

Genomics Education, Minority Health and Health Disparities

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**Inter-Society Coordinating Committee for
Practitioner Education in Genomics**

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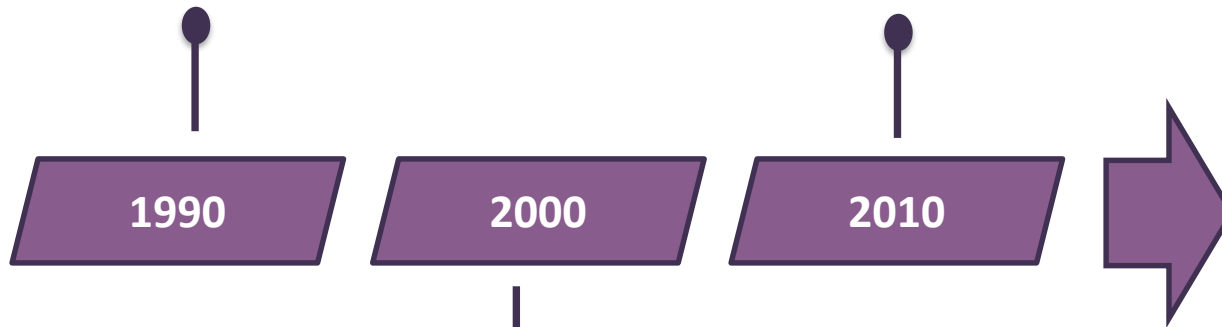


NIH National Institute
on Minority Health
and Health Disparities

NIMHD History

Established as an Office
under the NIH Director
through HHS Secretary
Louis W. Sullivan M.D. in
1990

Established as an
Institute in 2010 as
part of ACA



Transitioned to a Center
through legislation
championed by
Representative Louis
Stokes (D-OH) in 2000

- John Ruffin, PhD was director until he retired in March 2014
- Eliseo J. Pérez-Stable, MD started as Director September 2015



Minority Health Definition

- **Minority Health Research focuses on health determinants that lead to specific outcomes within a minority group and in comparison to others**
- **Race and ethnic minorities share a social disadvantage based on being subject to discrimination as a common theme**



OMB Race/Ethnic Classification

- **African American or Black**
- **Asian**
- **American Indian and Alaska Native**
- **Native Hawaiian and other Pacific Islander**
- **Latino or Hispanic**
- **White**



Life Expectancy in the U.S., 2014

	Men	Women
Whites	76.5	81.1
Blacks	72.0	78.1
Latinos	79.2	84.0
AI/AN and NH (2007-09)	68.0	74.3

Arias E, NCHS, CDC, 2016



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Race/Ethnicity and Genetic Ancestry

- **103,006 participants in Kaiser Northern California GERA Cohort**
- **Elect from 23 race/ethnic categories collapsed into 7**
- **Self-report: 83.8% White, 19.2% minority**
- **93.8% endorsed a single category; 6.2% endorsed ≥ 2**
- **12% were genetically admixed**

Banda Y, et al. Genetics 200:1285-95, 2015



Self-Reported Category Compared to Genetic Ancestry

	European/ West Asian	African	East Asian	Indigenous	Pacific Islander	South Asian
White	1.000	0.003	0.004	0.009	0	0.043
African Am	0.910	0.997	0.005	0.013	0	0.021
East Asian	0.034	0.001	1.000	0.005	0.217	0.008
Am Indian	0.999	0.022	0.022	0.144	0	0.037
Latino	0.999	0.277	0.008	0.942	0	0.024
Pacific Islander	0.576	0	0.913	0	0.663	0.261
South Asian	0.307	0.007	0.109	0.004	0.050	0.961



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Mixed Ancestry Populations

- **Latin America has been a mixture laboratory for 500 years**
- **South Asian mixture for >20,000 years –
– White and African mostly**
- **Hawaii 200 years: Pacific Islanders, Whites, East Asians**
- **African Americans in the US have moderate admixture**
- **Opportunity to understand etiology: resource for study of complex diseases**

