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Research Methods

Consent for Use of Genetic Data among US Hispanics/Latinos: Results from the Hispanic Community Health Study/ Study of Latinos

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Inclusion of historically underrepresented populations in biomedical research is critical for large precision medicine research initiatives. Among 13,721 Hispanic Community Health Study/Study of Latinos (HCHS/SOL) enrollees, we used multivariable-adjusted prevalence ratios to describe characteristics associated with participants' willingness to consent to different levels of biospecimen and genetic data analysis and sharing. At baseline (2008-2011), HCHS/SOL participants almost universally consented to the use of biospecimens and genetic data by study investigators and their collaborators (97.6%; 95%CI: 97.1, 98.0). Fewer consented to biospecimen and genetic data sharing with investigators not affiliated with the HCHS/SOL research team (81%, 95%CI: 80, 82) or any data sharing with commercial/for-profit entities (75%, 95%CI: 74, 76). Those refusing to share their data beyond the study investigators group were more often females, Spanish language-speakers and non-US born individuals. As expected, participants who were retained and reconsented at the six-year follow up visit tended to embrace broader data sharing, although this varied by group. Over time, Puerto Ricans and Dominicans were more likely to convert to broader data sharing than individuals of a Mexican background. Our analysis suggests that acculturation and immigration status of specific Hispanic/Latino communities may influence decisions about participation in genomic research projects and biobanks. *Ethn Dis*. 2021;31(4):547-558; doi:10.18865/ed.31.4.547

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Introduction

A major weakness of large-scale genetic association studies has been the reliance on non-Hispanic White populations.[1,2] Race/ethnic minority populations are underrepresented in biomedical research and the gap in participation of genomic studies is particularly large.[3,4] Genetic research often attains lower participation rates compared with non-genetic studies[5,6] and racial/ethnic groups may not be equally willing to give biospecimens.[7] In large research efforts such as the All of Us Research Program,[8] representativeness will help ensure that the entire US population benefits from the results and will maximize genomic variation as well as diversity in environmental and life course exposures.[9] Achieving inclusiveness will not only promote equity, but also will increase power to identify genomic influences of disease and to identify gene-by-environment interactions that mediate pathways from the genome to disease.[10,11]

While individuals of Mexican background have demonstrated willingness to participate in both non-genetic and genetic studies to a similar

extent as their non-Hispanic White counterparts,[5] to our knowledge the consent rates of other Hispanic/Latino background groups have not been explored. Large-scale genetic research initiatives will require broad sharing of resources; however, in studies in which the majority of participants agreed to the proposed genetic applications, the access to participant genetic data for researchers from private firms was the element most commonly refused.[12] Hispanic/Latino populations are heterogeneous with wide variation of birthplace, length of stay in the United States, levels of acculturation and socioeconomic status.[13]

The Hispanic Community Health Study/ Study of Latinos (HCHS/SOL) is a large prospective study of Hispanic/Latino adults of diverse backgrounds, ancestry and sociodemographic characteristics from metropolitan areas that offers a unique opportunity to understand the consent trends of the Hispanic community in order to understand potential selection biases in genomic research. In the present study, we examined the extent to which participants consented to sharing biospecimens and data with investigators and commercial/for-profit entities (hereafter referred to as commercial entities); our findings identify variation in levels of consent by sociodemographic and health characteristics.

Methods

Study Population and Data Collection Procedures

HCHS/SOL is a community-based longitudinal study of self-identified Hispanic/Latino adults, aged 18 to 74 years, from randomly selected households in four US field centers (Chicago, IL; Miami, FL; Bronx, NY; San Diego, CA).[14] The overall purpose of the study is to identify disease risk factors and determine the role of acculturation in the occurrence of disease.[14] The study was limited to those who could communicate in English or Spanish. HCHS/SOL achieved a 41.7% participation rate, which is comparable to other large NHLBI cohorts.[15,16] The institutional review boards at each field center approved the study, and all participants gave written informed consent to participate. During 2008-2011, 16,415 participants underwent baseline clinical evaluation, biospecimen collection and interviews. HCHS/SOL conducted annual follow-up interviews to determine health outcomes of interest and, from 2014 to 2017, 71% of the cohort attended the six-year in-person clinical re-examination (Visit-2).

This analysis is restricted to the 13,721 participants who completed the final version tiered informed consent document (ICD) at baseline. The analysis of the change of consent responses at Visit-2 is restricted to participants who completed the re-examination visit (n=9,838).

Ascertainment of Informed Consent to Collection and Sharing of Genetic and Non-genetic Data

We used a tiered consent that offered participants the opportunity to opt in or opt out of study components. They were asked about their willingness to have their data and specimens used for various purposes including: 1) biospecimens and non-genetic data used by HCHS/SOL investigators and their collaborators; 2) genetic data used by HCHS/SOL investigators and their collaborators; 3) non-genetic data used by not-for-profit investigators nonaffiliated to HCHS/SOL; 4) genetic data used by not-for-profit investigators nonaffiliated to HCHS/SOL; and 5) non-genetic and genetic data used by commercial entities (Table 1).

