GENETICS AND PRECISION HEALTH

28TH BEST PRACTICES FORUM

MARCH 24, 2018

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EL RIO HEALTH

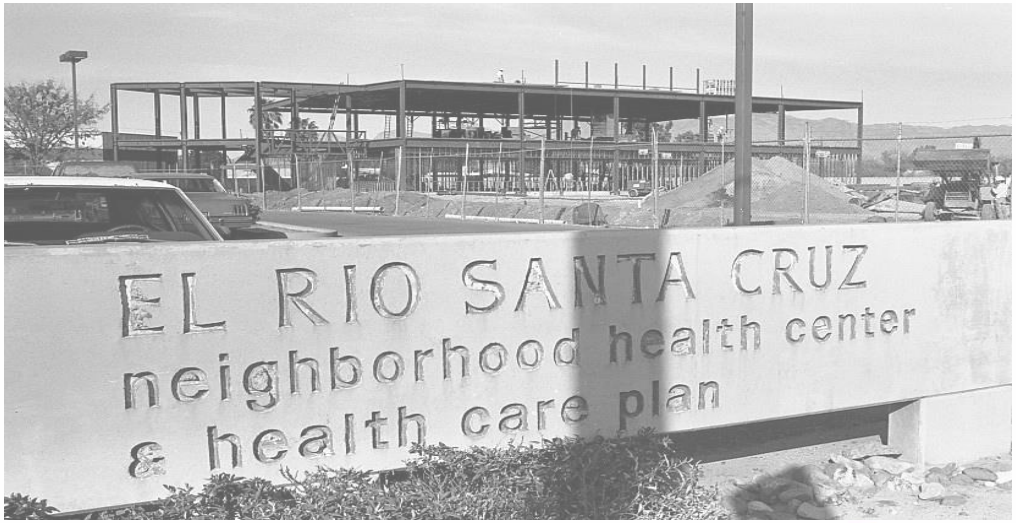
Patient-Centered Medical Home NCQA RECOGNIZED PRACTICE

THE JOINT COMMISSION NATIONAL QUALITY APPROVAL

LEADER IN LGBT HEALTHCARE EQUALITY 2016 HEALTHCARE EQUALITY INDEX

Our History

- El Rio Community Health Center opened to serve patients in October 1970 as El Rio Santa Cruz Neighborhood Health Center
- El Rio was incorporated in 1974 as a private non-profit corporation



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Our Practice

2017 UDS Data

Total Number of Patients Served	**101, 563**
Total Number of Patient Visits	**389, 303**
Number of Employees	**1, 156**
Number of Unique Clinic Sites	**14**
Number of Providers	**170- Medical** **31- Dental** **24- BH**

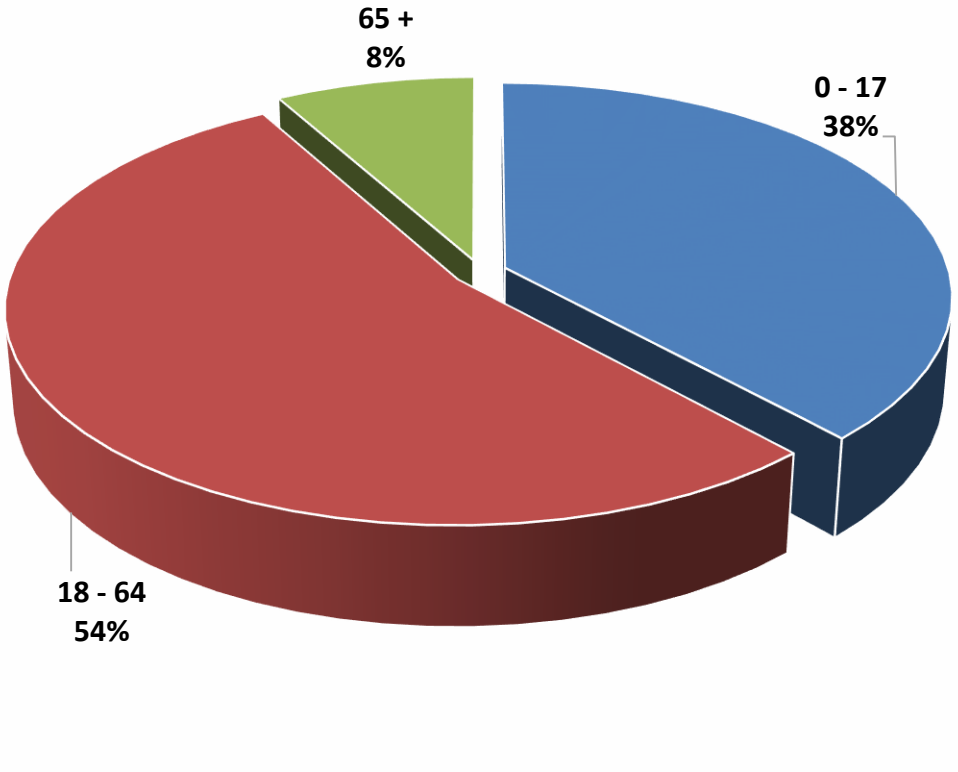
EL RIO HEALTH

Who do we serve?

Demographics

- A health care home for 101,536 patients.
- 64% of El Rio's patients live below the Federal Poverty Line.

Patients by Age



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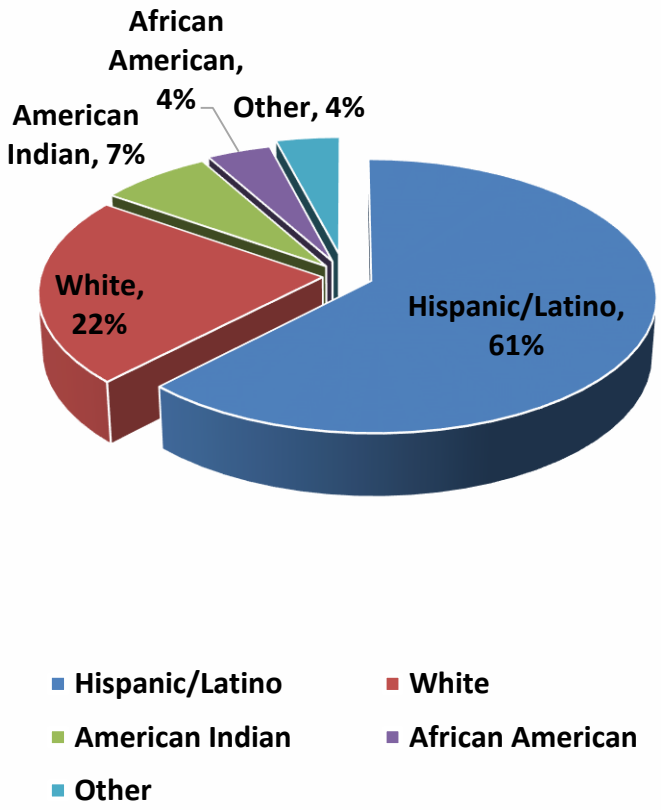
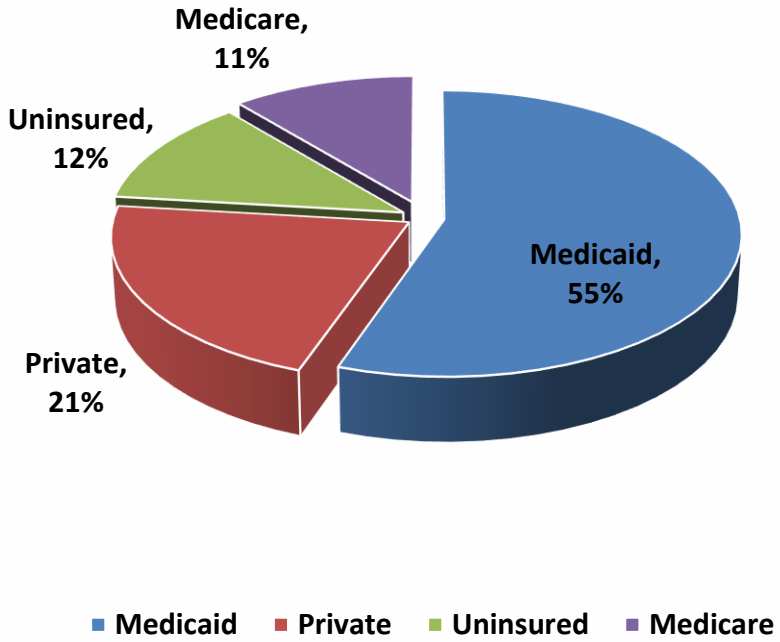
Our Patients

