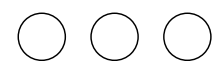




GROW: Gestational Diabetes and Related Health Outcomes Among American Samoan Women

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Type 2 & Gestational Diabetes

GLOBAL



In 2022, 14% of adults 18 and older were living with diabetes, an increase from 7% in 1990 (WHO)

UNITED STATES



Crude estimates for 2021 (CDC):

- **14.7% of adults aged 18 and older**
- Disparities by race-ethnicity

AMERICAN SAMOA



Estimated prevalence 33.6% (2018)

Gestational Diabetes (GDM) prevalence may be as high as 40.0%

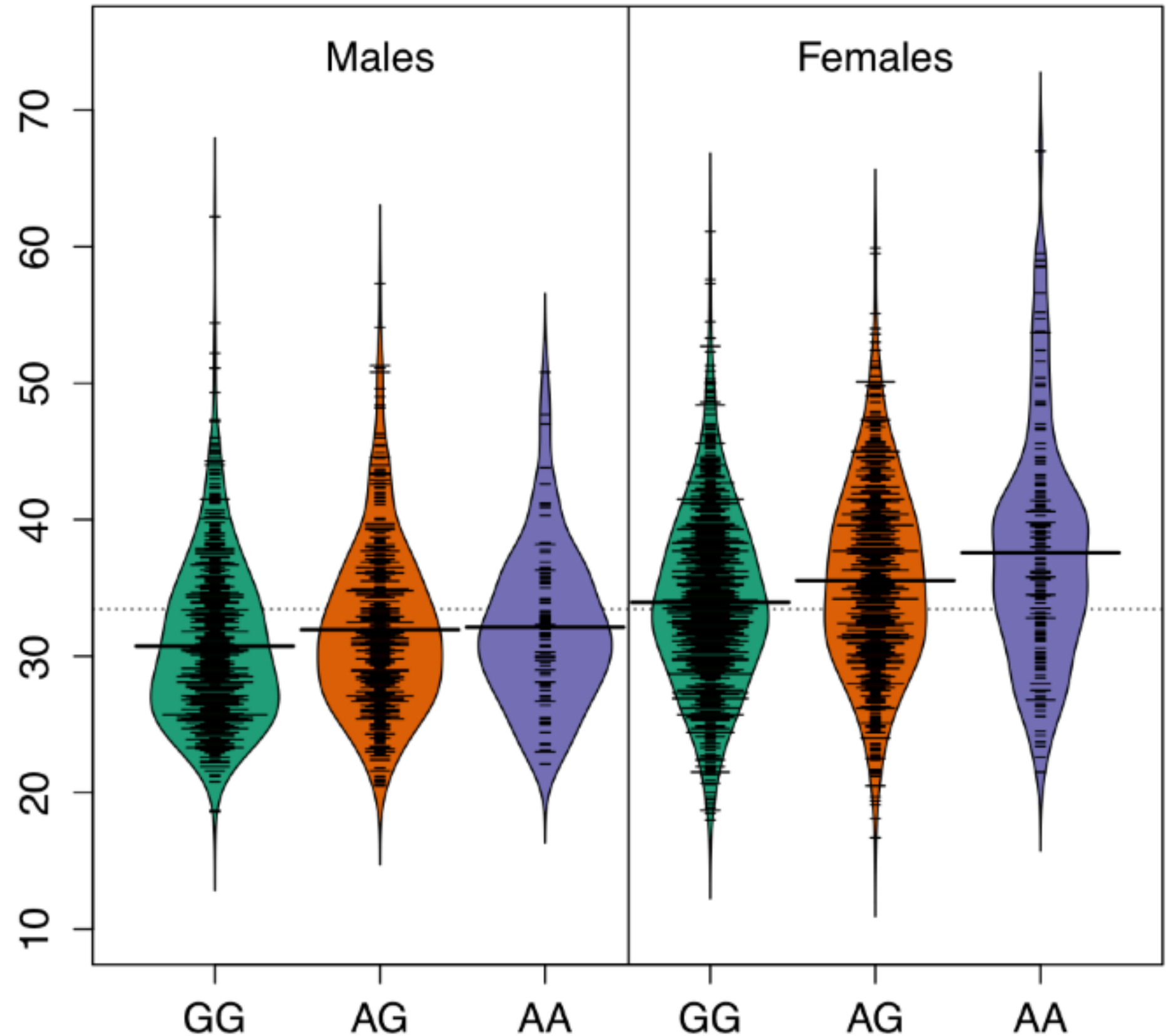
Knowledge and practice gaps: No research on etiology of GDM, no interventions, no understanding of transition to postpartum Type 2 Diabetes