Each field center developed the ICD in conjunction with their IRB, following guidance from NHLBI and the HCHS/SOL coordinating center. Detailed informed consent procedures are available at www2.cscc.unc.edu/hchs/. Prior to completing the consent process, HCHS/SOL participants viewed a video describing the study components, including the purpose and use of genomic material and the participant's ability to exercise control over these options (video available at https://sites.cscc.unc.edu/hchs/public-relations-AV-pub). Trained bilingual staff administered the ICD in English or Spanish depending on participant preference. Unlike other field centers, which presented the informed consent materials during the recruitment encounter, the San Diego site mailed the ICD and recruitment documents in advance to prospective participants, and attempted induction into the study at a subsequent recontact, as required by its local IRB.

Covariates

HCHS/SOL assessed through self-report the following characteristics: Hispanic/Latino background (Dominican, Central American, Cuban, Mexican or Mexican-American,

Table 1. Proportion consenting to use of genetic and non-genetic biospecimen and/or data with HCHS/SOL study investigators and their collaborators, not-for-profit nonaffiliated investigators, and commercial entities: HCHS/SOL, 2008-2011

Type of sharing	Data type	ICT form item	N	Weighted % (95% CI)
HCHS/SOL investigators and their collaborators	Non-genetic	I agree to allow my samples (blood, urine) to be used for current and future research done by scientists who collaborate with the HCHS/SOL investigators	13642	99 (99, 99)
HCHS/SOL investigators and their collaborators	Genetic	I agree to allow my blood to be used to obtain genetic material (DNA/RNA) to be stored for future use by HCHS/SOL and investigators they work with	13446	98 (97, 98)
Not-for-profit nonaffiliated with HCHS/SOL investigators	Non-genetic	I agree to share my non-genetic data, information, and samples available to investigators not associated to HCHS/SOL and specialized laboratories	11220	84 (83, 85)
Not-for-profit nonaffiliated with HCHS/SOL investigators	Genetic	I agree to share my genetic data, information, and samples available to investigators not associated to HCHS/SOL and specialized laboratories	10910	81 (80, 82)
Commercial/for-profit entities	Non-genetic and genetic	Commercial or for-profit companies that are not part of HCHS/SOL may use my genetic and non-genetic information, data and samples to do research to develop new diagnostic tests and medical treatments that may benefit many people	9990	75 (74, 76)

Puerto Rican, South American, more than one background, other); educational attainment; annual household income; employment status; health insurance status; place of birth (US mainland vs outside US mainland); time since relocation to the mainland United States; age; self-rated health status (fair, poor, good, very good, excellent); and known personal and family history of several conditions.

We created a disease burden score to reflect the number of prevalent self-reported chronic conditions, namely coronary heart disease (CHD; myocardial infarction, balloon angioplasty, stent, or coronary bypass surgery), stroke, diabetes, and cancer. Each condition contributed 1 point to summary count measures. We constructed a family history of disease burden score by first assigning a score of 0, 1, or 2 points to participants with 0, 1, or ≥2 first-degree family relatives with a history of each condition; each individual disease score was then summed across conditions, yielding a maximum score of 8. To assess perceived discrimination, we used the Brief Perceived Ethnic Discrimination Questionnaire-Community Version,[17] which has been previously validated.[18,19]

Data Analyses

The goal of the data analyses was to examine participants' permission on the tiered consent and their willingness to agree to data sharing. All analyses were weighted to account for unequal probabilities of selection due to the sampling design.[14] Sampling weights were non-response adjusted, trimmed, and calibrated by age, sex, and Hispanic/Latino group to the characteristics of each field center's target population from the 2010 US Census. Analyses were performed using SAS version 9.3 (SAS Institute, Cary, NC) and SUDAAN release 11.0.1 (RTI International, Research Triangle Park, NC).

We used chi-squared tests to assess differences in consent restrictions according to participant characteristics. To characterize participants according to their data/specimen sharing restrictions, we defined two outcomes: 1) refusal to share with (not-for-profit) investigators beyond the HCHS/SOL study group; and 2) refusal to share with commercial entities. There was high agreement between consent to use of genetic and non-genetic data by not-for-profit investigators nonaffiliated to HCHS/SOL (Kappa=.86, P<.0001). Therefore, for further analyses we created a composite outcome representing agreement to allow use of genetic and non-genetic data by all HCHS/SOL investigators, collaborators, and by not-for-profit outside

