American Journal of Epidemiology **Submitted Manuscript**

Special Collection: N/A

Title: The Puerto Rico Young Adults' Stress, Contextual, Behavioral & Cardiometabolic Risk (PR-OUTLOOK) Study: Design and Methods

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Key words: Cardiovascular health, risk factors, prospective cohort study, young adults, Hispanics/Latinos, Puerto Ricans, stress, resiliency.

Acknowledgments[1]**:** We acknowledge the contributions of the Hispanic Alliance for Clinical and Translational Research (National Institute of General Medical Sciences, grant U54GM133807), the community partner clinics, the study participants, and the PR-OUTLOOK research staff and assistants.

Funding: This work was supported by the National Heart, Lung, and Blood Institute (grant R01HL149119 to M.C.R. and C.M.P.)

Conflict of Interest: The authors have no conflict of interest to disclose.

Disclaimer: The content is solely the responsibility of the authors and does necessarily represent the official views of the National Heart, Lung, and Blood Institute.

[1] Study investigators, conference presentations, preprint publication information, thanks.

Data Availability Statement: PR-OUTLOOK data will be available from the study Principal Investigators (Drs. Pérez and Rosal) upon reasonable request and compliance with the study's data request processes.

Abbreviations: CVH, Cardiovascular health; CVD, Cardiovascular disease; BPRHS, Boston Puerto Rican Health Study; BMI, Body mass index; COVID-19, Coronavirus disease 2019; HCHS/SOL, Hispanic Community Health Study/Study of Latinos; LE8, Life's Essential 8; REDCap, Research Electronic Data Capture; PROSPECT, Puerto Rican Observational Study of Psychosocial, Environmental, and Chronic Disease Trends; PR-OUTLOOK, Puerto Rico (PR) Young Adults' Stress, Contextual, Behavioral & Cardiometabolic Risk Study.

Abstract

The Puerto Rico (PR) Young Adults' Stress, Contextual, Behavioral & Cardiometabolic Risk Study (PR-OUTLOOK) is investigating overall and component-specific cardiovascular health (CVH) and cardiovascular disease (CVD) risk factors in a sample of young (age 18-29) Puerto Rican adults in PR (target n=3,000) and examining relationships between individual-, family/social- and neighborhood-level stress and resilience factors and CVH and CVD risk factors. The study is conducting standardized measurements of CVH and CVD risk factors and demographic, behavioral, psychosocial, neighborhood, and contextual variables and establishing a biorepository of blood, saliva, urine, stool, and hair samples. The assessment methods are aligned with other National Heart, Lung, and Blood Institute funded studies: the Puerto Rico Observational Study of Psychosocial, Environmental, and Chronic Disease Trends (PROSPECT) of adults 30-75 years, the Hispanic Community Health Study/Study of Latinos (HCHS/SOL), the Boston Puerto Rican Health Study (BPRHS), and the Coronary Artery Risk Development in Young Adults (CARDIA). PR-OUTLOOK data and its biorepository will facilitate future longitudinal studies of the temporality of associations between stress and resilient factors and CVH and CVD risk factors among young Puerto Ricans, with remarkable potential for advancing the scientific understanding of these conditions in a high-risk but understudied young population.

Although cardiovascular disease (CVD) risk has declined among older groups in the US population, CVD risk factors among young adults (typically defined as encompassing the age range of 18-35 y) have increased,[1] and incident CVD (e.g., heart failure) and some CVD outcomes (e.g., myocardial infarction) have not declined, or have increased (e.g., acute ischemic stroke and CVD mortality).[2-5] Life's Essential 8, a metric of four behavioral (smoking, physical activity, diet quality, and sleep) and four health (blood pressure, fasting glucose, non-high-density lipoprotein cholesterol, and body mass index) factors, has been proposed as an overall measure of Cardiovascular Health (CVH).[6] Understanding overall CVH rather than just assessing the presence of individual CVD risk factors is vital in young adulthood, a generation that grew up during the dual epidemic of obesity and type 2 diabetes[7,8] and unhealthy lifestyle behaviors.[9-20]