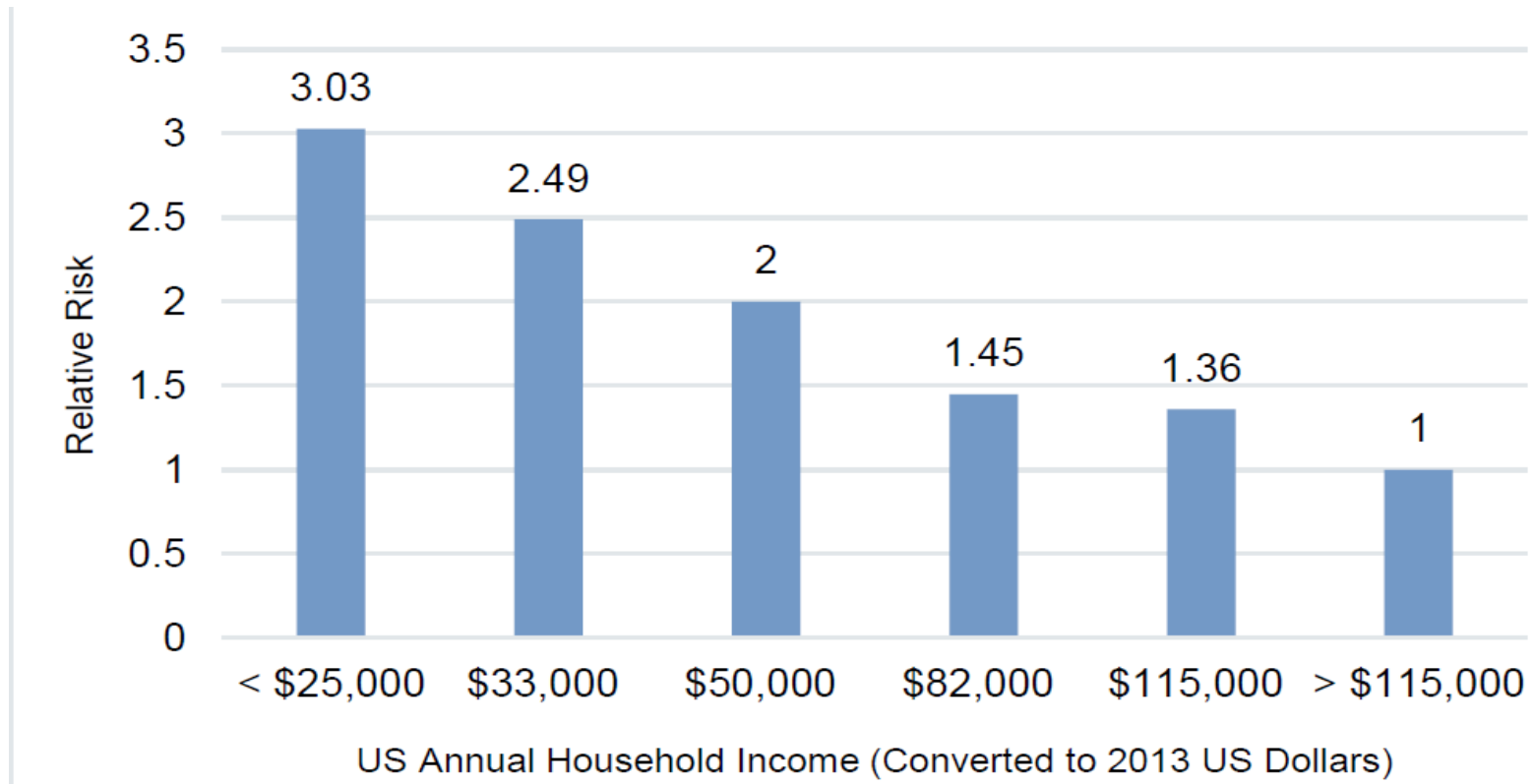


Health Disparity Populations

- Health disparity populations include:
 - racial and ethnic minorities
 - less privileged socio-economic status
 - underserved rural residents, and/or
 - sexual gender minorities
- Populations have poorer health outcomes often attributed in part to social disadvantage, being subject to discrimination, and underserved in the full spectrum of health care.



Relative risk of All-Cause Mortality by US Annual Household Income Level



Assessment of Socioeconomic Status or Social Class in Clinical Medicine

- **Education – in years or categories**
- **Income –annual household/dependents**
- **Occupation categories – Whitehall**
- **Life course SES — effects understudied**
- **Parental education (children)**
- **Type of insurance**
- **Wealth or total assets**



Social Determinants of Health

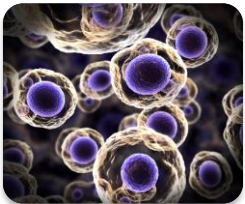
- **Age, gender, race/ethnicity, SES, occupation**
- **National origin or family background**
- **Urban or rural residence or geographic region**
- **Cultural identity, Religion, religiosity**
- **Immigrant, generation, documentation**
- **Language proficiency, acculturation**
- **Literacy, numeracy, food insecurity**
- **Sexual orientation, gender identity**



Mechanisms Leading to Health Disparities



Individual Behaviors, Lifestyle, Beliefs and Response to chronic Stress: racism, childhood adverse conditions, food insecurity, witness to or victim of violence, immigrant, limited English proficiency



Biological Processes and Genetics: earlier age of onset, gene variants, metabolic differences, susceptibility, faster progression or greater severity, brain networks, microbiome, extracellular RNA







Physical and Cultural Environment: place, social system, neighborhood, infrastructure, family, social interactions, network, community cohesion



Clinical Events and Health Care: differential treatments, poor communication, adverse events to medications, falls, progression of disease, access, use/abuse of appropriate services, end of life care



National Institute on Minority Health and Health Disparities Research Framework

		Levels of Influence*			
		Individual	Interpersonal	Community	Societal
Domains of Influence (Over the Lifecourse)	Biological	Biological Vulnerability and Mechanisms	Caregiver–Child Interaction Family Microbiome	Community Illness Exposure Herd Immunity	Sanitation Immunization Pathogen Exposure
	Behavioral	Health Behaviors Coping Strategies	Family Functioning School/Work Functioning	Community Functioning	Policies and Laws
	Physical/Built Environment	Personal Environment	Household Environment School/Work Environment	Community Environment Community Resources	Societal Structure
	Sociocultural Environment	Sociodemographics Limited English Cultural Identity Response to Discrimination	Social Networks Family/Peer Norms Interpersonal Discrimination	Community Norms Local Structural Discrimination	Social Norms Societal Structural Discrimination
	Health Care System	Insurance Coverage Health Literacy Treatment Preferences	Patient–Clinician Relationship Medical Decision-Making	Availability of Services Safety Net Services	Quality of Care Health Care Policies
Health Outcomes		 Individual Health	 Family/ Organizational Health	 Community Health	 Population Health