Table 2. Demographic characteristics at baseline visit, 2008-2011

	Target population (weighted)
	% (95% CI)
Sex	
Female	52 (51, 53)
Male	48 (47, 49)
Age, years	
18-24	17 (15, 18)
25-34	22 (21, 24)
35-44	22 (20, 23)
45-54	18 (17, 19)
55-64	13 (12, 14)
65-76	8 (8, 9)
Field center	
Bronx	29 (26, 32)
Chicago	15 (13, 17)
Miami	31 (26, 36)
San Diego	25 (22, 29)
Annual household income	
<$10,000	14 (13, 15)
$10,001-$20,000	29 (27, 30)
$20,001-$40,000	30 (28, 31)
$40,001-$75,000	13 (12, 14)
>$75,000	5 (4, 7)
Not reported	10 (9, 11)
Years of education	
<9th grade	16 (15, 17)
Some high school	16 (15, 17)
HS graduate/equivalent	27 (26, 28)
Trade/vocational school	12 (11, 13)
College or higher	29 (27, 31)
Language preference	
Spanish	75 (73, 77)
English	25 (23, 27)
Place of birth	
Outside US mainland	77 (76, 79)
Within US mainland	23 (21, 25)
Years in the US mainland (among foreign-born)	
0-<5 years	18 (16, 20)
5-<10 years	19 (17, 20)
10-<15 years	16 (15, 17)
≥15 years	48 (45, 50)

investigators. Adjusted prevalence ratios (aPR) for refusals to share were derived at baseline from multivariable Poisson regression models with robust variance estimation, while excluding those with incomplete data for key covariates (n=469; 3.4%). Initial models were adjusted for sex, age (continuous), and field center. Subsequent models further adjusted for sociodemographic and acculturation variables. Because Puerto Rican background was associated with somewhat higher rates of consent, as well as a disproportionate burden of chronic disease and unique distributions with respect to relocation and acculturation-related variables,[20] we conducted sensitivity analyses after excluding participants of Puerto Rican background. We used multivariable-adjusted models to identify characteristics of participants who changed their consent over time about sharing data with scientists outside the HCHS/SOL investigator group and with commercial entities.

Results

Population Characteristics

The weighted mean age of the population in the enrollment communities was 41 years (range: 18-76 years) and 52% were female. The population had a wide range of education attainment (9th grade or lower, 16%, and educated beyond high school, 41%). (Table 2) Most (75%) preferred to receive study materials in Spanish, and 50% had some form of health insurance. The majority of participants (86%) reported being free of diabetes, CHD, stroke, or cancer at baseline visit.

Consent to Use of Genetic and Non-genetic Biospecimen Data

Most participants consented to current and future use of biospecimens by HCHS/SOL investigators and their collaborators, whether for genetic or non-genetic studies (Table 1). Fewer agreed to data and specimen resource sharing with not-for-profit investigators who are not affiliated with HCHS/SOL. Specifically, 84% (95%CI: 83, 85) agreed

Table 3. Proportion (95% CI) consenting to sharing of genetic and non-genetic data with not-for profit and commercial investigators at baseline and Visit 2