Multiple factors may reduce CVH in young adults, including high stress levels (i.e., financial, school-to-work, and social/family transitions), a peak in behavioral risks, and undervaluing of health care/prevention.[21,22] However, CVH and CVD risk have been understudied among young adults, especially Hispanic/Latino adults. The Coronary Artery Risk Development in Young Adults (CARDIA) study, initiated in 1985, examined CVD risk among young Black and White adults but excluded Hispanics/Latinos individuals.[23] The Hispanic Community Health Study/Study of Latinos (HCHS/SOL), a study of adults aged 18-74 in the continental US, shows marked variations in risk, prevalence, and outcomes among Hispanic/Latino subgroups, with Puerto Ricans having strikingly greater CVD risk and burden, and poorer overall CVH, than other groups.[10,24-28] However, little is known regarding CVH and CVD risk factors of young adults residing in Puerto Rico (PR).

Existing literature links psychosocial and contextual stress and CVD risk,[29-32] but these

associations have not been studied among young adults in PR. In the past few years, Puerto Ricans have suffered major stressors (i.e., a financial crisis, earthquakes, three hurricanes, and COVID-19).[33-35] Poverty, present in 40.5% of the population[36], may exacerbate these stressors. With young adults facing considerable social, economic, and contextual challenges,[21] it is critical to understand how these stressors may contribute to CVH. Similarly, it is essential to understand the role of culture-specific factors, such as family/social support, spirituality, and religiosity as potential protective influences. With atherosclerosis developing well before its clinical manifestation, studies of CVH and CVD risk in young Puerto Ricans may facilitate early CVD prevention.[22,37-47]

This article describes the methods of the PR-OUTLOOK (Puerto Rico (PR) Young Adults' Stress, Contextual, Behavioral & Cardiometabolic Risk) study established to address critical gaps in our understanding of CVH and CVD risk factors (Table 1) among young adults in PR. The study objectives are:

1. To describe CVH metrics and CVD risk factors in a community sample of young adults in PR.
2. To examine associations between psychosocial and neighborhood stress and CVH metrics and CVD risk factors.

   Hypothesis: Stress is negatively associated with CVH metrics and positively associated with CVD risk factors.
3. To assess the modifying effect of culture-specific resilience factors on associations between psychosocial and neighborhood stress and CVH metrics and CVD risk factors.

   Hypothesis: Resilience factors modify associations of stress and CVH metrics and CVD risk factors.

PR-OUTLOOK is guided by a biopsychosocial perspective[48] which argues that ethnic health disparities are influenced by differential exposure to psychosocial adversities, with moderation by the level of access to material, emotional, and other resources over time; that an imbalance between stress and resources is created by socioeconomic factors defining the social hierarchy and life opportunities; and that this disadvantaged status is maintained and worsened by debilitating environments of poverty and deprivation.

METHODS

Study design

PR-OUTLOOK is establishing a cohort of 3,000 men and women aged 18-29 across the island of PR using community-based approaches and conducting comprehensive survey and clinical assessments, followed by brief bi-annual telephone contacts. A randomly selected sub-sample of 1,500 participants, stratified by sex and socioeconomic position index,[49] completes actigraphy measures. Recruitment started in September 2020 and will continue for 3.5 years, with bi-annual contacts projected to end in 2024. The University of Puerto Rico-Medical Sciences Campus Institutional Review Board approved the study.

Participant eligibility, recruitment, and consent

Eligible individuals are: (1) aged 18 to 29 years old; (2) self-identify as Puerto Rican, born in PR, or have at least one Puerto Rican-born parent; (3) reside in PR; (4) have phone access; (5) have no cognitive, psychiatric, or physical conditions that preclude participation; (6) are not on active military duty; and (7) have no immediate relatives participating in the study.