National Institute on Minority Health and Health Disparities, 2018

*Health Disparity Populations: Race/Ethnicity, Low SES, Rural, Sexual/Gender Minority

Other Fundamental Characteristics: Sex/Gender, Disability, Geographic Region

NIMHD Research Divisions of Scientific Programs



Clinical and
Health
Services
Research



Integrative
Biological and
Behavioral
Sciences



Community
Health and
Population
Sciences



NIMHD Research FOAs

- Immigrant Populations: etiology/interventions
- Disparities in Surgical Care and Outcomes
- **Social Epigenomics**
- Caribbean Initiative
- Sleep Disparities
- Liver Cancer and Chronic Liver Disease
- Opioid Use Disorders
- Simulation Modeling and Systems Science
- Lung Cancer Etiology, Screening and Care
- Health Information Technologies



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Inclusion of Diverse Participants

- **All disparity populations are historically underrepresented in biomedical research**
- **Social justice, good science, and common sense mandate inclusion (40% US population)**
- **About 26% of participants in NIH-funded clinical studies are from race/ethnic minority groups**
- **Accountability, granularity, diverse workforce**



How Does Racial Inequity Harm Health

- **Measure Interpersonal: major experiences or events, everyday discrimination (9-items), heightened vigilance scale – potential reality**
- **Effect on physical and mental health status of African Americans in cohort study**
- **Effect of racism on physiological measures such as SBP or levels of inflammatory markers**
- **53% Blacks and 36% Latinos report discrimination experiences in past 30 days**
- **Discrimination impacts health behaviors: smoking, problem drinking, substance use**



Breast Cancer Screening, 2015 among women age 50-74

	Up-to-date on Mammography
White	71.8%
Black	74.3%
Asian and Pacific Islander	66.1%
AI/AN	56.7%
Latina	72.1%
Education Level	Up-to-date on Mammography
< High School	60.3%
High School / GED	68.3%
Some College / Tech	71.0%
College Graduate	78.9%

White A, et al. MMWR 2017; 66: 201-206



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Breast Cancer Risk Perception

1160 women in San Francisco Clinics

Kim S, et al. Archives of Internal Medicine 2008; 168: 728-734

	White (29%)	African America (14%)	Latina (21%)	Asian (36%)
No risk	2	7	10	48
Very low risk	27	24	20	18
Somewhat/ low risk	35	27	33	23
Moderate	27	28	19	8
High/very high risk	8	14	18	3



Odds Ratios of Correct/Incorrect Use of Wall of Women Visuals (Wong S, et al, Patient Educ Counsel 2012;

87(3):327-35)

Variable	Total Wall	Wall of 100	Wall of 10k
< High school	0.55 (0.35-0.90)	0.44 (0.25-0.78)	0.52 (0.16-1.69)
African Ams	0.36 (0.22-0.61)	0.30 (0.17-0.54)	0.62 (0.18-2.11)
Chinese	0.68 (0.41-1.13)	0.49 (0.27-0.89)	1.54 (0.55-4.31)
Latinas	0.36 (0.22-0.60)	0.34 (0.19-0.61)	0.25 (0.07-0.83)
Numeracy Score	1.30 (1.21-1.40)	1.29 (1.18-1.41)	1.37 (1.15-1.64)



Cancer Risk Perception and Shared Decision Making (SDM)

- **Dominant paradigm in health care — “gold standard” in communication**
- **SDM leads to better health outcomes**
- **Perceived risk varied by race/ethnicity**
- **Understanding risk: numeracy and education — qualitative factor?**
- **Intent to have screening at baseline did not predict test at 2 y in minority women — role of clinician communication?**



Cancer Incidence by Site and Race/Ethnicity in Women, U.S. 2010 – 2014 (per 100,000 age-adjusted)

	African American	Asian/PI	White	Latina
Breast	125.1	98.5	134.1	93.1
Lung	49.0	27.9	52.7	24.2
Colon	33.1	19.8	26.0	21.0
Uterus	25.7	21.8	28.4	24.0
Cervix	8.7	6.1	6.9	9.1

Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov)



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Protective Variants for BC on 6q25

Only present in women with Indigenous ancestry

rs140068132/rs147157845	OR	95% CI	P-value	MAF
Discovery	0.60	0.49-0.72	3×10^{-7}	9%
Replication Mexicans	0.63	0.53-0.75	3×10^{-7}	15%
Replication COLUMBUS	0.54	0.41-0.71	1×10^{-5}	10%
Replication WHI	0.61	0.31-1.22	0.16	7%
Meta-Analysis all samples	0.60	0.53-0.67	9×10^{-18}	