rs373863828 (p.ArgGln) *CREBRF*

- Discovery Sample: +1.36 kg/m² per copy
- Explains 1.93% of variation in BMI

COMPARISON WITH FTO:

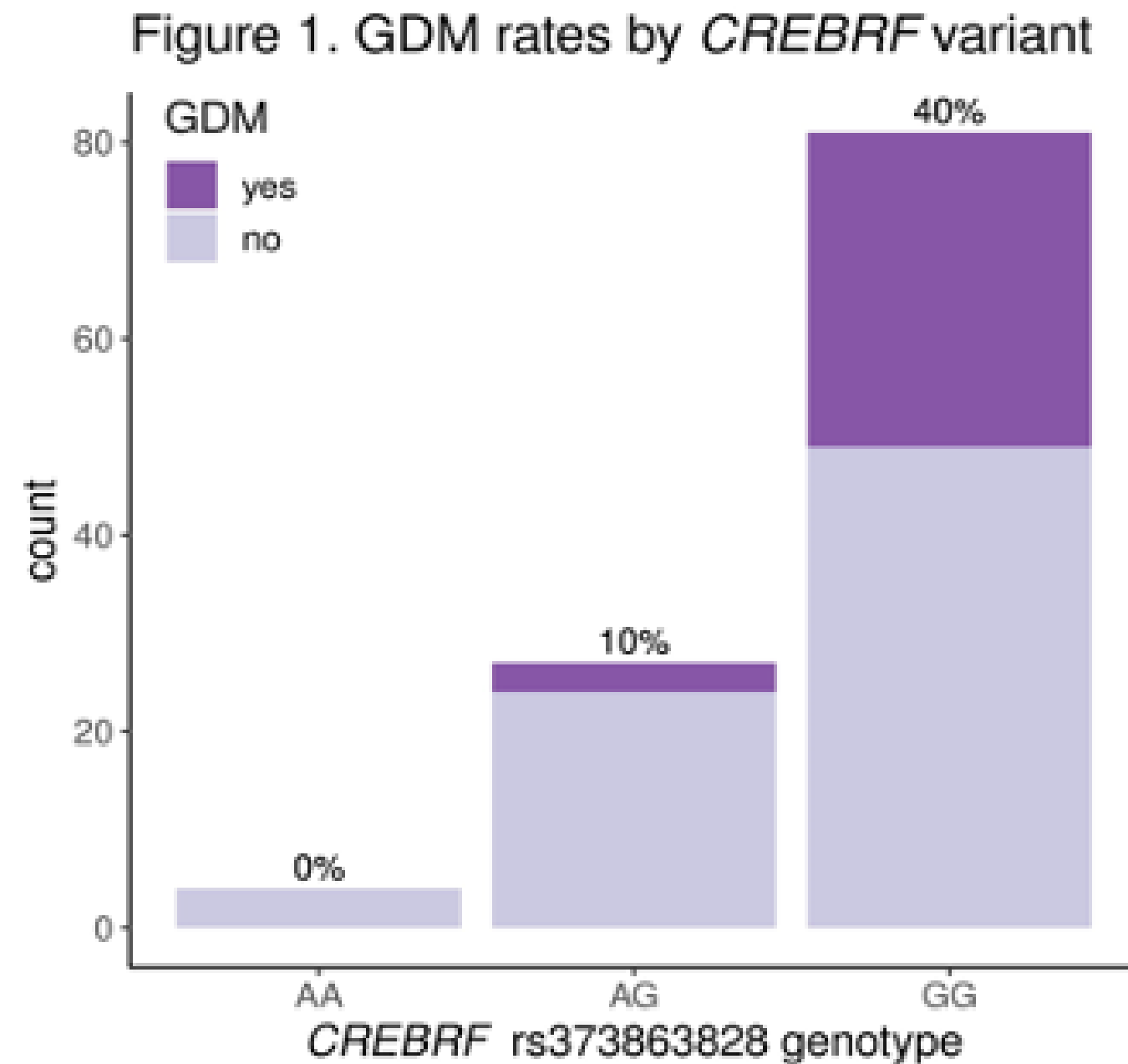
- 0.25-0.41 kg/m² per copy
- 0.10-0.34% of variation in BMI
- **~45% of Samoans have at least one copy of the variant**