Participants are recruited throughout the island via public announcements on traditional and social media; press releases; electronic and print advertisements; referrals; and community outreach activities. Pre-eligibility is assessed by telephone or online (Research Electronic Data

Capture (REDCap) survey),[50] and recruiters determine final eligibility via telephone. We originally planned a population-based stratified random sampling design for recruitment, which the SARS-COVID-19 pandemic made unfeasible. Thus, we reverted to the more opportunistic recruitment strategy described above. Although this change may make our findings potentially less generalizable, our approach is not uncommon in community-based studies[51-54] and will still provide valuable and needed information. Also, we will address potential recruitment bias, as described in the analysis section below.

Upon confirming eligibility, research staff members conduct consenting procedures: explain study activities and risks and benefits to participants and obtain written consent (online with secure access, in person, or by mail) with ample time for individuals to read the consent form and ask questions.

Assessment

The study assessment includes a survey and a clinical visit. Variables assessed are listed in Table 1 and procedures are described below.

Survey: The survey assesses demographics, medical and health care history, health behaviors, psychosocial variables, and contextual factors. Participants who complete the survey online (computer, tablet, or smartphone) receive an email with a unique access link. Participants who prefer or need (i.e., no internet access) oral administration of the survey are offered interviewer-conducted telephone administration.

Demographic and socioeconomic characteristics: The survey assesses age, sex at birth, race, nativity, migration history, gender identity, sexual orientation, marital status, children's ages (if any), living arrangements, educational attainment, work status, annual household income, perceived social standing (MacArthur Scale of Subjective Social Status),[55] food insecurity (6-

item US Department of Agriculture Household Food Security Scale),[56] current economic[57] and housing instability, childhood material deprivation,[58] health insurance, health literacy,[59] and self-reported skin color.[60]

Medical and health care history: Participants complete a checklist of cardiovascular and other chronic diseases that they or their first-degree family members have experienced. Those who respond affirmatively to 'female' in sex-at-birth are asked about contraceptive use, history of polycystic ovarian syndrome, and hysterectomy. Other questions include perceived health,[57] healthcare provider access, last provider visit date, COVID-19 perceptions, and preventive behaviors.

Health behaviors: The survey assesses cigarette smoking and secondhand nicotine exposure,[61] vaping,[62] and use of energy drinks, street drugs, and sexual stimulants.[62] It also includes measures of physical activity (frequency, duration, and intensity),[63,64] sedentariness,[65] and sleep (duration and variability,[66] quality,[67,68] napping,[69] morningness and eveningness,[66,70] sleep problems,[67] sleep apnea symptoms[66] and daytime dysfunction).[71]

Psychosocial factors: The survey assesses symptoms of depression (10-item Center for Epidemiological Studies of Depression Scale (CESD-10),[27,72] trait anxiety (10-item Spielberger's State-Trait Anxiety Inventory (STAI-10),[73] post-traumatic stress (2-item PTSD Checklist for Civilians),[74] and the experience of a cultural syndrome known as ′ataque de nervios′ (2-item measure from the National Latino and Asian American Survey).[75]

Also assessed are individual-level stressors and resources, including perceived stress (Perceived Stress Scale (PSS-4)),[76] the experience of individual chronic stressors (Chronic Burden Scale),[77] traumatic stress from natural disasters (2018 World Values Survey for PR),[78] perceived discrimination (Everyday Discrimination Scale),[79] loneliness (UCLA Loneliness

Scale),[80] caregiving,[81] and beliefs about caregiving obligations (Norms Toward Obligation and Solidarity Scale).[57] Assessed individual-level resources include stress coping (Shift-and-Persist Scale),[82] optimism (Revised Life Orientation Test),[83] religiosity (National Institute of Mental Health Collaborative Psychiatric Epidemiology Survey),[84] and spirituality (Daily Spiritual Experience Scale).[85,86] The survey also assesses social support and strain from spouse/partner, family, and friends (Midlife Development in the United States Survey),[87] overall satisfaction with life, trust in others (Social Networks and Social Resources module of the 2017 International Social Survey Programme),[57] and pet ownership and type.[88]