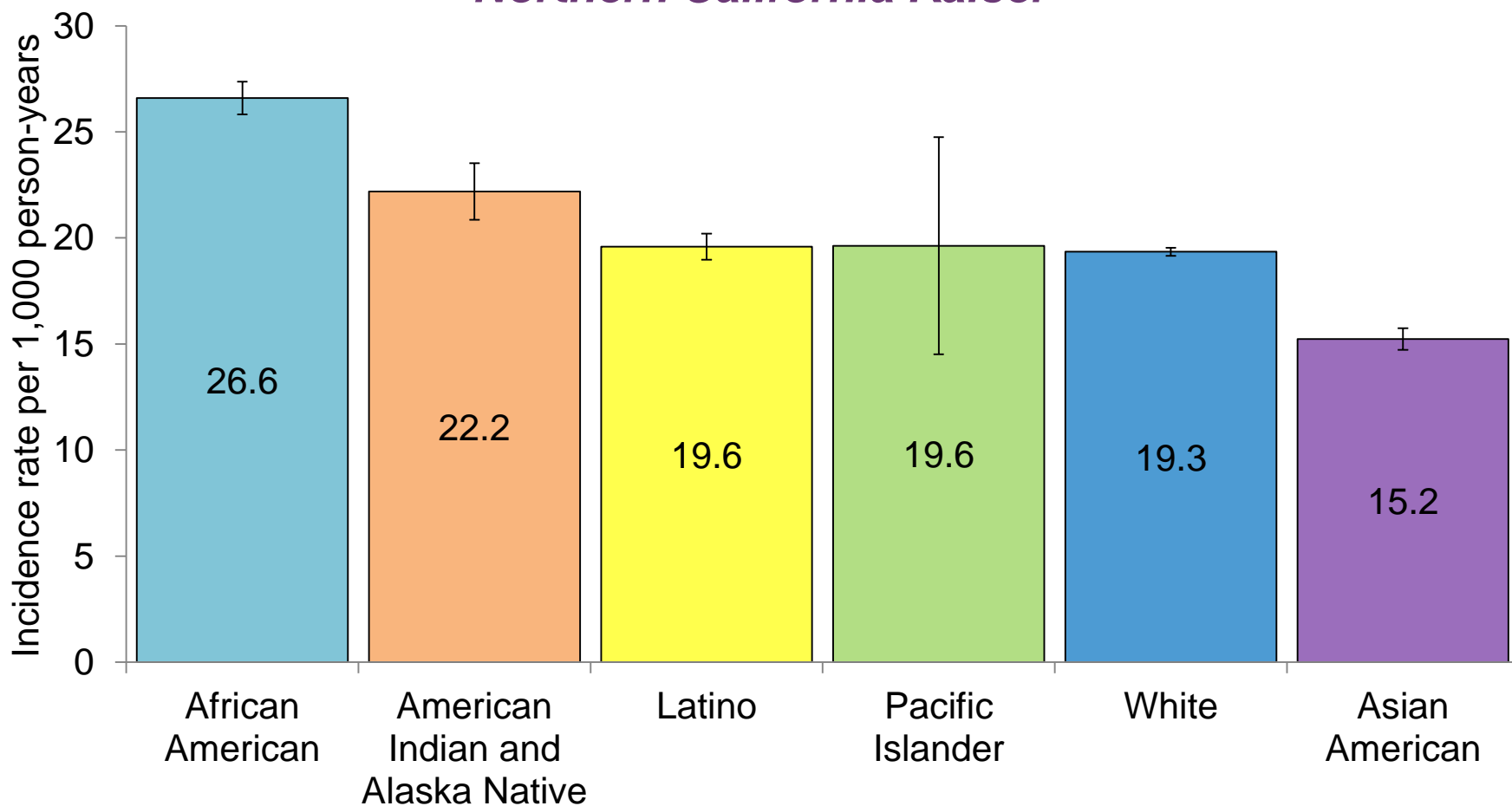


**GG Homozygous women 2.8 fold reduction
of the odds of developing breast cancer**



Age-standardized Dementia Incidence Rates by Race/Ethnicity, 2000-2013

Northern California Kaiser

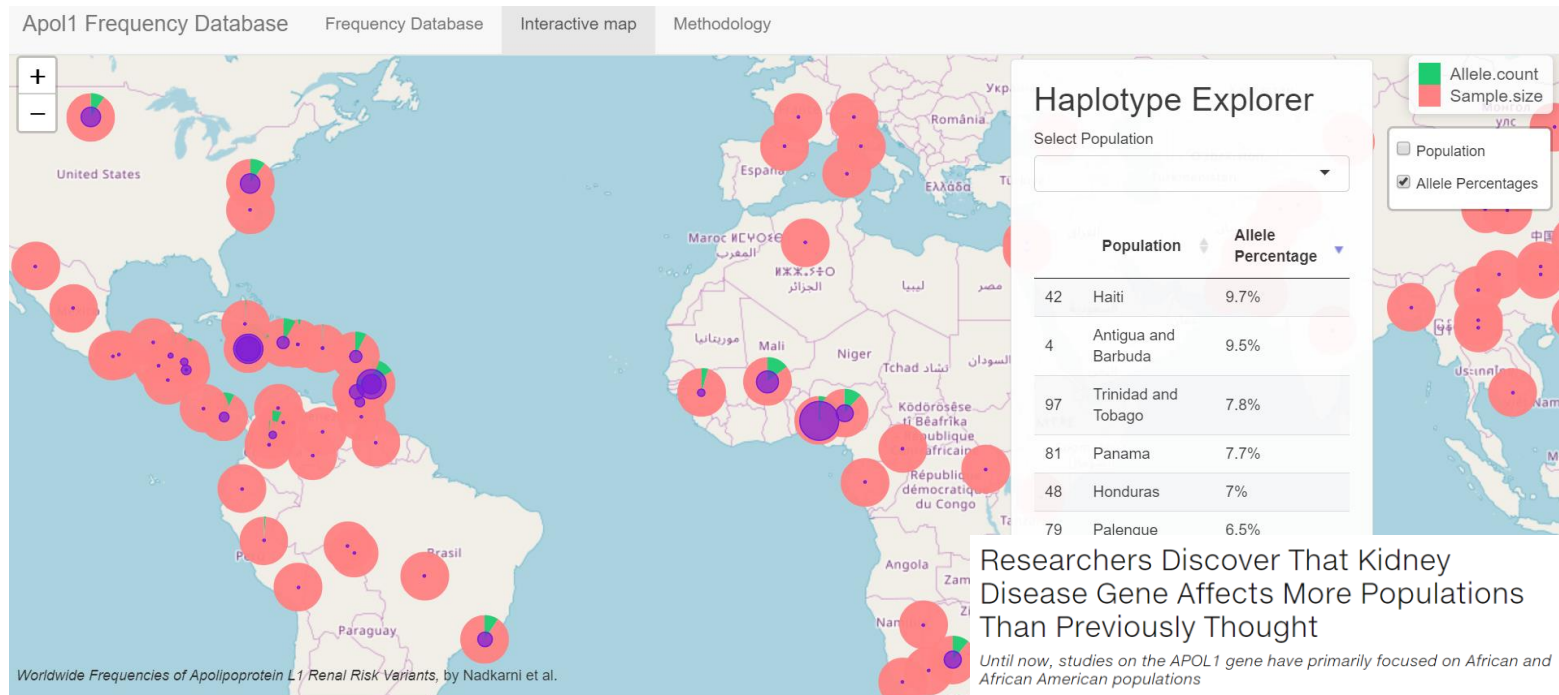


Examples of Race/Ethnicity Effects in Understanding Mechanisms: What about Genetics?

- **Optimal BMI cut points to define risk: 23, 25,28?**
- **Low LDL AA family led to PCSK9 inhibitors**
- **Epigenetic clock differences**
- **Post-transplant outcomes worse for AA recipients**
- **Optimal Cotinine cut points to define smoking**
- **Clopidogrel did not work in Pacific Islanders**
- **APOL 1-CKD among African ancestry populations**
- **Response to albuterol and normal PFT curves**