El Rio Patients by Race/Ethnicity (2017 UDS Data)



El Rio Patients by Payer Source (2017 UDS Data)



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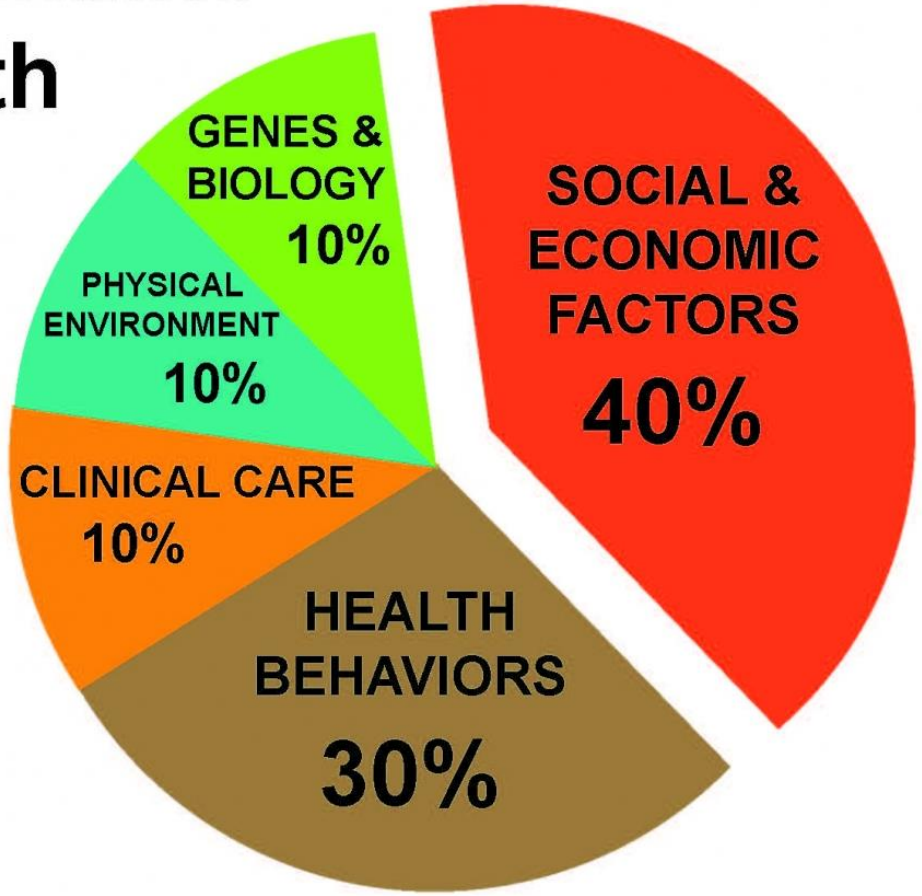
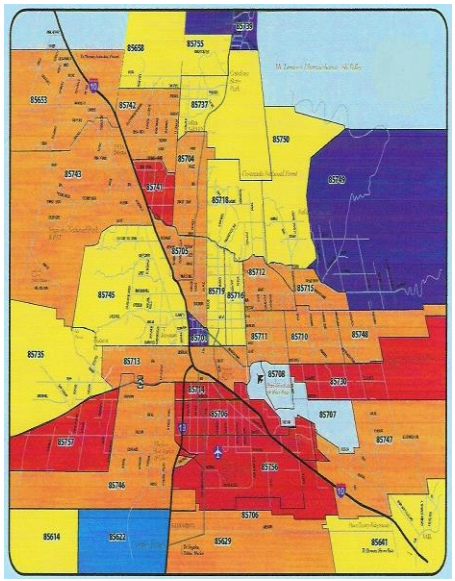
Why Implement Precision Medicine in the Community Clinic Setting?

- Diversity of population
- Disproportionate disease burden/healthcare disparities
- Social determinants of health
- Inequitable resource allocation
- Clinically relevant research to CHC community

Determinants of Health



ZIP Code VS. GENETIC Code



"Your longevity and health are more determined by your ZIP code than they are by your genetic code."