Neighborhood characteristics and resources: The survey assesses seven social and physical neighborhood environment features that may be associated with CVD risk, namely violence, safety, aesthetic quality, walking environment, availability of healthy foods, social cohesion, and neighborhood integration (MESA Neighborhood Conditions Scales).[89] It also assesses social and political participation (i.e., professional, sports, or social groups), social relations, support systems, and reciprocity within these groups (Social Networks and Social Resources module of the 2017 International Social Survey Programme).[57]

Clinic Visit: Following survey completion, participants attend an in-person clinic visit. A mailing provides 1) directions to the clinic; 2) instructions to refrain from eating, smoking/substances, and vigorous physical activity on the morning of the visit, wear light clothing, and bring all their prescribed and over-the-counter medications; and 3) a kit with instructions for a stool sample collection within 24 hours of their visit. A subsample of participants receives a wrist-worn actigraph (GENEActiv Original) with wear instructions (i.e., non-dominant wrist, seven consecutive days) and a sleep diary. On the morning of the visit, participants are screened for COVID-19 symptoms (online or by telephone). The clinic visit is conducted by rigorously

trained staff and structured as follows:

Reception: Upon arrival, the research staff welcomes the participant and briefly explains the procedures.

Stool sample: The participant's stool sample is stored at -20°C. Participants who do not bring this sample may collect it at the visit.

Accelerometer and sleep diary: For the sub-sample of participants in the sleep study, the research staff collects the actigraph and sleep diary.

Urine sample: Participants are instructed to collect a urine specimen in a labeled cup.The voiding time is recorded.

Saliva sample: Participants provide whole saliva samples in two labeled 2 mL cryovials using the SalivaBio's passive drool method and the Saliva Collection Aid (Salimetrics, State College, PA).

Anthropometry: Height, weight, and waist and hip circumferences are measured using standardized protocols.[90] Height is measured using a SECA 213 portable stadiometer and rounded to the nearest centimeter. Weight is measured with a Tanita WB800-S Plus Digital Scale and rounded to the nearest tenth kilogram. Using an ADC measuring tape, waist circumference is measured at the level of the umbilicus and hip circumference at the maximal protrusion of the gluteal muscles to the nearest 0.1 centimeters. All measurements, except weight, are taken twice in a standing position (light clothing, no shoes) .

Blood pressure and pulse: After a ten-minute rest period in a sitting position, systolic and diastolic blood pressures are measured by placing an appropriately sized cuff on the participant's right arm. Three measures are taken at two-minute intervals using a digital automatic blood pressure monitor (Omron HEM-907XL).

Blood samples: With the participant seated, a certified phlebotomist follows standard protocols

and uses pre-coded (ID, collection date, and time) tubes to collect 37.7 ml of blood by venipuncture from an arm vein in the following order: one 2.7 ml BD Vacutainer® buffered sodium citrate, one 9 ml Vacuette® tube serum clot activator, one 9 ml Vacuette® tube serum separator clot activator, three 4 ml BD Vacutainer® K2EDTA, one 2.5 ml Paxgene® blood RNA tube, and one 2.5 ml Paxgene® blood DNA tube. An additional 15.7 ml of blood are collected for quality validation in a random subsample (10% of participants).

Hair sample: Between three and five strands (1-3 cm) of hair are cut from the posterior vertex of the participant's skull,[91] wrapped in aluminum foil, and placed in an envelope. Additionally, participants are queried about the frequency of hair washing and salon treatments over the previous three months, hair care products used, and steroids' use.

Skin spectroscopy: The NIX Mini 2 color sensor device (Nix Sensor Ltd., Ontario, Canada) measures skin color. With the participant sitting with arms flat on a table and head roughly in line with the torsos, four skin color measures are taken by placing the device flat against the skin on the outer arm, inner arm, cheek, and forehead. The device is connected to a smartphone that transfers spectroscopy data directly into the study's database. *Dietary/nutritional intake*: Dietary intake in the previous year is assessed using a food frequency questionnaire adapted and validated for the Puerto Rican population.[92,93] This tool is administered using visual aids to facilitate portion size estimation. Analysis of food and nutrients is performed using the Nutrition Data System for Research (University of Minnesota, Minneapolis, MN).