rs373863828 (p.ArgGln) *CREBRF*

Genotype	Obesity	Diabetes
GG	52.1% ^y	19.7% ^s
GA	58.0%	14.2%
AA	65.2%	9.5%
Each Copy of A	Relative Risk 12.6% ↑	26.9% ↓

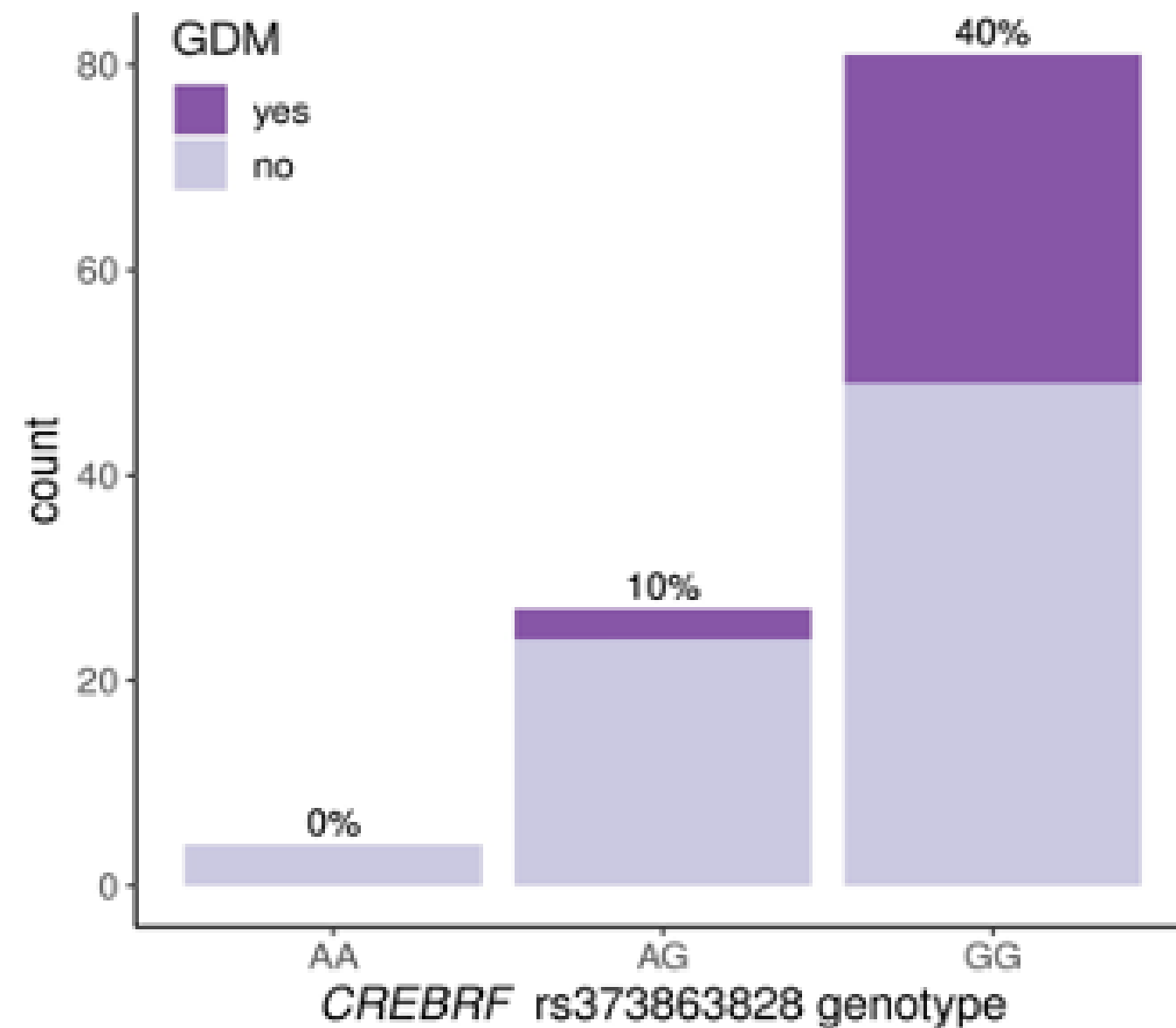
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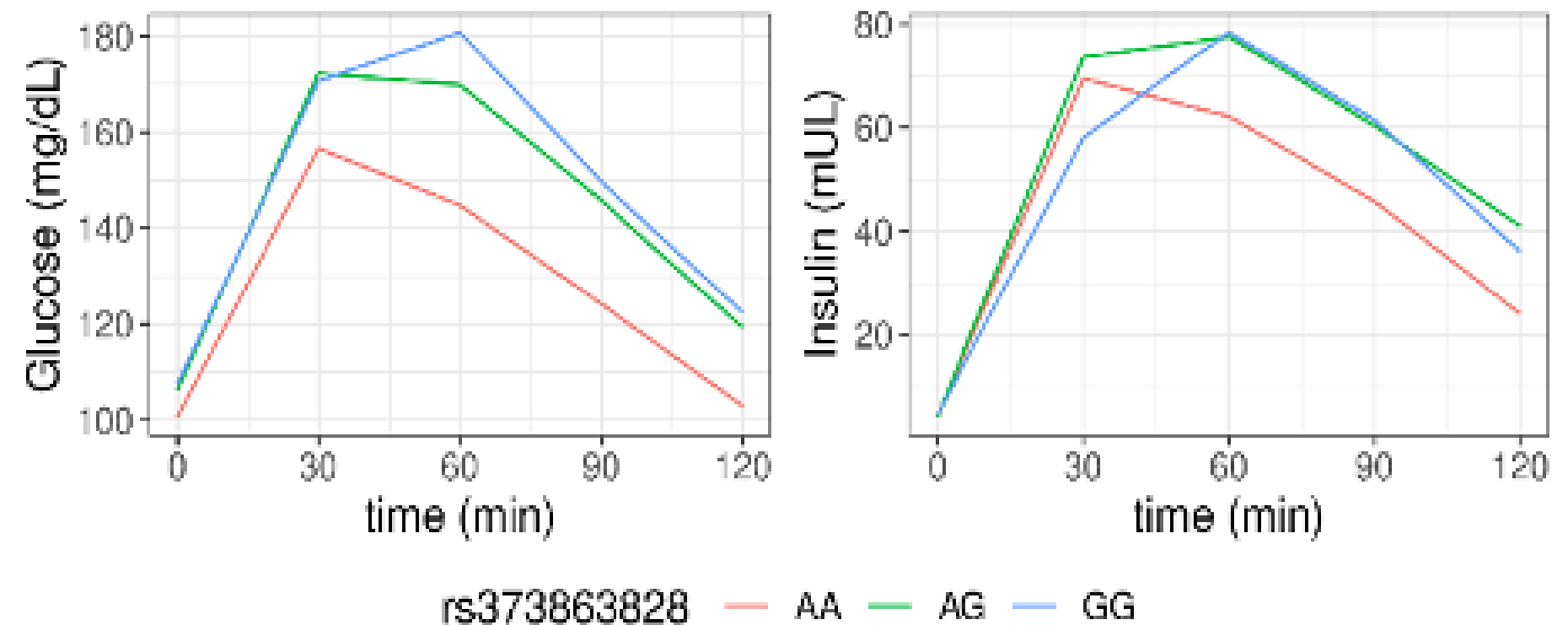