Tom Frieden, M.D., M.P.H.; CDC Director

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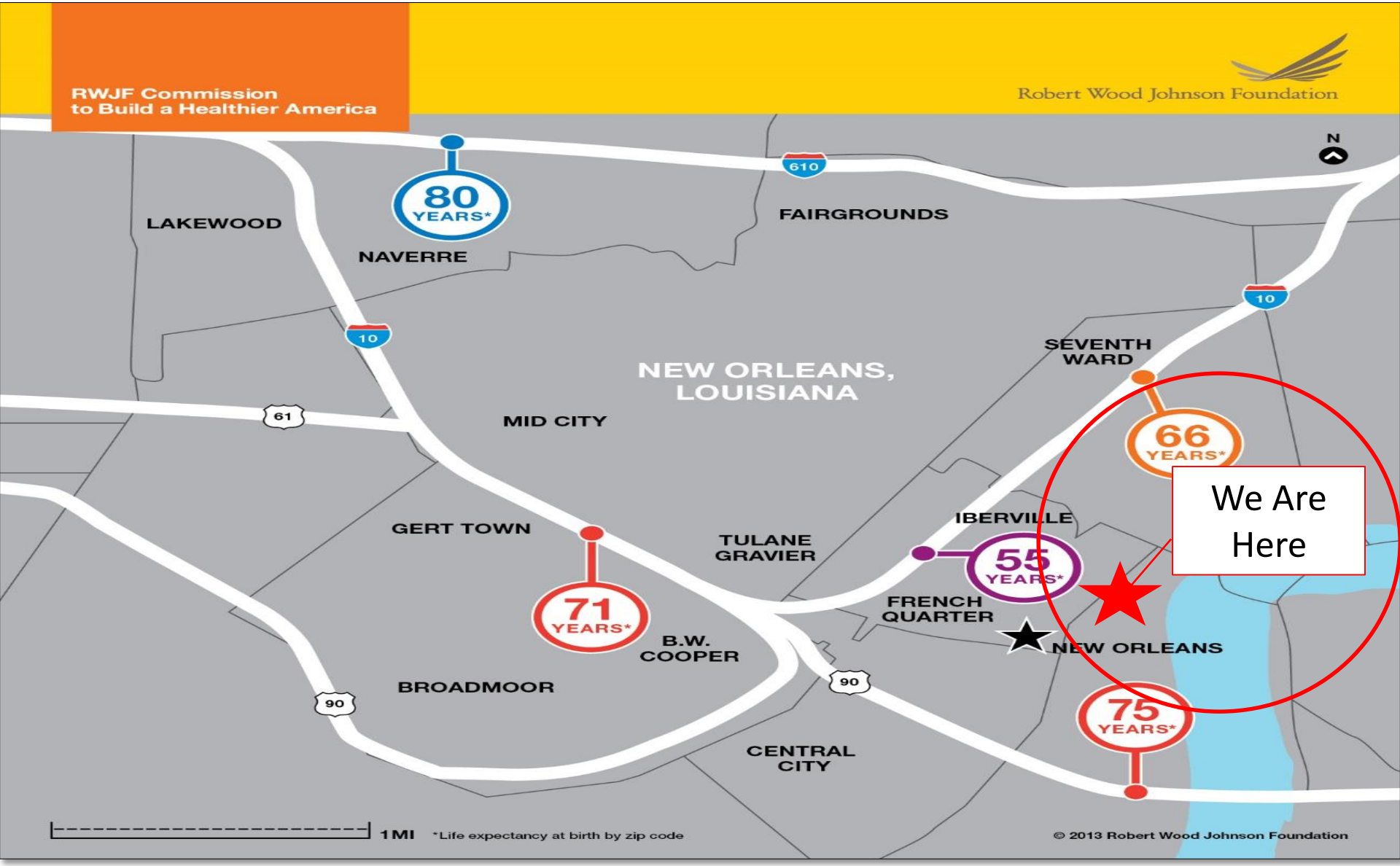
And The Gap Is Widening

Birth Place and Life Expectancy: New Orleans



Critical for Implementation of Precision Medicine: Disease as a Phenotype

- The disease phenotype results from the combination of biology (often viewed as a genotype) with the environment (physical, psychosocial, cultural, and behavioral factors).
- So which is more important in disease development, your Zip Code (environment), or your Genetic Code?
- **Both, but to what extent?**

Resiliency: The Ability to Adapt to Stress, Trauma and Adversity (Wilson et al, Archives of Public Health.2017; 75:56)