Medications: The research staff records medication names and doses from the participant's drug containers or provided pictures of drug containers and self-reported reasons for use.

Exit procedures: At the end of the visit, research staff verify the completion of all assessments and provide participants with a copy of anthropometric, heart rate, and blood pressure

measurements. Participants receive a monetary incentive ($100). They also receive their laboratory test results, a brochure explaining the tests performed, and a thank-you card within two weeks.

Post-clinic visit procedures

Specimens are processed and prepared for transfer. A total of 15.7 ml of blood, and an additional 15.7 ml for a QA sample, are processed for same-day cardiometabolic assays (i.e., total cholesterol, HDL cholesterol, triglycerides, fasting glucose, insulin, glycosylated hemoglobin, and high-sensitive C Reactive Protein) (Table 2). Plasma and serum are separated within one hour of venipuncture in a centrifuge, and samples are refrigerated at 8°C or frozen at -20°C until collected by a local clinical reference laboratory. All other specimens, including whole blood, plasma, serum, buffy coat, Paxgene DNA, Paxgene RNA, saliva, urine, stool, and hair, are prepared and transferred to the study's biorepository at FDI Clinical Research for long-term storage (specimens are stored at -80°C; hair samples are stored at -20°C). For the sleep study subsample, data are extracted from the actigraph, and sleep diaries are scanned and uploaded to REDCap.

Biannual Contacts

At brief biannual calls (5-10 minutes), study staff update participants' contact information and document any health information, including a new diagnosis of CVD risk factors or events, emergency room visits, CVD-related hospitalizations, or procedures. Any new diagnosis or hospitalization triggers a request for medical records or death certificates for potentially CVD-related events and adjudication.[94] Because calls are primarily carried out for cohort retention purposes, we do not expect to observe important health changes in this young sample. Any data collected regarding CVD-related events will be used solely for descriptive purposes.

Cohort Retention

To boost the potential for the study cohort to remain prospectively, we use various strategies to maintain participant engagement over time.[95,96] At enrollment, the research staff collect contact information for the participant and three alternate contacts. Participants receive a toll-free number to facilitate contact with the study staff. To enable assessment completion, we contact participants at different times of the day and week and schedule clinic visits at convenient times. Participants receive reminder calls to complete the survey and to confirm the clinic visit.

We also maintain contact with participants by mailing holiday and birthday cards, annual newsletters, and token gifts with the study logo, and encouraging logging into the study website, which includes study updates and health information that might interest young adults. To regain contact with participants whose contact information may have changed, we conduct postal tracing and computer searches, mail handwritten letters, call personal contacts provided by the participant, and do home visits.

Training and certification of research staff

Study staff are fully trained in human subjects' research ethics, rapport building, and interviewing techniques, REDCap, study procedures described in the manual of operations, and data privacy and security.

Data quality assurance, management, and requests

Quality control procedures include 1) a manual of operations with study protocols; 2) training and retraining of staff for measurement standardization; 3) periodic checking and re-calibrating equipment and ongoing monitoring of examiner performance; 4) system validation rules for data entry and comprehensive edits after data submission; 5) validation and verification of data collection completion and quality checks; 6) descriptive analyses to identify errors in the

data collection process; 7) calculation of invalid rates of food frequency questionnaire records; and 8) review of progress reports to identify and promptly resolve any difficulties. Data are stored in a password-protected database, with access limited to investigators and key data management staff.

In compliance with the NIH's 2003 Data Sharing Policy[97] that existed at the study's outset, our data sharing plan includes the creation of de-identified datasets and accompanying documentation, provision for sharing of data used in publications, and release of data to appropriate investigators under the establishment and signing of a data use agreement.

