hx (1st,2nd degree),
- gestational DM,
- SGA / LGA,
- Race,
- **+ Depressive Symptoms**

Medical conditions associated with insulin resistance:
- acanthosis nigricans,
- fatty liver disease,
- hypertension,
- dyslipidemia,
- polycystic ovary syndrome [PCOS])

Thank you!

Strong Heart Family Study

Great Plains Institutional Review Board (GPIRB)

Oklahoma Tribes and the Oklahoma City Area IHS IRB

Arizona Tribal Authority

Jessica Reese

Shelley Cole

Jack Kent

University of Washington

Jason Deen

Amanda Fretts

Sara Divall

Douglas Opel

Screening for T2D

- % A1C
- Pancreatic auto-antibodies: GAD-65, IA-2, ZnT8, IAA.

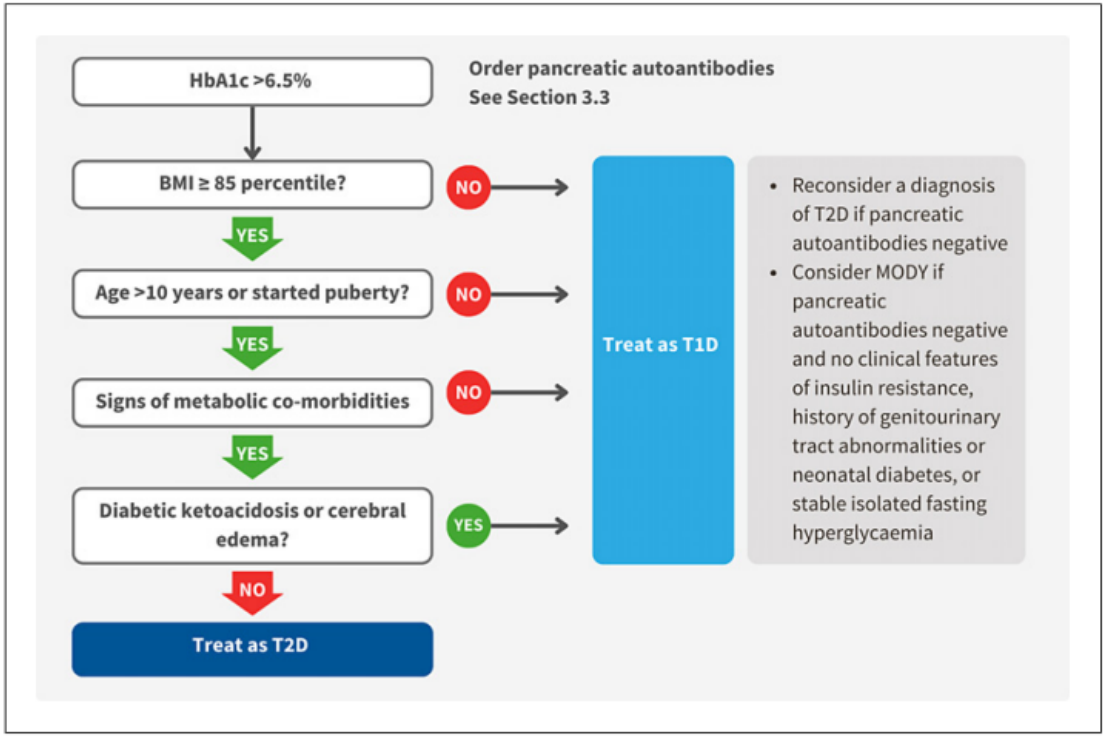


Fig. 1. Diagnosis of new onset diabetes in youth.