Association of Genotypes by Country and Population of Origin



December 27, 2018

N Engl J Med 2018; 379:2571-2572

DOI: 10.1056/NEJMc1800748

Diagnostic Utility for Exome Sequencing for Kidney Disease

- 3037 patients from 2 cohorts had exome sequencing and diagnostic analysis; 64.4% White, 14.6% Latino, 10.5% AA, 7.4% Asian
- Diagnostic variants in 9.3% for 66 monogenic disorders; 39 occurred in a single patient
- APOL1 in 29% Blacks and 7% Latinos with CKD; 14% of Black and 3% of Latino controls
- 2187 patients had clinical assessments, 1.6% had genetic findings for medically actionable disorders

Groopman EE, et al. NEJM 2018; December 26



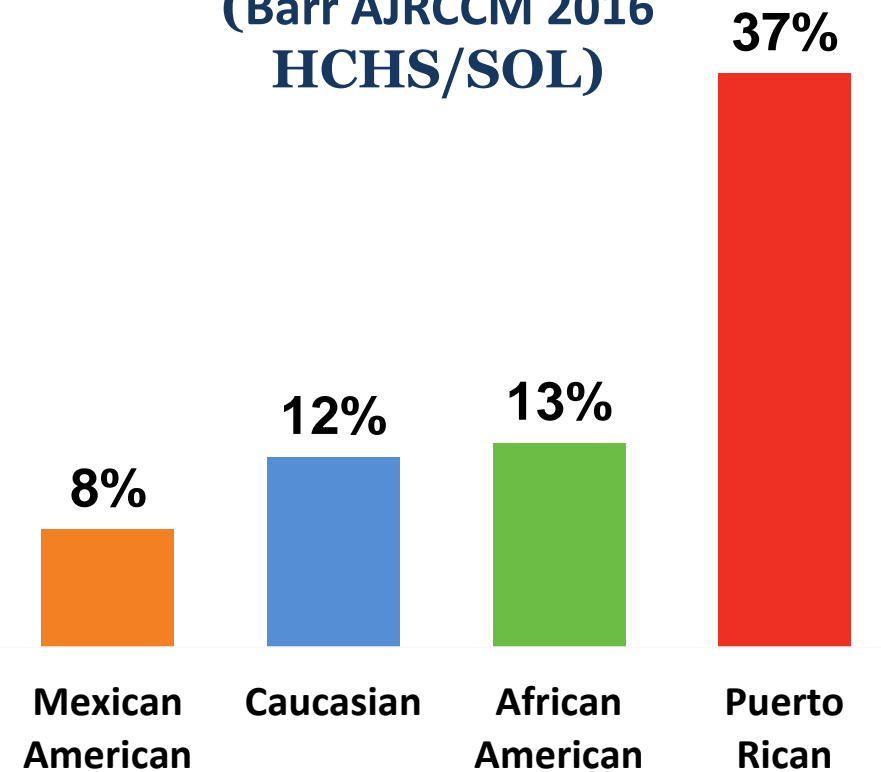
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Asthma Disparities