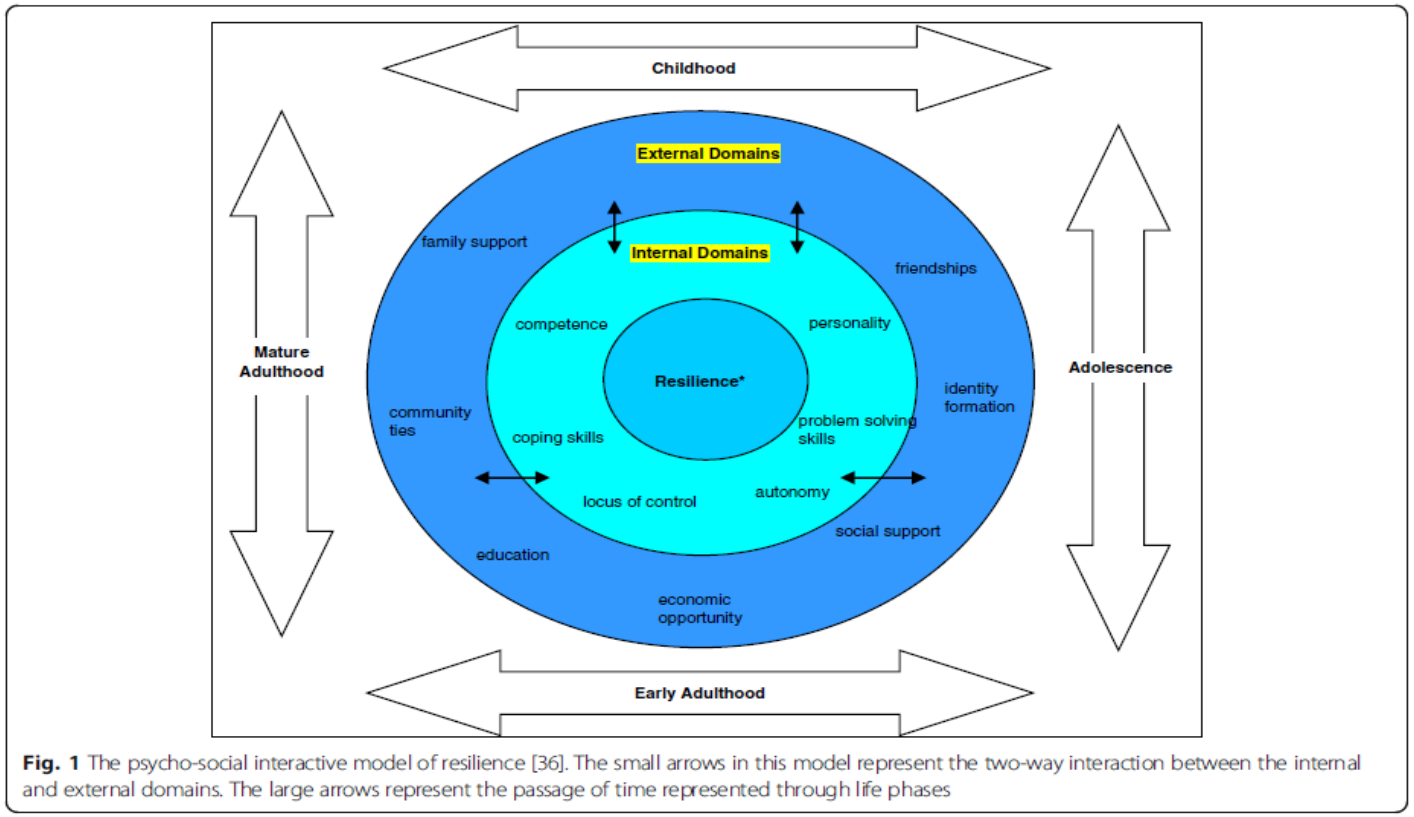


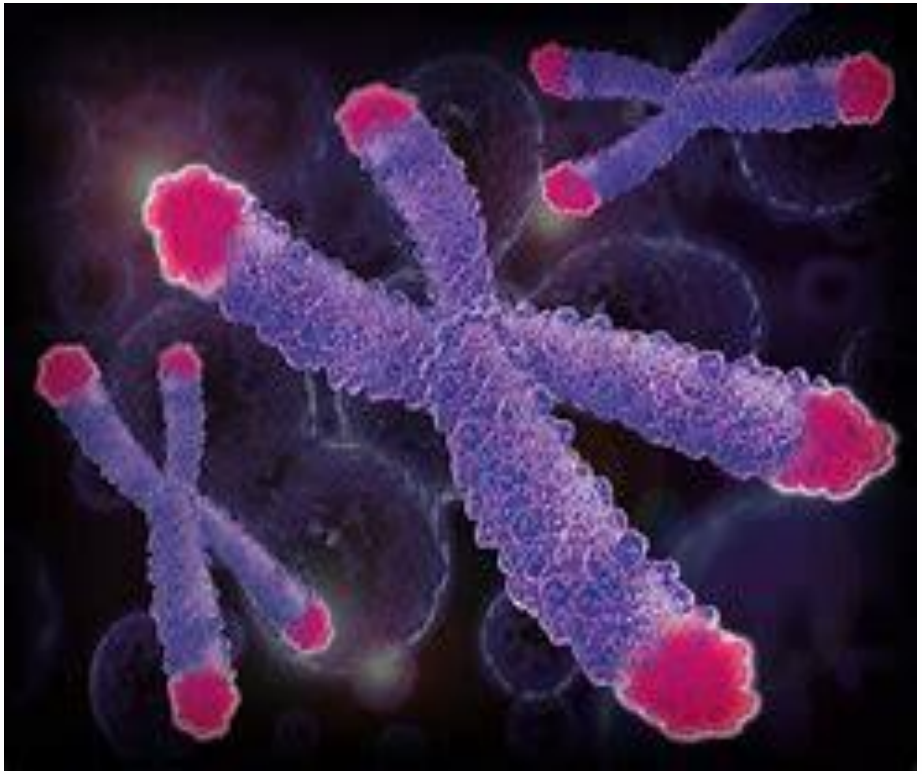
Fig. 1 The psycho-social interactive model of resilience [36]. The small arrows in this model represent the two-way interaction between the internal and external domains. The large arrows represent the passage of time represented through life phases

Stress Resilience and Risk of Type 2 DM in 1.5 Million Young Men (Crump et al, Diabetologia. 2016 April; 59(4):728-733)

Fig. 1.
Stress resilience (on a scale of 1–9) in 18-year-old men who did or did not develop type 2 diabetes in adulthood. Black bars, type 2 diabetes; grey bars, no type 2 diabetes

Telomeres

- DNA protein caps at the end of chromosomes
- Protect against genetic degradation
- Telomere length is a marker of cell aging
- Telomere shortening is associated with early adversity and chronic stressors
- Understanding Telomere biology evolving, but shortening linked to lower life expectancy, increased risk for cardiovascular disease and Alzheimer's dementia.



Lifespan Adversity and Later Adulthood Telomere Length in the Nationally Representative US Health and Retirement Study (Puterman et al Proceedings of National Academy of Sciences October 2016)

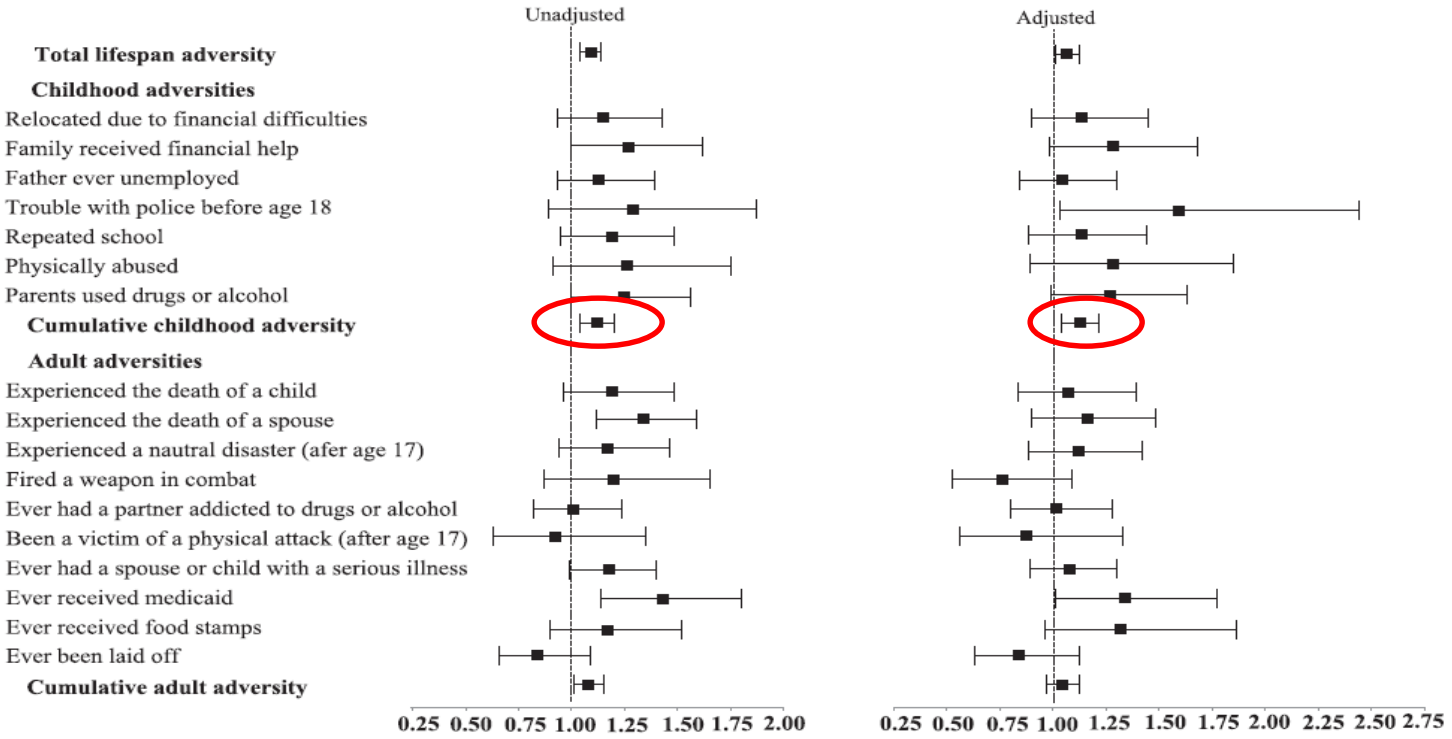


Fig. 1. ORs and 95% CI for total lifespan adversity, childhood adversities, adulthood adversities, and each independent item predicting odds of short telomeres (25th lowest percentile).