	Baseline Visit HCHS/SOL 2008-2011				
	Overall	**Bronx**	**Chicago**	**Miami**	**San Diego**
	N=13721	**N=3414**	**N=3455**	**N=3516**	**N=3336**
	N, % (95% CI)	**N, % (95% CI)**	**N,% (95% CI)**	**N, % (95% CI)**	**N, % (95% CI)**
Hispanic/Latino background	Consent to sharing with not-for-profit investigators[a]				
Overall	10731, 80 (79, 81)	2873, 83 (81, 85)	2505, 73 (71, 75)	3027, 87 (85, 88)	2326, 72 (69, 74)
Dominican, N=1307	1104, 83 (80, 86)	1025, 83 (79, 85)			
Central American, N=1371	1064, 78 (75, 80)		271, 80 (72, 85)	639, 77 (73, 80)	
Cuban, N=2130	1900, 89 (88, 90)			1850, 89 (88, 90)	
Mexican, N=5380	3783,72 (70, 74)		1442, 70 (67, 73)		2176, 71 (68, 74)
Puerto Rican, N=2176	1807, 84 (81, 86)	1269, 84 (81, 87)	453, 77 (73, 82)		
South American, N=902	707, 81 (77, 84)		238, 76 (69, 82)	320, 83 (77, 87)	
	Consent to sharing with commercial entities				
Overall	9990, 75 (74, 76)	2880, 85 (83, 87)	2262, 66 (63, 68)	2646, 77 (75, 79)	2202,68 (65, 70)
Dominican, N=1307	1061, 82 (79, 85)	997, 83 (79, 85)			
Central American, N=1371	936, 71 (68, 74)		231, 71 (64, 77)	553, 68 (63, 72)	
Cuban, N=2130	1668, 79 (77, 81)			1615, 79 (77, 81)	
Mexican, N=5380	3545, 67 (65, 70)		1315, 63 (60, 66)		2064,67 (64, 70)
Puerto Rican, N=2176	1792, 85 (83, 87)	1300, 89 (86, 91)	413, 72 (67, 77)		
South American, N=902	642, 73 (69, 77)		211, 65 (56, 74)	285, 73 (67, 78)	
	Visit-2 HCHS/SOL 2014-2017				
	Overall	**Bronx**	**Chicago**	**Miami**	**San Diego**
	N=9838	**N=2232**	**N=2584**	**N=2513**	**N=2509**
	N, % (95% CI)	**N, % (95% CI)**	**N, % (95% CI)**	**N, % (95% CI)**	**N, % (95% CI)**
Hispanic/Latino background	Consent to sharing with not-for-profit investigators[a]				
Overall	8479, 87 (86, 88)	2086, 92 (90, 94)	2099, 81 (78, 83)	2272, 90 (88, 92)	2022, 82 (80, 84)
Dominican, N=1307	838, 90 (86, 93)	776, 91 (88, 93)			
Central American, N=1371	833, 84 (81, 87)		217,81 (74, 87)	491,83 (80, 86)	
Cuban, N=2130	1408, 92 (90, 94)			1373, 93 (91, 95)	
Mexican, N=5380	3249, 82 (80, 84)		1222, 79 (76, 82)		1907,82 (79, 85)
Puerto Rican, N=2176	1338, 93 (91, 95)	896,94 (91, 96)	384,87 (83, 90)		
South American, N=902	576, 82 (78, 86)		199,78 (71, 84)	261,84 (78, 89)	
	Consent to sharing with commercial entities				
Overall	7651, 80 (79, 81)	2068, 92 (91, 94)	1914, 74 (72, 76)	2000, 80 (77, 82)	1669, 69 (66, 72)
Dominican, N=1307	832, 92 (89, 94)	777, 93 (90, 95)			
Central American, N=1371	740, 74 (70, 77)		200, 76 (70, 82)	423, 70 (66, 74)	
Cuban, N=2130	1257, 83 (80, 85)			1225, 83 (81, 86)	
Mexican, N=5380	2822, 73 (71, 75)		1119, 73 (70, 76)		1587, 68 (66, 71)
Puerto Rican, N=2176	1295, 90 (88, 92)	884, 94 (92, 96)	357, 78 (72, 83)		
South American, N=902	489, 70 (65, 74)		167, 65 (58, 72)	218, 69 (63, 75)	

Estimates for cells with <150 participants are hidden due to lack of precision; estimates are weighted to the target population and confidence intervals account for survey parameters.

a. Defined as consent to sharing to both non-genetic and genetic biospecimen and data with HCHS/SOL collaborators and not-for-profit nonaffiliated investigators.

for non-genetic analyses, and 81% (95%CI: 80, 82) agreed for genetic analyses. Still fewer participants consented to sharing non-genetic and genetic data with commercial entities (75%, 95%CI: 74, 76).

Individuals who remained in the study through Visit-2 generally became more likely over time to acquiesce to data and biospecimen sharing. Overall, agreement to allow investigators and their collaborators obtain

genetic material increased to 98.5% (95%CI 98.0, 98.8) (data not shown). Overall agreement to sharing with not-for-profit investigators and with commercial entities increased to 87% (95%CI: 86, 88) and 80% (95%CI: 79, 81), respectively (Table 3).

Sharing Data beyond HCHS/SOL: Not-for-Profit Investigators

The proportion agreeing to share their genetic and non-genetic data with not-for-profit investigators unaffiliated with the HCHS/SOL research centers varied by field center and national background (both P<.0001). At baseline, agreement with this type of sharing was relatively low among San Diego residents (72%, 95%CI: 69, 74) and individuals of Mexican/Mexican-American background (72%, 95%CI: 70, 74). The most likely to agree to this form of sharing were those in the Miami center (87%, 95%CI: 85, 88) and those of Cuban background (89%, 95%CI: 88, 90). Individuals of Mexican/Mexican-American background had lower rate of consent regardless of the field center in which they resided (Chicago, 70%, 95%CI: 67, 73, vs San Diego, 71%, 95% CI: 68, 74). When reconsented at Visit-2, individuals of Mexican background continued to show the lowest consent rate although agreement increased considerably from baseline (Table 3).

Sharing Data beyond HCHS/SOL: Commercial Entities

The agreement to share with commercial entities was less common than agreement to other types of data sharing. Of those consenting to use by not-for-profit investigators, 9.2% did not consent to commercial use of their data and specimens (data not shown). Across all background groups, those of Puerto Rican background had the highest proportion who consented to data sharing with commercial entities (85%, 95% CI: 83, 87) at baseline. However, we observed differences between Puerto Rican background residing in the Bronx and Chicago (89%, 95% CI:86, 91 and 72%, 95% CI: 67, 77, respectively). Individuals of Mexican and Central American background were relatively less willing to share with commercial entities, regardless of their region of residence (Table 3).