Statistical Analysis

Proportions and means with 95% confidence limits will be used to characterize categorical and continuous measures, respectively, of overall and component-specific CVH metrics (range: 0-100)[6] and CVD risk factors (presence/absence) at baseline (Aim 1). We will compare these measures across categories of socioeconomic indicators and urban/rural status using z-tests of proportions and means depending on the nature of the variable. Using generalized linear models, Aim 2 will examine the associations between psychosocial and neighborhood stress and CVH metrics and CVD risk factors. These models will be adjusted for age, sex at birth, and individual socioeconomic status, and will use the appropriate canonical link depending on the nature of the data. Directed acyclic graphs will be used to inform the choice of other covariates in the models.[98,99] We will also assess the impact of the time lag between the survey and clinical assessment on time-dependent variables and use this as a variable in sensitivity analysis and adjustments. To assess the modifying effect of resilience factors on associations observed in Aim 2, we will introduce these factors as interaction terms with stress (psychosocial and neighborhood) to determine the impact on CVH metrics and CVD risk factors. If the interactions

are significant, we will conduct subgroup analyses. All analyses will be performed using STATA (Stata Corporation, College Station, TX, US) and R (R Core Team, Vienna, Austria) softwares.

As selection bias may influence key characteristics in this non-probabilistic sampling, we designed a plan to compare the sample demographics against demographics from the 2020 US Census data for PR, to make corrections to our recruitment strategy. Particular attention will be given to age, sex, and socioeconomic indicators. To correct differences between the final sample and Census data, and to improve generalizability, we will use the statistical approach of Iterative Proportional Fitting (IPF), also known as raking.[100,101] In this approach, marginal totals from our primary covariates of interest (age, sex, and socioeconomic indicators) in the sample are compared to Census data. IPF iteratively adjusts the weight for each observation until the sample distribution aligns with the Census data for those variables. Using these weights that directly adjust counts in primary covariates of interest in our sample to those in the Census data will facilitate adjustment of results to approximate those of the target population and allow us to obtain prevalence estimates of CVD risk factors.

Power

As our plan was to develop a cohort, we based our power considerations on the preset sample size of n=3,000. We used a minimum detectable effect approach. For categorical measures, we conservatively assumed the base proportion of 0.5, the middle of the binomial distribution, where variability is highest. Because our original design included complex survey sampling, we also accounted for a design effect (DEFF), the ratio of the sampling variance obtained using a complex design relative to the variance that would have been obtained from a simple random sample without replacement.[102] We calculated an effective sample size by dividing the available sample by the DEFF, and used this to determine the minimum detectable effect. The DEFF was

allowed to vary based on the expected mean cluster size. As the new design no longer uses complex survey sampling, the DEFF is no longer needed, and the available and effective sample sizes are the same.

For Aim 1, a sample size of n=3,000 produces a two-sided 95% confidence interval with a width equal to 0.036 when the sample proportion is 0.5 (a 95% confidence interval as tight as (0.482, 0.518)). For Aim 2, our comparisons of interest include four possible scenarios: continuous predictor and outcome; categorical predictor and outcome; categorical predictor and continuous outcome; and continuous predictor and categorical outcome. For simplicity, we only present power consideration for the first scenario. Although we will employ more complex approaches to analyze the data, using more straightforward power calculation approaches with fewer assumptions is commonly accepted. For two continuous variables (e.g., stress and BMI), we will have 80% power to detect a correlation as small as 0.05 in the main study (n=3,000) and 0.09 in the sleep study (n=1,000, e.g., actigraphy and survey measures), based on a two-sided linear regression test with r=0 for one normally distributed covariate X, with a =0.05. For Aim 3, there are numerous possible interactions. Therefore, we focused on the impact of subgroup analysis on the minimum detectable effect. An example is the possible modification of the relationship between stress and CVH (both continuous) by functional support (operationalized here as two equal-sized groups). Using a similar approach as Aim 2 but reducing the sample size to n=1,500 (one level of functional support), we will have 80% to detect a correlation as small as 0.07. If functional support is categorized into, for example, four groups (n=750) in each group, we will still have 80% to detect a correlation as small as 0.10.

Preliminary results

Because recruitment is near completion, initial analyses were conducted to assess potential

selection bias by describing the baseline demographics of the first 2,744 participants along with the demographic characteristics of a similarly aged sample from the US Census 2021 PR Community Survey (Table 3).[103] Data show that our sample has more younger adults, women, married individuals, and privately insured adults than in the Census. Any differences in sociodemographic characteristics between the final sample and Census data will be corrected using the statistical approach of IPF.