Academic: Community Health Center Partnerships

EL RIO COMMUNITY HEALTH CENTER

MARIPOSA COMMUNITY HEALTH CENTER

Center for Disparities in Diabetes, Obesity & Metabolism

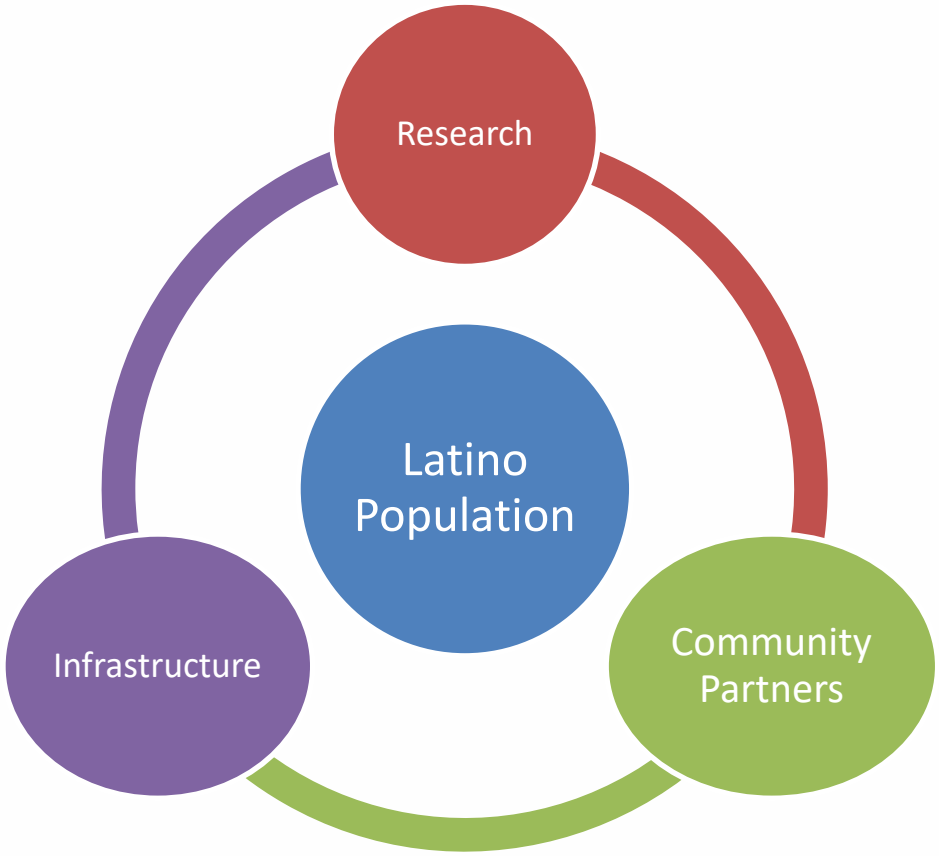
CDDOM Biobank Research Initiative Goals

- ***Biospecimen Registry*:** Creation of a resource of consented patients with a biobank of their genetic material
- ***Research:*** To **serve as a nucleus for interdisciplinary research** to advance evidence-based clinical care in the community.
- ***Outreach and Public Service:*** To **facilitate development of innovative approaches to delivery of care and prevention**, within a diverse population, and speeding the time from knowledge development to clinical care.

Funding Specifics

- 4.5 million start up funding for a 5 year project (proof of concept) by the University of Arizona Health Sciences
- PI: Lawrence Mandarino, PhD, Director of the UA Center for Disparities in Diabetes, Obesity and Metabolism
- Collaboration with FQHC's: El Rio and Mariposa Health Centers

Specific Objectives



- To understand the **social, clinical, and biological reasons** for poor glycemic control in patients with type 2 diabetes.
- To reduce the percentage of El Rio and Mariposa patients with HbA1c > 9.0%
- Recruit approximately 2,500 poorly controlled patients and their family members.

Proband Inclusion Criteria

- Diabetic patients with HbA1c > 9.0% and their multigenerational families (parents, children, spouses, etc.)
- Age between 18 and 75
- Self-identified as Latino

Healthy People 2020 Comparative Results

Measure	HP 2020 Goal	AACHC	2015 El Rio UDS	2016 El Rio UDS	2017 El Rio UDS	Current El Rio Performance (February 2018)
All Patients w/ Hba1c >9%	16.10%	48.71%	32.2%	35.6%	35.1%	35.2%

Diabetic HbA1c Uncontrolled >9.0% [18-75]: 1Q14 - 4Q17

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Goal	Decrease the percentage of diabetic patients aged 18-75 whose most recent HbA1c reading was >9%
Benchmark	16.2% (Healthy People 2020 Target) 33.0% (2016 HEDIS Commercial HMO Mean) 43.3% (2016 HEDIS Medicaid HMO Mean) 26.3% (2016 HEDIS Medicare HMO Mean)
Numerator	3,243 patients aged 18-75 whose most recent HbA1c test results was >9%
Denominator	9, 387 diabetic patients aged 18-75 who were seen during the measurement year
Quarter	4th Quarter 2017 (October—December 2017)

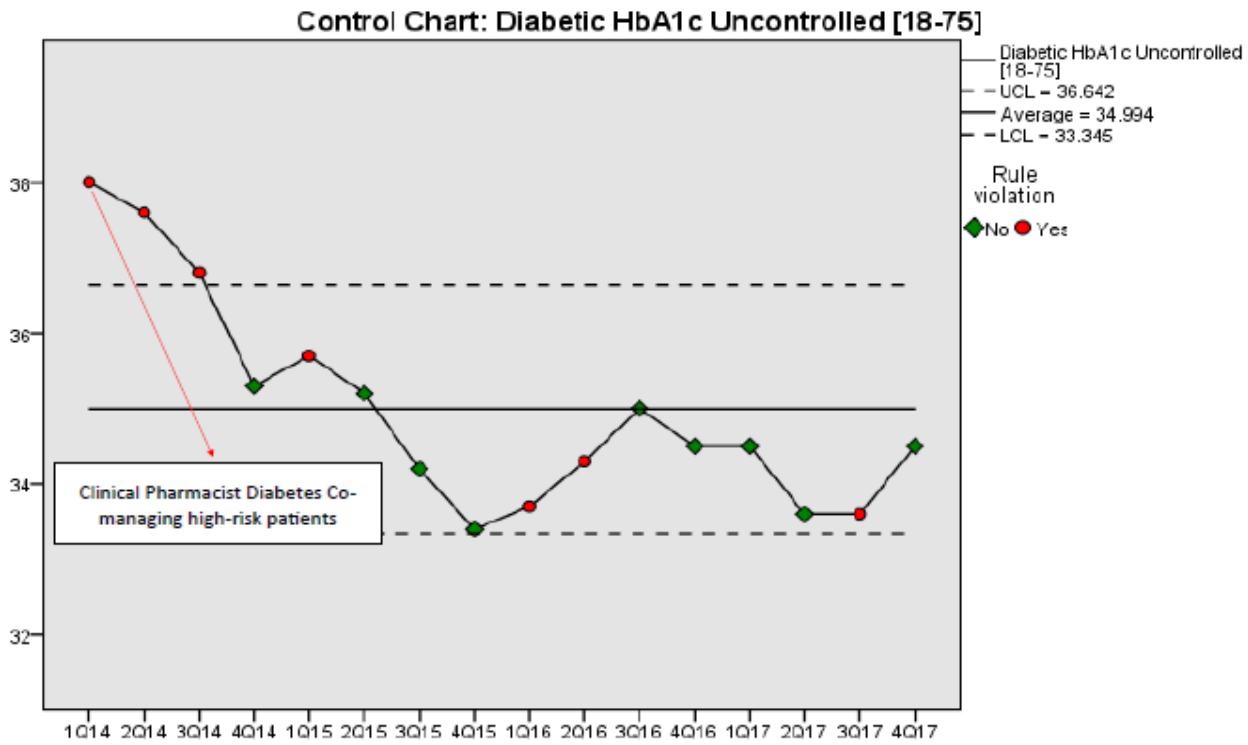
Interpretation	Beginning in 1Q14 a statistically significant decrease in patients whose most recent HbA1c was >9%. This is likely the result of clinical pharmacists co-managing high-risk diabetic patients as part of the medical team.
Action Plan	Clinical pharmacists will continue to co-manage high-risk diabetic patients as part of the medical team with the aim of continuing to drive a decrease in patients whose most recent HbA1c being >9%