Figure 1. GDM rates by *CREBRF* variant



1. Can we replicate this in a larger, more generalizable sample?
2. Is there also an impact on transition to postpartum diabetes?
3. What is the mechanism?

Figure 4. OGTT curves - women without diabetes (weight-adjusted)





GROW

$n = 350$ women

- ≥ 18 years of age
- Samoan (four Samoan/PI grandparents)
- < 14 w based on ultrasound
- Singleton pregnancy
- Completion of prenatal care enrollment
- Planned residence in American Samoa until 18m postpartum

Exclusion Criteria:

- Pre-existing Type 1 or Type 2 Diabetes
- Conditions that would interfere with glucose homeostasis or other key study variables

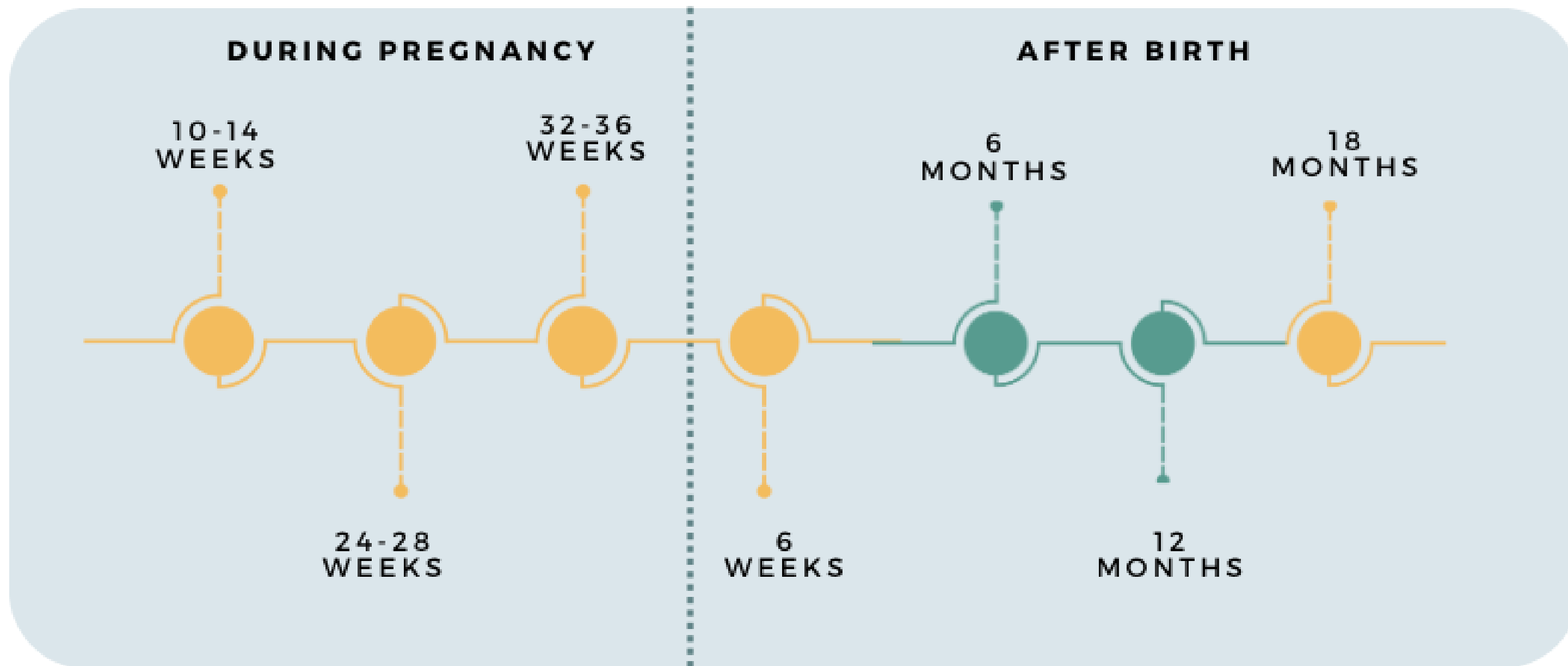
Note: We will include those with pre-diabetes