Multivariable-adjusted Predictors of Consent to Data Sharing

Models adjusted for age, sex, and field center and other potential confounders identified risk factors for refusing to share with nonaffiliated not-for-profit investigators (Table 4). Men were 15% less likely (95% CI:.05, .23) than women, and those in the oldest age group (65-76 years) were 41% less likely (95% CI:.24,.54) than the youngest age group (18-24 years; P across age groups, .0002), to refuse sharing with not-for-profit investigators. Individuals of Cuban background were significantly less likely to refuse sharing compared with those of Mexican background (aPR, .57; 95%CI: .45,.72). Those born in the US mainland were less likely to refuse sharing with not-for-profit investigators (aPR, .84; 95%CI: .71, .99), as were English speakers in a finding that was just above the level of statistical significance (P=.05). Although a prior CHD diagnosis was associated with a reduced probability of data sharing refusal (aPR, .68; 95%CI: .48, .95; P=.03), prior diagnosis of stroke, diabetes, or cancer was not, nor were family history or perceived discrimination variables (all P>0.1).

Those born in the US mainland were significantly less likely to refuse consent to sharing with commercial entities (vs foreign-born, aPR, .84; 95%CI: .73, .97), as were males compared with females (aPR, .88; 95%CI: .81, .96) (Table 4). After adjustment for place of birth and other covariates, English language preference was associated with a 23% lower prevalence ratio for refusing resource sharing with commercial entities (95% CI: .11,.44 lower prevalence). Those with the lowest level of education (below 9th grade) were the most likely to agree to resource sharing with commercial entities, while for those with education levels of high school and beyond, adjusted prevalence ratios were above 1 for likelihood of refusal (P<.001). In addition, individuals with >1 first degree relatives having a cancer history were 25% less likely to refuse sharing with commercial entities (95% CI:.05, .41). However, consent to sharing with commercial entities did not differ across age groups (P=.37) or by prior CHD diagnosis (P=.51).

Analyses that were repeated after exclusion of Puerto Rican background participants generally confirmed key aspects of the above results. In this sensitivity analysis, association of family history of cancer was not statistically significantly associated with consent to sharing with commercial entities, while this analysis also showed that having at least

Table 4. Multivariable adjusted prevalence ratios for refusal to share genetic or non-genetic biospecimens and data with nonaffiliated not-for profit investigators and commercial entities, among individuals consenting to use of genetic data by study investigators (N=13,252): HCHS/SOL, 2008-2011