Control Rules (Special Cause Variation)

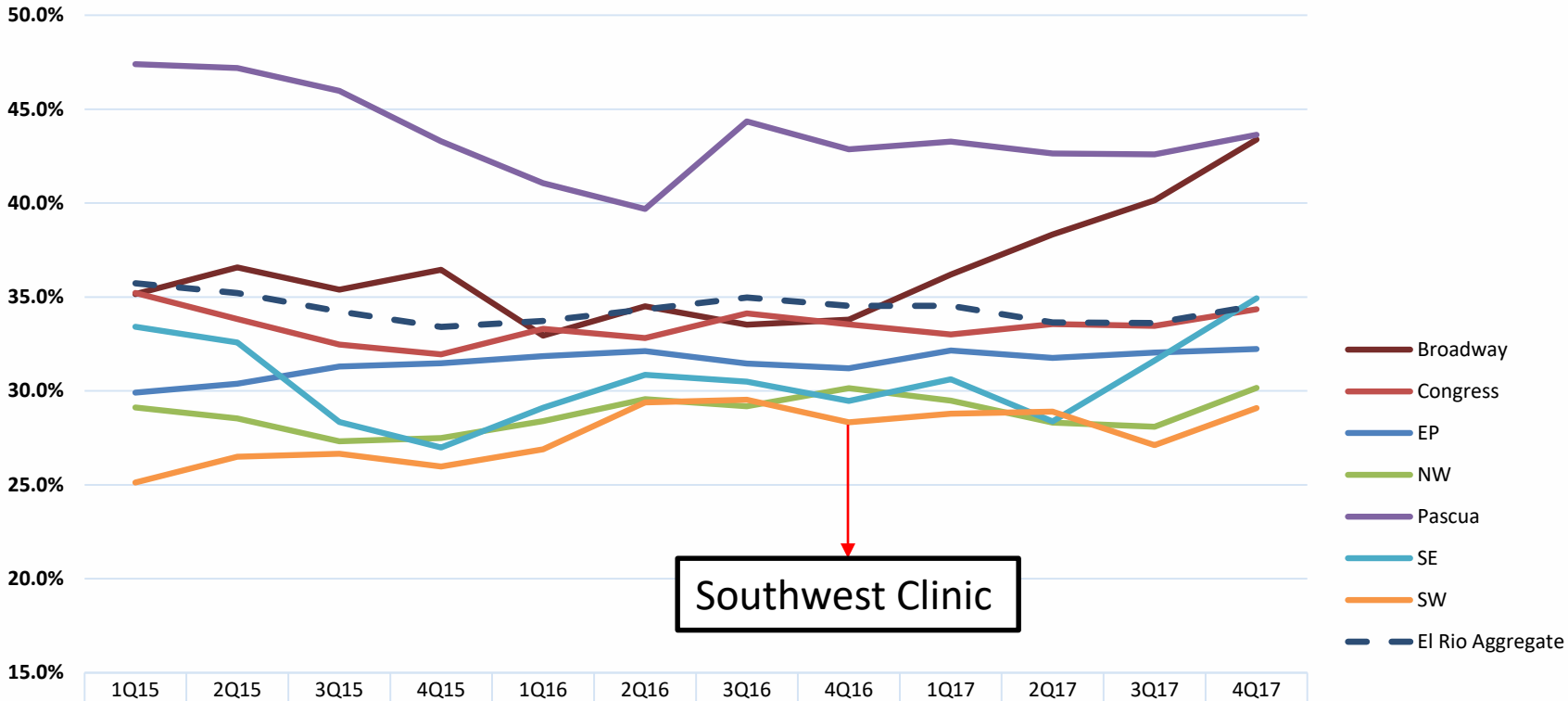
- One point outside the upper or lower control limits (3 SD)
- Two out of three successive points more than 2 SD from the mean on the same side of the center line
- Four out of five successive points more than 1 SD from the mean on the same side of the center line
- Eight successive points on the same side of center line
- Six successive points increasing or decreasing (a trend)

Rule Violations

Month	Violation
1Q14	Greater than +3 sigma
2Q14	Greater than +3 sigma, 2 points out of the last 3 above +2 sigma
3Q14	Greater than +3 sigma, 2 points out of the last 3 above +2 sigma
1Q15	4 points out of the last 5 above +1 sigma
1Q16	2 points out of the last 3 below –2 sigma
2Q16	4 points out of the last 5 below –1 sigma
3Q17	2 points out of the last 3 below –2 sigma