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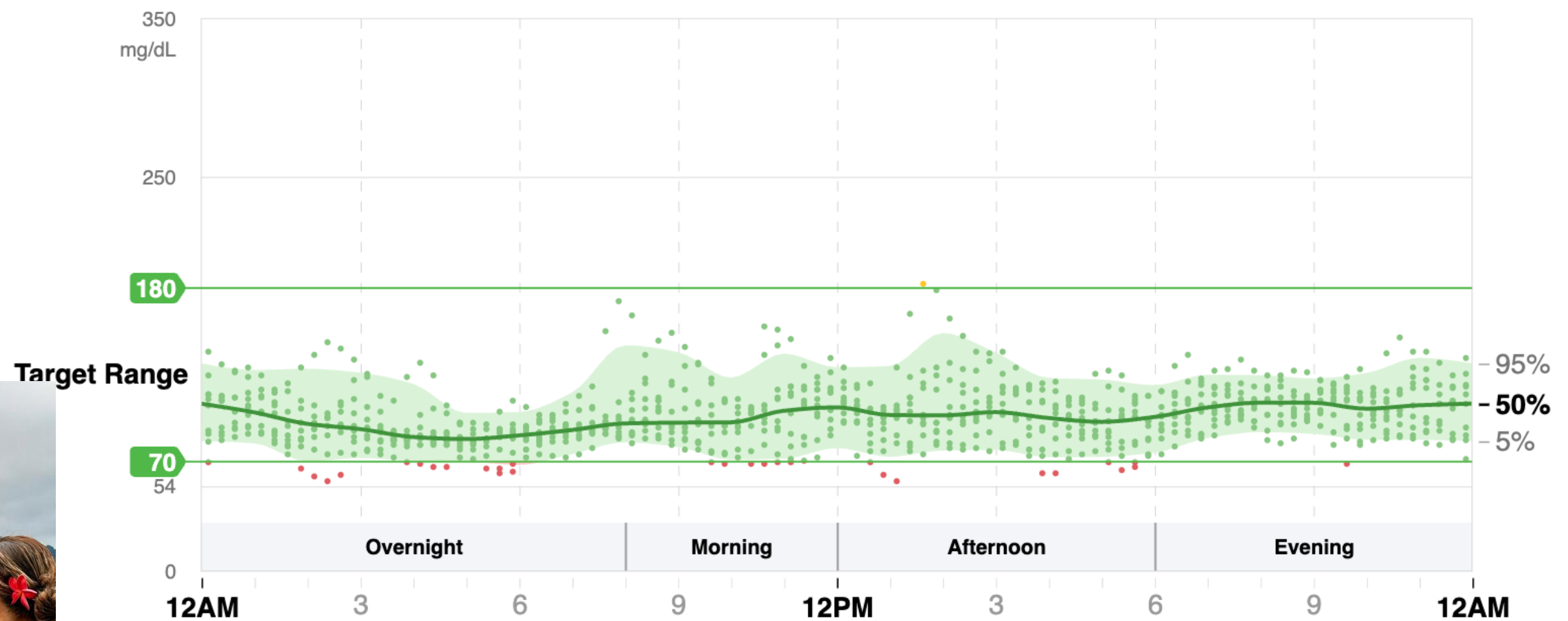
- fs-OGTT, HbA1c, CGM (10-14w, 24-28w, 32-36w, 6w, 18m)
- Anthropometry & body composition, blood pressure
- Questionnaires



GROW

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GROW - Clinical & Public Health Questions

$n = 350$ women

- How common is GDM?
- Are there patterns of early glycemic control that are associated with GDM diagnosis?
- Are there behavioral factors associated with development of GDM or postpartum T2DM?
- What support do women with GDM need?