	Refusal to share with HCHS/SOL non-affiliated, not-for-profit investigators[a]		Refusal to share with commercial entities	
Characteristic	**aPR (95%CI)**	**P[d]**	**aPR (95%CI)**	**P[d]**
Men (ref, women)	.85 (.77, .95)	.003	.88 (.81, .96)	.003
Age (ref, aged 18-24 years)		.0002		.37
25-34	.97 (.82, 1.15)		1.10 (.92, 1.32)	
35-44	.84 (.70, 1.00)		1.07 (.90, 1.26)	
45-54	.78 (.66, .92)		1.05 (.90, 1.23)	
55-64	.74 (.62, .88)		1.05 (.88, 1.26)	
65-76	.59 (.46, .76)		.87 (.70, 1.09)	
Hispanic/Latino background (ref, Mexican)		<.0001		<.0001
Dominican	.82 (.60, 1.13)		.96 (.71, 1.29)	
Central American	1.01 (.83, 1.24)		1.01 (.85, 1.21)	
Cuban	.57 (.45, .72)		.71 (.58, .87)	
Puerto Rican	.85 (.70, 1.05)		.74 (.59, .92)	
South American	.87 (.69, 1.09)		.89 (.72, 1.11)	
Other/>1/not reported	.88 (.65, 1.19)		.98 (.75, 1.30)	
Annual household income (ref, <$10,000)		.22		.54
$10,001-$20,000	1.20 (1.00, 1.43)		1.05 (.91, 1.21)	
$20,001-$40,000	1.17 (.97, 1.41)		1.05 (.91, 1.21)	
$40,001-$75,000	1.05 (.84, 1.32)		.94 (.78, 1.12)	
>$75,000	1.07 (.75, 1.52)		.97 (.75, 1.25)	
Years of education (ref, <9th grade)		.17		.01
Some high school	1.02 (.85, 1.22)		1.25 (1.06, 1.48)	
HS graduate/equivalent	.88 (.76, 1.02)		1.11 (.98, 1.25)	
More than HS	.93 (.81, 1.07)		1.21 (1.07, 1.37)	
English language preference (ref, Spanish)	.85 (.72, 1.00)	.05	.77 (.66, .89)	.0005
Born in US mainland (ref, foreign-born)	.84 (.71, 0.99)	.038	.84 (.73, .97)	.02
Has health insurance (ref, no insurance)	.92 (.82, 1.03)	.13	1.01 (.92, 1.11)	.79
Fair or poor self-reported health (ref, excellent through good)	.97 (.87, 1.08)	.55	.98 (.90, 1.08)	.71
Treated unfairly because Hispanic/Latino (ref, never)		.88		.30
Sometimes	1.03 (.91, 1.17)		1.03 (.94, 1.13)	
Often or always	1.01 (.87, 1.17)		.95 (.85, 1.06)	
Chronic disease burden score[b] (ref, 0)		.12		.22
1	.85 (.72, .99)		.89 (.78, 1.02)	
2 or more	.93 (.64, 1.35)		.87 (.51, 1.51)	
History of CHD (ref, no history)	.68 (.48, .95)	.03	.85 (.52, 1.38)	.51
History of stroke (ref, no history)	.87 (.57, 1.34)	.53	.72 (.49, 1.06)	.10
History of diabetes (ref, no history)	.95 (.80, 1.12)	.55	.91 (.79, 1.05)	.20
History of cancer (ref, no history)	.89 (.64, 1.22)	.46	.95 (.66, 1.35)	.76
Family history disease burden score[c] (ref, 0)		.32		.50
1	.90 (.80, 1.03)		.93 (.83, 1.04)	
2	.96 (.84, 1.10)		1.00 (.89, 1.13)	
3 or more	.90 (.77, 1.05)		.96 (.84, 1.10)	
Family history of CHD (ref, none)		.19		.70
1 first degree relative	.89 (.78, 1.01)		.96 (.87, 1.07)	
>1 first degree relatives	1.00 (.78, 1.28)		.94 (.78, 1.14)	
Family history of stroke (ref, none)		.83		.56
1 first degree relative	1.04 (.88, 1.21)		1.05 (.94, 1.18)	
>1 first degree relatives	.91 (.59, 1.40)		1.12 (.81, 1.55)	
Family history of diabetes (ref, none)		.65		.54
1 first degree relative	.99 (.88, 1.12)		1.06 (.96, 1.17)	
>1 first degree relatives	.94 (.81, 1.08)		1.01 (.89, 1.14)	
Family history of cancer (ref, none)		.54		.05
1 first degree relative	1.03 (.91, 1.16)		1.01 (.91, 1.12)	
>1 first degree relatives	.88 (.68, 1.14)		.75 (.59, .95)	

a. Values represent the prevalence ratios (95%CI) for refusal to biospecimen use relative to the reference group derived from Poisson regression models with robust variance estimation adjusted for sex, age (continuous), field center, years of education (continuous), household income, Hispanic/Latino national background, language preference, place of birth (within vs outside mainland US), and duration of US residence (among foreign-born).

b. 1 point each for self -report CHD, stroke, diabetes and cancer.

c. Family history score calculated by first assigning 0,1, or 2 points for first degree relatives with a history of each of CHD, stroke, diabetes, and cancer and then by summing each individual disease score.

d. P-values reflect Wald tests for any difference across categories.

one chronic disease was associated with a reduced probability of refusing to share study resources (P for group difference, .038) (data not shown).

Change of Consent Status over Time

As shown in Table 5, only 10% of participants who consented to sharing biospecimen and data with commercial entities changed their response to refused at Visit-2. Comparing baseline to Visit-2, age was the only variable significantly associated with withdrawal of consent to share data at P<.1, with the <44-year-old age group being more likely than older individuals to withdraw consent to share with outside investigators. Conversely, almost two-thirds (63%) of participants who refused data sharing at baseline did agree to sharing with these entities at Visit 2. Individuals of Puerto Rican or Dominican background were less likely than those of Mexican background to change their mind and refuse sharing with commercial entities at Visit-2 (aPR, .26; 95%CI: .16, .14; and aPR, .32; 95%CI: .23, .45, respectively, P for group differences <.0001). Consistently, individuals of Puerto Rican and Dominican background who refused at baseline were more likely than Mexicans to change their mind and consent to sharing at Visit-2 (aPR, 1.40; 95%CI: 1.25, 1.58; and aPR, 1.18; 95%CI: 1.03, 1.34, respectively, P for group differences <.0001) (Table 5). Rate of changing consent from refusal to agreement for data sharing with commercial entities was higher among of Puerto Ricans in the Bronx 81% (95% CI: 70, 89) than among Puerto Ricans in Chicago 59% (95% CI: 47, 70) (data not shown).

The element of consent most commonly refused in our study was access to biospecimens and data by commercial entities.