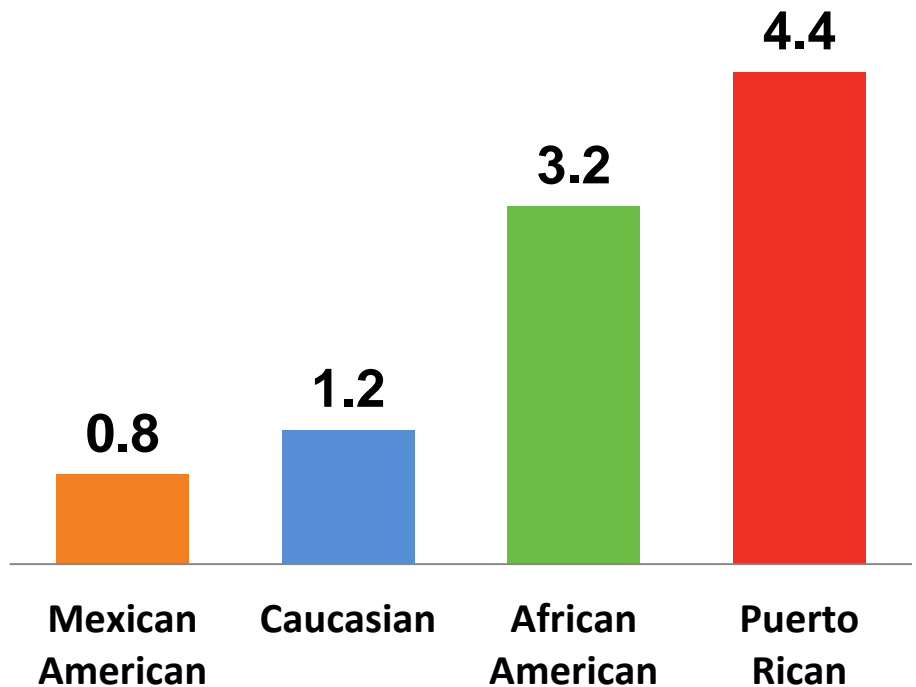
Prevalence

(Barr AJRCCM 2016
HCHS/SOL)