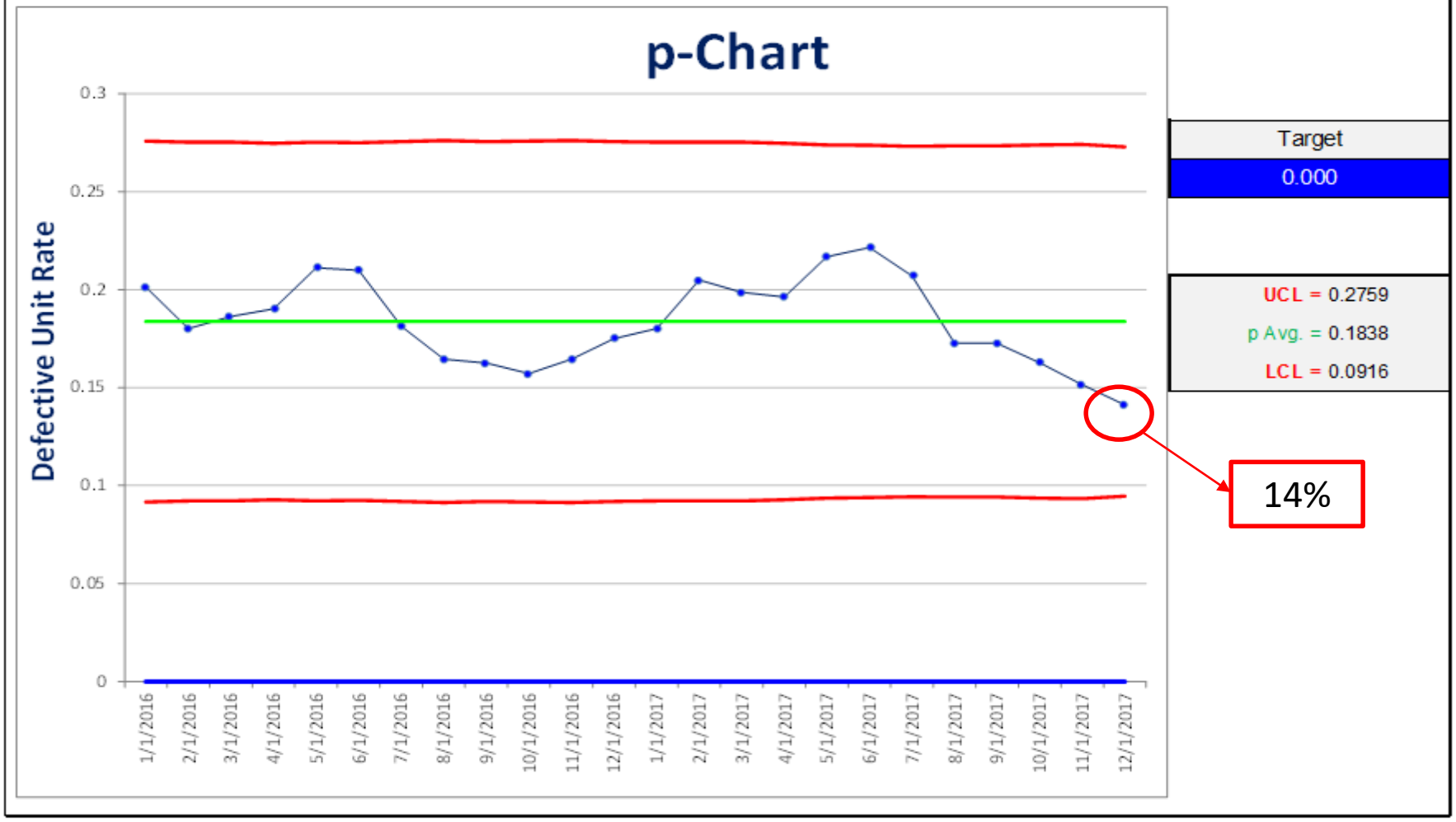


Diabetic HbA1c Poor Control >9.0% by Location



	1Q15	2Q15	3Q15	4Q15	1Q16	2Q16	3Q16	4Q16	1Q17	2Q17	3Q17	4Q17
Broadway	35.2%	36.6%	35.4%	36.4%	32.9%	34.5%	33.5%	33.8%	36.2%	38.3%	40.1%	43.4%
Congress	35.2%	33.8%	32.5%	31.9%	33.3%	32.8%	34.1%	33.5%	33.0%	33.6%	33.5%	34.3%
EP	29.9%	30.4%	31.3%	31.5%	31.9%	32.1%	31.4%	31.2%	32.2%	31.8%	32.0%	32.2%
NW	29.1%	28.5%	27.3%	27.5%	28.4%	29.6%	29.2%	30.1%	29.5%	28.3%	28.1%	30.2%
Pascua	47.4%	47.2%	46.0%	43.3%	41.1%	39.7%	44.4%	42.9%	43.3%	42.6%	42.6%	43.6%
SE	33.4%	32.6%	28.3%	27.0%	29.1%	30.9%	30.5%	29.5%	30.6%	28.4%	31.6%	34.9%
SW	25.1%	26.5%	26.7%	26.0%	26.9%	29.4%	29.5%	28.3%	28.8%	28.9%	27.1%	29.1%
El Rio Aggregate	35.7%	35.2%	34.2%	33.4%	33.7%	34.3%	35.0%	34.5%	34.5%	33.6%	33.6%	34.5%