Table 1. Questionnaire Measures			
Assessment	Data Collected	Measure	Time Point
Demographic characteristics	Age, education, household income	Investigator-developed	10-14w
Health History	Prior diagnoses, medication use, family history of diabetes		10-14w*
Tobacco and Alcohol	Use of tobacco products, vaping, alcohol consumption; 30d recall		All
Dietary Intake	Intake of fruits and vegetables, sugar-sweetened beverages, desserts, salty snacks, fast food, water; 30d recall	Brief dietary screener	All
Physical Activity**	Time spent in 32 activities: household/caregiving, occupational, sports/exercise, transportation, and inactivity; current trimester recall	Pregnancy Physical Activity Questionnaire	All pregnancy
	Time spent in moderate and vigorous leisure, work, and transportation activities; 7d recall	International Physical Activity Questionnaire	All postpartum
Sleep	Global sleep quality score and component scores (subjective sleep quality, sleep duration, etc.); 30d recall	Pittsburgh Sleep Quality Index	All
Psychosocial Health	Depression, anxiety, social support	PHQ-9, GAD-7, MSPSS	All
Infant Feeding	Mode of infant feeding (breastfeeding, formula, mixed-feeding)	Investigator-developed	All postpartum
Usual Routines	Illnesses during CGM, changes to usual routine (diet & physical activity)	Investigator-developed	All CGM

d: day; w: week; CGM: continuous glucose monitoring. *Diagnoses and medication use throughout pregnancy will be extracted from medical records (Section C.5.f); **Min/week of light, moderate and vigorous activity will be used in analyses

GROW

Planned Analyses

Aim 1: Associations of CREBRF and GDM

- Primary: Incidence of GDM, plasma glucose during the 24-28w OGTT
- Secondary: glucose during 10-14w and 32-36w OGTTs, CGM (Time In Range)
- Exploratory: CGM profiles by genotype among women diagnosed with GDM



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Aim 2: Associations of CREBRF with changes in glucose homeostasis and pre-DM/T2DM risk postpartum

- Primary: Changes in fasting glucose and A1c from 10-14w gestation to 18m postpartum
- Secondary: Incident pre-DM/T2DM at 18m postpartum, CGM profiles and incident pre-DM/T2DM
- Exploratory: Body composition as a potential mediator



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Aim 3: Evaluate to what extent improvements in insulin secretion mediate the pathway between CREBRF genotype and diabetes risk

- CREBRF - 10-14 w insulin response - GDM
- CREBRF - 24-28 w insulin response - T2DM postpartum



GROW+

$n = 320$ infants

Specific Aims:

1. Determine associations between **maternal glycemia** in pregnancy and **infant body size, composition, and metabolic markers** and assess the moderating role of infant *CREBRF*
2. Determine the extent to which **body composition mediates the association between maternal glycemia in pregnancy and infant metabolic markers** (and assess direct and indirect effects of infant CREBF)
3. Determine associations between maternal-infant **CREBRF genotype combination** and (a) maternal glycemia, (b) infant body size/composition, and (c) metabolic markers

GROW+

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- Genotyping
- Anthropometry (weight, length, skinfolds)
- Body composition (DXA)
- Metabolic markers: glucose, insulin, proinsulin, c-peptide, leptin, adiponectin, IGF1, IGF2
- CGM - 12m
- Questionnaires (feeding)



Summary

- Pregnancy is a uniquely important moment to both understand how NCD risk is established and to intervene
- Understanding unique genetic contributors to risk may open doors to intervention or help guide limited resources
- Our work will examine risk for gestational diabetes (GDM) and impacts of GDM on child health and growth in the first 18 months of life



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