Mortality

Akinbami L. CDC/NCHS

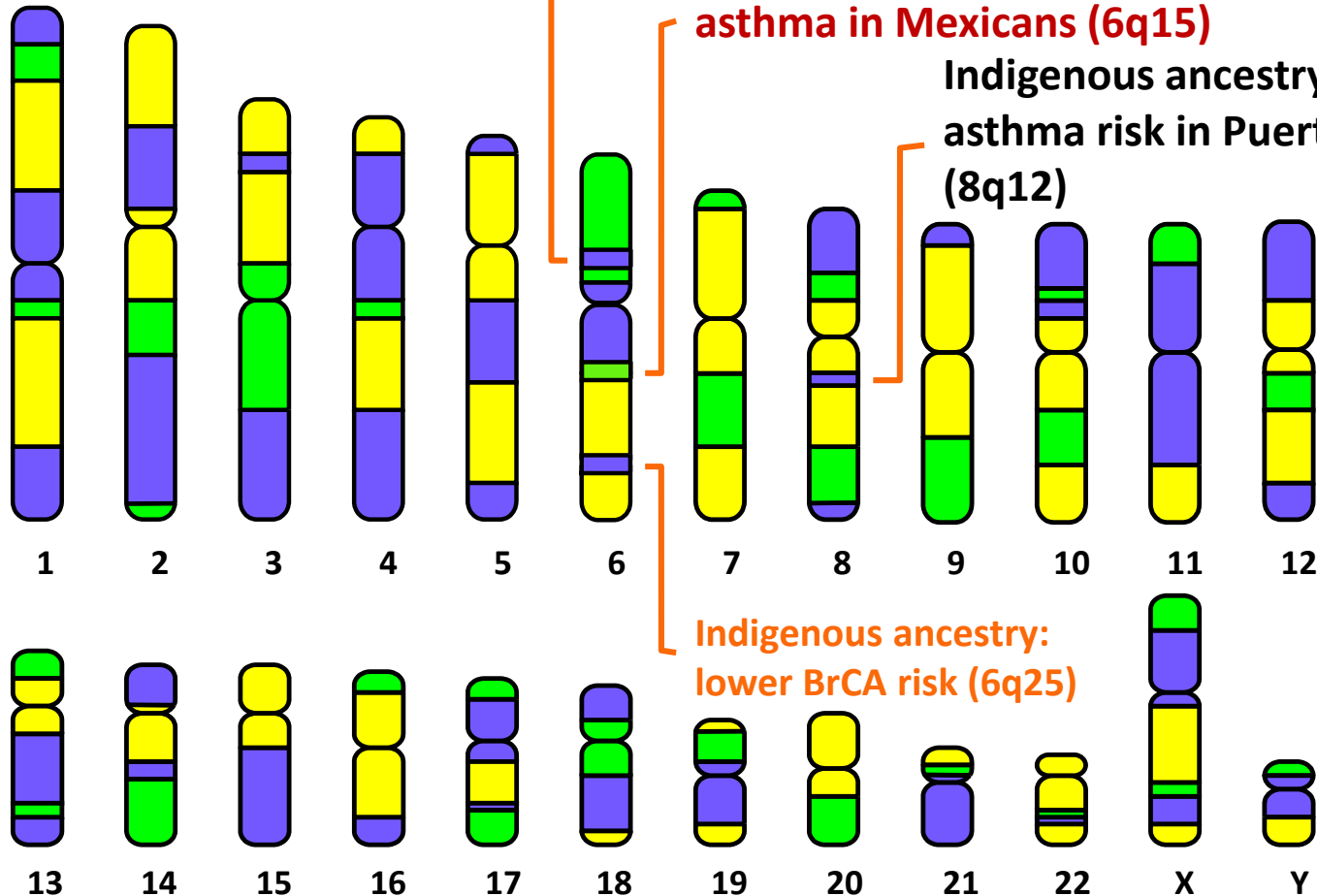


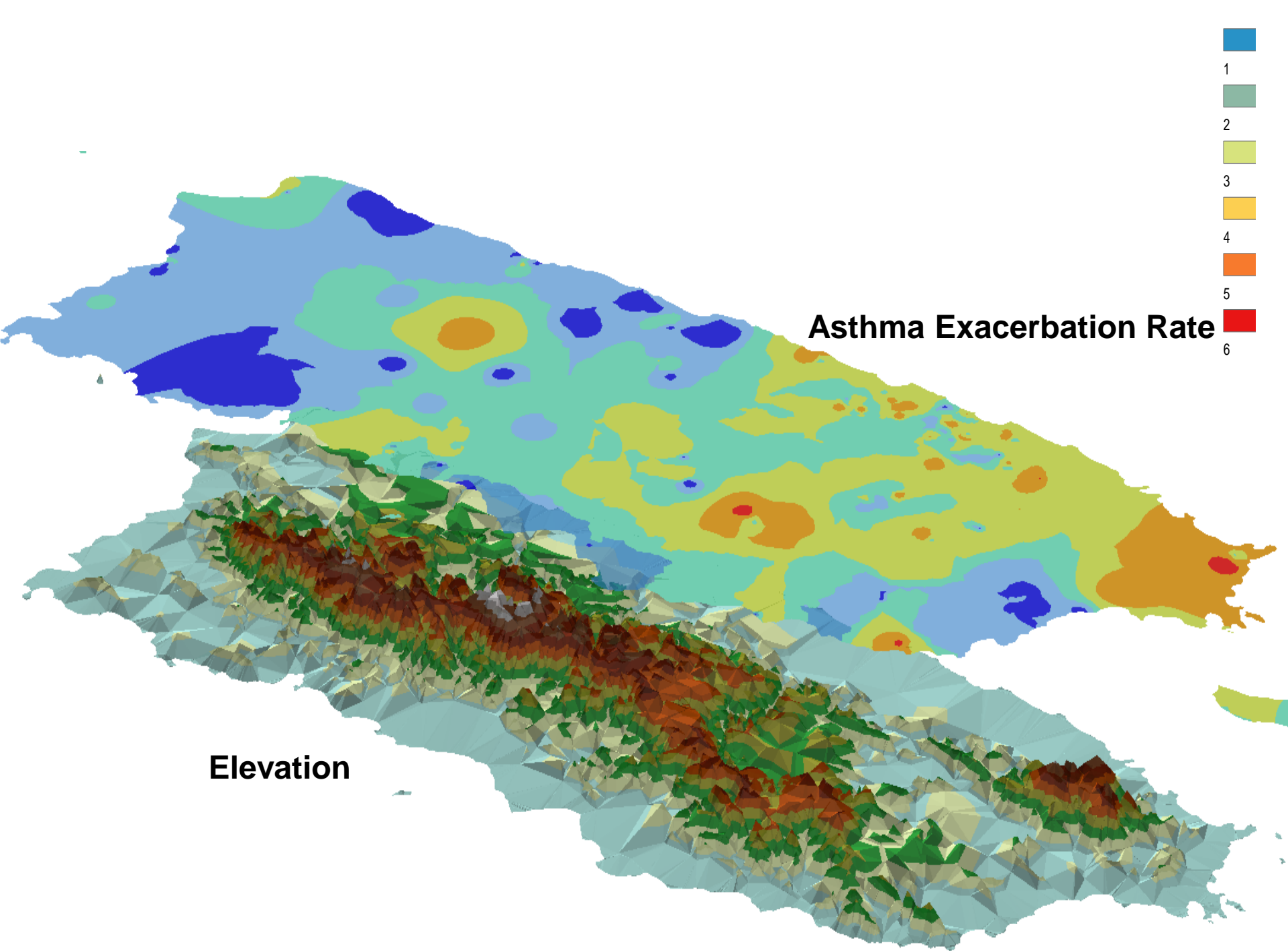
Locus Specific Ancestry

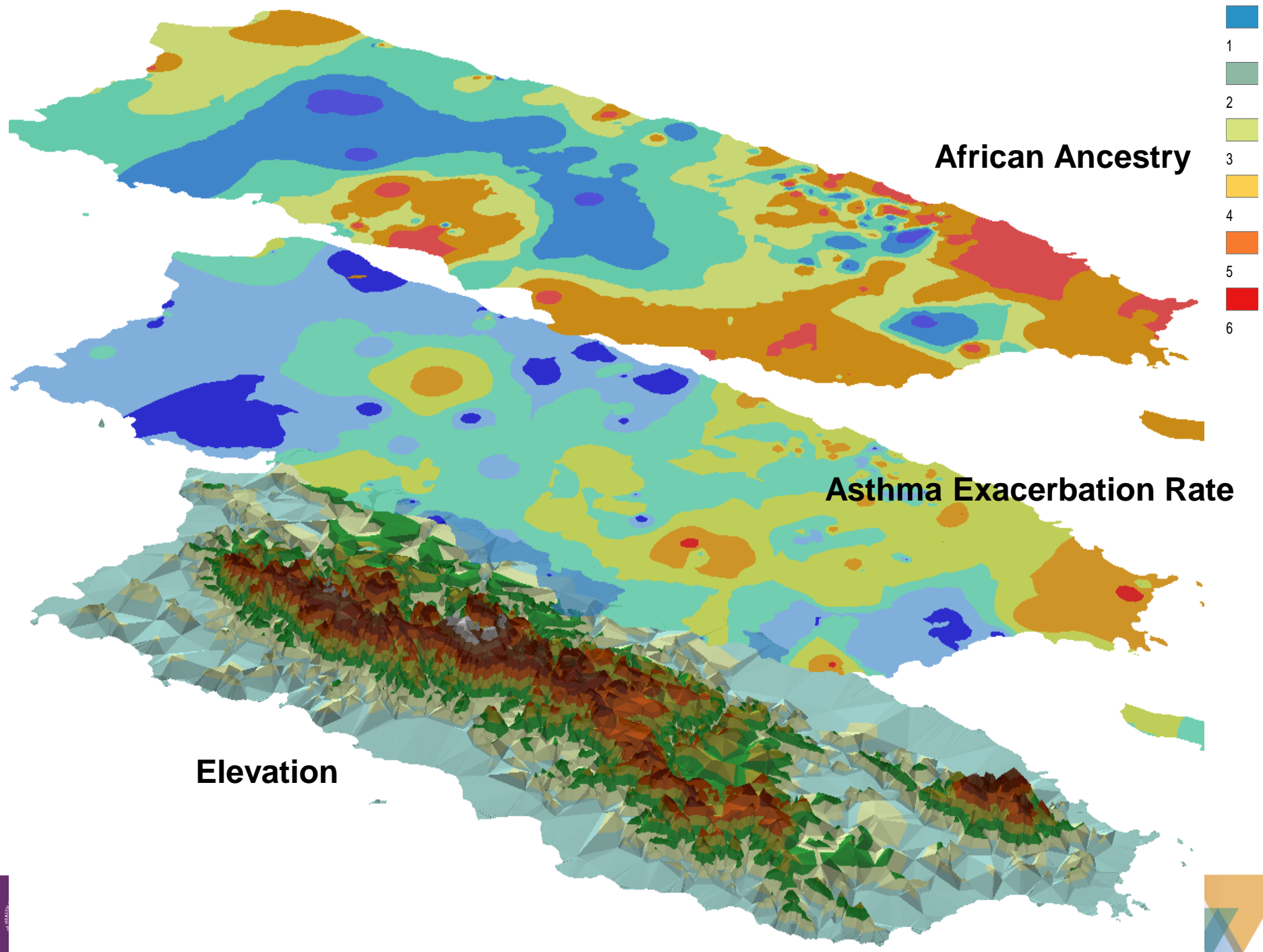
Indigenous ancestry: lower IgE levels in Latinos (6p21)

African ancestry protective for asthma in Mexicans (6q15)

Indigenous ancestry increases asthma risk in Puerto Ricans (8q12)







Promoting Health Equity in Health Care to Reduce Disparities

- **Expand Access: Health insurance, place and clinician as fundamental**
- **Public Health Consensus**
- **Coordination of Care: Systems, navigators, and target conditions**
- **Patient-Centered: PCMH, effective communication, cultural competence**
- **Performance measurement in populations**



Precision Medicine and Clinical Care

- **When is “more precise” individualized approach better than a standard one with demonstrated efficacy?**
- **One size fits all approach can work to improve outcomes in many clinical situations**
- **New is not always better and is usually more expensive — cost has to be considered**
- **Precision in patient-clinician interactions**
- **Enhance cultural competence/humility and reduce structural discrimination**



Challenges for ISCC Practitioner Education

- **Genetic profiles have contributed to understanding etiological pathways of developing or protection from disease**
- **Pharmacogenomics has highlighted clinically relevant differences by subpopulations**
- **Sequencing may lead to identifying clinically actionable risk for common and rare diseases**
- **Emphasis on patient-clinician interactions in communication of risk addressing cultural differences and structural discrimination**



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