Discussion

Research among Hispanic/Latinos can provide novel insights of the role of ancestry and genetics in health risks,[21] yet more research in ancestrally diverse populations is needed.[22] In the community-based HCHS/SOL study, which recruited during 2008 to 2011, participants' (98%) willingness to consent to genetic research conducted by study-affiliated scientists compares favorably vs other population-based research in different populations. For example, 85% of participants in the National Health and Nutrition Examination Survey consented to genetic research[5] whereas in the Multiethnic Study of Atherosclerosis (MESA), 79% agreed to participate.[12] In the Framingham Heart Study, more than 99% of participants granted permission for DNA extraction and genetic research.[16]

Lack of trust in researchers and medical professionals has been associated with difficulty to recruit for biomedical research. Our results support the notion that community members may have particularly negative responses to the idea that others may profit from their specimens or data.[23,24] The element of consent most commonly refused in our study was access to biospecimens and data by commercial entities. Twenty-five percent refused sharing genetic and non-genetic information with commercial entities. This suggests greater unwillingness to participate in this form of data and specimen resource sharing among Hispanics than has been reported in other populations.[16] At the same time, the proportion that agreed to broad sharing was high overall, which is notable when considering that the Hispanic/Latino community tends to have a relatively high degree of medical mistrust.[25]

The HCHS/SOL research teams obtained community consultations on issues related to Hispanic/Latino cultural sensitivities and values during the study design and conduct phases, which might have contributed to participant satisfaction, and the ability to build trust with participants thereby increasing community interest in genetic research.[26] As the study continued over time, participant consent rates for sharing with investigators not associated with the HCHS/SOL study increased. At the six-year follow-up visit, consent for data sharing with commercial entities continued to be the element most commonly refused although the proportion agreeing increased over time to 80% whereas consent to sharing with non-for profit investigators non-affiliated with HCHS/SOL increased to 87%. It is possible that increasing acculturation over time may be a factor, and it is also possible that either in-

Table 5. Multivariate analyses of characteristics of participants who changed consent in sharing of genetic and non-genetic biospecimens and data with commercial entities and nonaffiliated not-for profit investigators: HCHS/SOL, 2008-2017

	Sharing with commercial entities				Sharing with HCHS/SOL nonaffiliated, not-for-profit investigators			
	Change from yes at baseline to no at Visit 2		Change from no at baseline to yes at Visit 2		Change from yes at baseline to no at Visit 2		Change from no at baseline to yes at Visit 2	
	N=1198		N=1709		N=780		N=1517	
	aPR (95% CI)	P	aPR (95% CI)	P	aPR (95% CI)	P	aPR (95% CI)	P
Sex		.10		.12		.08		.14
Women vs men	1.12 (.98, 1.29)		.95 (.88, 1.02)		1.21 (.98, 1.50)		.95 (.88, 1.02)	
Age at Visit 2		.24		.87		.001		.64
45-54 vs 23-44	.91 (.73, 1.13)		.97 (.87, 1.09)		.64 (.50, .81)		.98 (.89, 1.09)	
55-64 vs 23-44	1.09 (.87, 1.36)		1.00 (.89, 1.11)		.67 (.52, .87)		1.04 (.96, 1.14)	
65-95 vs 23-44	1.14 (.88, 1.49)		.95 (.82, 1.09)		.79 (.54, 1.14)		1.00 (.90, 1.11)	
Hispanic/Latino background (ref, Mexican)		<.0001		<.0001		<.0001		
Dominican	.26 (.16, .41)		1.40 (1.25, 1.58)		.55 (.35, .88)			
Central American	.88 (.66, 1.18)		1.00 (.87, 1.15)		.89 (.66, 1.19)			
Cuban	.64 (.52, .80)		1.23 (1.09, 1.39)		.49 (.33, .74)			
Puerto Rican	.32 (.23, .45)		1.18 (1.03, 1.34)		.39 (.26, 0.58)			
South American	1.04 (.81, 1.33)		.85 (.68, 1.05)		.92 (.65, 1.30)			
Other/>1/not reported	.86 (.54, 1.37)		1.20 (.98, 1.47)		.61 (.30, 1.24)			
Language preference		.45		.08		.78		.31
Spanish vs English	1.11 (.85, 1.45)		1.13 (.98, 1.29)		1.05 (.75, 1.46)		1.07 (.94, 1.22)	
Place of birth		.03		.96		.06		.37
Foreign born vs US mainland born	1.37 (1.03, 1.80)		1.00 (.86, 1.17)		1.43 (.99, 2.06)		.95 (.85, 1.06)	
Has health insurance at Visit 2		.66				.46		
No vs yes	1.04 (.87, 1.23)				1.09 (.86, 1.38)			

P's are from Chi square tests in comparison with reference. Characteristics are from Visit 1 unless noted otherwise.
Included age, sex and variables with P<.10 in univariate analyses.

creased personal knowledge or changing community values about genetics and medical research may have favored higher consent rates at the 6-year follow-up visit than at baseline.