Soltani- HbA1c Uncontrolled >9.0%

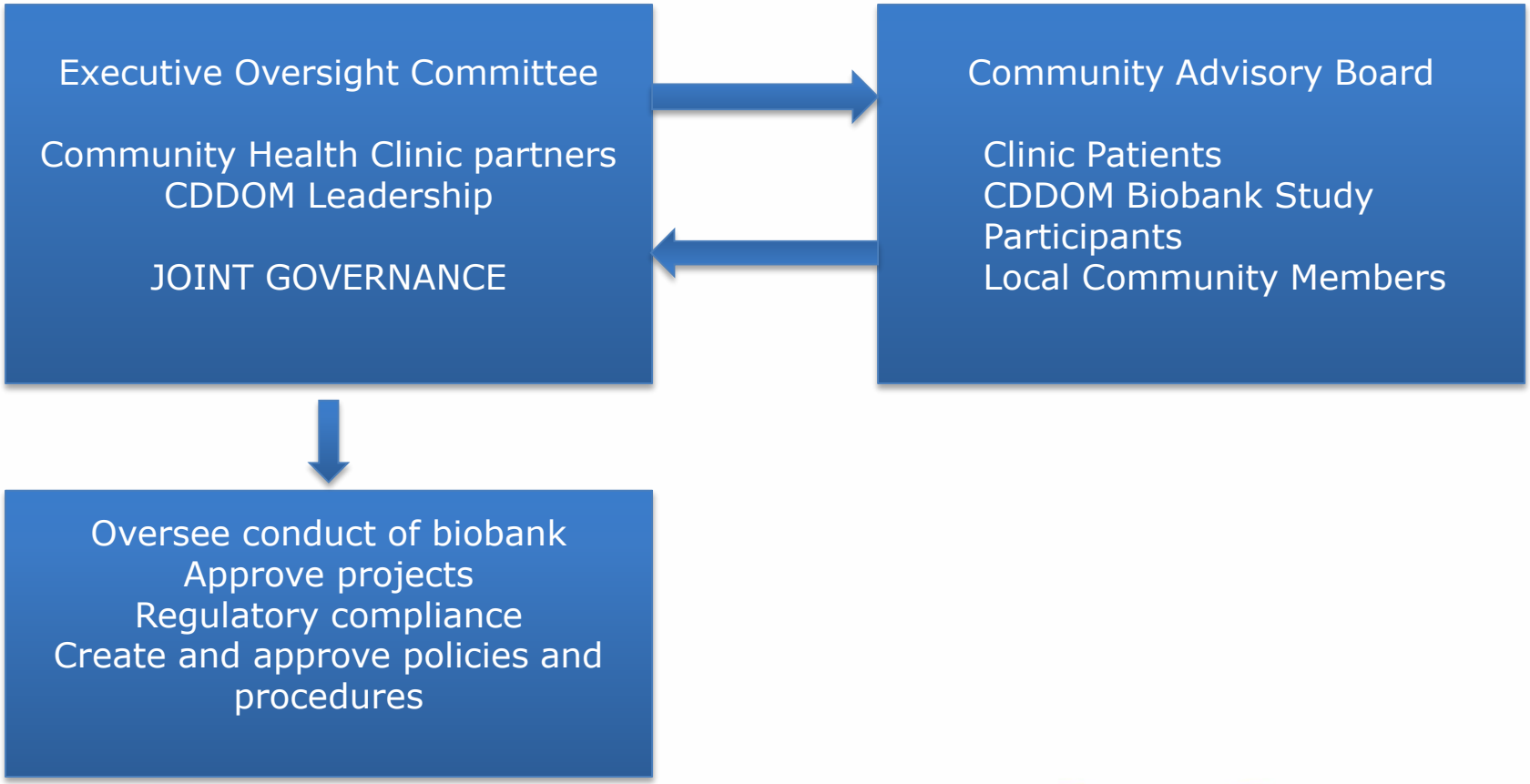


NON DUALISTIC APPLIED RESEARCH

Application and Impact of Biobank and Data

- **Testing effectiveness of family-based interventions** to improve glycemic control and prevent diabetes
- **Testing pharmacogenomic treatment interventions** to improve glycemic control and prevent diabetes.
- **Community Based Research** with patient, community, clinician and researcher input.

CDDOM Biobank Research Initiative: Governance and Advisory Committees



Next Steps

- Enrollment just begun: to date 10 families recruited, 13 total individuals
- Depression study proposal with OneOme: use of antidepressant pharmacogenomics in treatment of depression in an FQHC setting.

Genotype/Phenotype Summary

ONEOME®

Making prescriptions personal

Gene and phenotype summary

Gene	Genotype		Phenotype summary / Metabolic status
CYP1A2	*1A/*1F		**Rapid** Increased activity. Drugs converted to active metabolite(s) may cause side effects or toxicity. Active drugs converted to inactive metabolite(s) may lack efficacy.
CYP2B6	*1/*5		**Intermediate to Normal** Decreased activity. Drugs converted to active metabolite(s) may have reduced efficacy. Active drugs converted to inactive metabolite(s) may cause side effects or toxicity.
CYP2C9	*1/*3		**Intermediate** Decreased activity. Drugs converted to active metabolite(s) may have reduced efficacy. Active drugs converted to inactive metabolite(s) may cause side effects or toxicity.
CYP2C19	*17/*17		**Ultrarapid** Increased activity. Drugs converted to active metabolite(s) may cause side effects or toxicity. Active drugs converted to inactive metabolite(s) may lack efficacy.
CYP2D6	*1/*1		**Normal** Normal level of activity. Drugs metabolized at a normal rate.
CYP3A4	*1/*1		**Normal** Normal level of activity. Drugs metabolized at a normal rate.

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Genotype-derived Therapy

ONEOME®

Making prescriptions personal

Genotype-derived recommendations for medications

Antidepressant

Major gene-drug interaction

- Amitriptyline [1, 2, 20, 100]
- Citalopram [1, 2, 6, 8, 15, 19, 22, 23, 24, 27, 36, 37, 40, 42, 44, 50, 52, 55, 60, 65, 70, 71, 101]
- Clomipramine [1, 2, 20]
- Doxepin [1, 2, 20]
- Escitalopram [1, 2, 6, 8, 15, 19, 23, 24, 27, 40, 44, 50, 55, 60, 71, 101]
- Imipramine [1, 2, 20, 99]
- Trimipramine [1, 2, 20, 39]

Moderate gene-drug interaction

- Duloxetine [1]
- Selegiline [21, 32, 79]
- Sertraline [1, 2, 14, 16, 19, 45, 57, 59, 62, 75, 77, 93, 98]

Minimal gene-drug interaction

- Bupropion [1]
- Desipramine [1, 2, 20]
- Fluoxetine [1, 18, 27, 31, 45, 49, 69, 74, 86, 104]
- Fluvoxamine [1, 19, 30, 33, 34, 81, 82, 84, 85, 86, 89, 106]
- Levomilnacipran [1]
- Mirtazapine [1, 2, 38, 46, 88, 90]
- Nefazodone [1, 76, 96]
- Nortriptyline [1, 2, 20, 64, 95]
- Paroxetine [1, 2, 19, 29, 35, 56, 72, 78, 86, 91, 103]
- Protriptyline [1]
- Trazodone [1]
- Venlafaxine [1, 2, 97]
- Vilazodone [1]
- Vortioxetine [1]

Limited genetic impact

- Desvenlafaxine [1, 13]
- Milnacipran [1]

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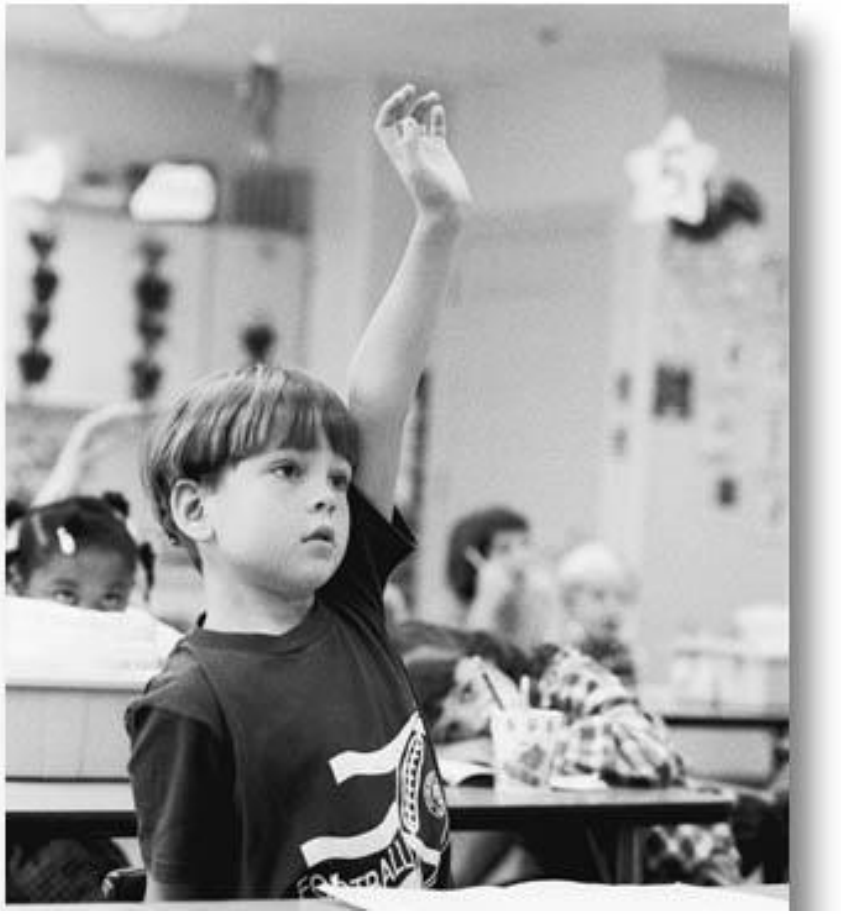
QUESTIONS?



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