Important predictors of refusal to share data and specimens were female sex, Spanish language-speaking preference and birthplace outside the United States. Latinas, and particularly those who are dominant Spanish speakers, when compared with women from other race/ethnic background, have been found to have a higher degree of medical mistrust and worries about potential misuses or disadvantages of clinical genetic testing information.[27] Relatively less is known, however, about the Hispanic population's views about genomic research studies like ours, as opposed to clinical genetic testing. Our study suggests that characteristics related to acculturation may influence decisions about Hispanic/Latino participation in large-scale community-based genomic projects. Thus, certain demographic groups within the Hispanic community may need tailored efforts to optimize their enrollment. Likelihood of consenting to genetic data sharing was unaffected by socioeconomic status, except for the finding that those with a 9th grade or lower educational attainment were more likely to agree to data and specimen resource sharing than those with an education beyond 9th grade.

Fears of genetic discrimination have been reported previously and may play a role in refusals to participate in genetic research and data sharing activities.[28,29] Prior surveys indicate that only 25% would trust their health insurer and 16% would

trust their employer to have access to genetic test results.[28] Half of unaffected individuals with family history of colorectal cancer enrolled in the Johns Hopkins Hereditary Colorectal Cancer Registry rated their level of concern about genetic discrimination as high.[30] To reduce concerns, HCHS/SOL informed participants of the Certificate of Confidentiality issued by NIH to protect their privacy by withholding their identities from all persons not connected with HCHS/SOL. The study ICD mentioned the Genetic Information Nondiscrimination Act of 2008, a federal law that prevents discrimination to obtain certain insurance products against anyone based on their genetic information. Despite these safeguards, HCHS/SOL rates of consent to sharing with unaffiliated not-for-profit and commercial entities were lower among individuals who lacked health insurance. Further research may ascertain whether this was driven by potential discrimination concerns against high-risk individuals that could prevent them from obtaining insurance or lead to higher premiums and eligibility issues.

On the other hand, self-reported family history of illness has been associated with positive attitudes toward genetic studies[31,32] and previous studies suggest that people being studied for a prevalent symptomatic condition under investigation were more likely to consent.[33] HCHS/SOL did not recruit participants to study a disease that necessarily affected them, which may account for differences in consent rates as compared with Hispanics/Latinos in other study settings. However, prior CHD diagnosis was associated with a reduced probability of refusal to share data in HCHS/SOL whereas prior diagnosis of stroke or diabetes, and family history of disease did not have any apparent effect. Individuals with >1 first degree relative having a cancer history were 25% less likely to refuse sharing with commercial entities which might be due to participant awareness of drug development for cancer including investments by private companies.[34]

Differences in consent rates within the Hispanic population highlight the importance of assessing attitudes of the different Hispanic/Latino background groups concerning genetic research and data sharing. Major differences in consent rates for sharing with study collaborators vs outside investigators and higher agreement at Visit-2 suggest trust is a key element in encouraging consent. Among individuals who remained in HCHS/SOL for the second in-person examination, there were more participants who changed their mind and ended up agreeing to genetic research over time than withdrawals of their consent to genetic research.

Study Limitations

Data from our urban cohort might not be generalizable to Hispanics/Latinos living in rural or suburban areas. Although consent language was standardized across sites, it is impossible to exclude the possibility that the way information was conveyed to participants may have differed across sites, and there may have been a potential impact of differences in the recruitment process across sites.

Conclusion

Our study emphasizes the importance of taking acculturation into account in recruitment plans and highlights the opportunity of adding genetic components to ongoing longitudinal research to facilitate the collection of genetic data. By following our project's model of employing bilingual staff who are culturally concordant with study communities,[35] ongoing projects in the field of precision medicine can engage adequate numbers of Hispanic/Latino participants.

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Conflict of Interest

No conflicts of interest to report.

Author Contributions

Research concept and design: Gonzalez, Strizich, Isasi, Thyagarajan, Perreira, Talavera, Giachello, Schneiderman, Kaplan; Acquisition of data: Perreira, Talavera, Daviglus, Schneiderman, Kaplan; Data analysis and interpretation: Gonzalez, Strizich, Isasi, Hua, Comas, Sofer, Thyagarajan, Perreira, Talavera, Nelson, Giachello, Kaplan; Manuscript draft: Gonzalez, Strizich, Isasi, Hua, Comas, Sofer, Thyagarajan, Daviglus, Nelson, Giachello, Kaplan; Statistical expertise: Strizich, Isasi, Hua, Talavera, Kaplan; Acquisition of funding: Perreira, Talavera, Daviglus, Schneiderman, Kaplan; Administrative: Gonzalez, Hua, Comas, Sofer, Thyagarajan, Perreira, Talavera, Nelson, Giachello, Kaplan; Supervision: Isasi, Perreira, Kaplan

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