DISCUSSION

Previous studies of Puerto Ricans have shown that this population experiences a considerable burden of cardiovascular disparities.[24,104-109] However, these studies have primarily focused on middle- and older-aged adults. To our knowledge, PR-OUTLOOK is the largest and only study inclusive of young adults throughout Puerto Rico. It will comprehensively assess the overall CVH profile and CVD risk factors of a community sample of n=3,000 young adults. The study will describe behavioral and cardiometabolic risk factors early, during young adulthood, before they develop or progress to clinical CVD. PR-OUTLOOK will also evaluate associations between psychosocial- and neighborhood-level factors and CVH and CVD risk factors in this sample.

The results of PR-OUTLOOK will provide targets for early CVD prevention and prioritization of public health programs, help generate research questions for future longitudinal cohort follow-up, and inform future CVD prevention interventions. Our rich dataset and comprehensive biorepository will offer opportunities to evaluate countless scientific hypotheses, furthering insights into the complex interactions between psychosocial and environmental determinants, behaviors, and CVH of young adults. Future longitudinal observations of this cohort will help resolve questions on the temporality of associations between individual- and

neighborhood stress, resilient factors, sociodemographic variables, and behavioral and CVH and CVD risk. The study also lays a solid foundation for comparing young and middle-aged and older adults on the island (comparisons with PROSPECT)[54] and in the US (comparisons with HCHS/SOL[61] and BPRHS[104]) facilitated by shared methods and measures. These comparisons will provide insights for understanding both health advantages and disparities of young adults living in the continental US versus PR, with distinct migration and acculturation dynamics and social and environmental conditions. Research capacity in PR will be strengthened by providing specialized training to research staff and opportunities for hands-on research experience for students and early career investigators, predominantly from underrepresented minoritized groups, as stated in Objective 8 of the National Heart, Lung, and Blood Institute's strategic vision.[110]

Table 1. Variables assessed at the survey and clinical assessment of PR-OUTLOOK

Domain	Variables assessed
Demographic and socioeconomic characteristics	• Age, marital status, children's ages (if any), and living arrangements • Race, nativity, and migration history • Skin color self-described[60] and objectively measured (Nix Sensor Ltd., Ontario, Canada) • Sex at birth, gender identity, and sexual orientation • Education (self and parents), annual household income, work status, health insurance, and health literacy[59] • Municipality of residence • Place of residence (urban vs. rural) • Perceived social standing[55] • Food insecurity[56] • Economic insecurity[57] • Housing instability • Material deprivation in childhood[58]
Medical and health care history	• Self-reported CVD history (self and family) and other chronic diseases • Women's health questions • Perceived health[57] • Medications type, dose, frequency, and reason (prescribed and over-the-counter) • Height and weight (measured); Body mass index (calculated)[90]

	• Waist and hip circumferences (measured); waist-to-hip ratio[90] • Systolic and diastolic blood pressures and heart rate (measured) • Total cholesterol, HDL cholesterol, and triglycerides (laboratory assays) and estimated LDL cholesterol • Blood glucose, hemoglobin A1c, and insulin (laboratory assays) • High-sensitive C reactive protein (hs-CRP) and fibrinogen (laboratory assays) • Healthcare provider access and last provider visit date
Health behaviors	Use of nicotine and substances: • Self-reported cigarette smoking and secondhand nicotine exposure[61] • Self-reported vaping frequency, devices, and substances[62] • Self-reported use of nonprescribed medications, stimulants to improve sexual performance, energy drinks, marijuana, and cocaine[62]
	Physical activity: • Self-reported physical activity (frequency, duration, and intensity)[63-64] • Self-reported sedentariness[65] • Objectively measured activity/sedentariness in a subsample (GENEActiv Original device (Activinsights, Cambridgeshire, UK))
	Sleep:

	• Objectively measured (GENEActiv Original device (Activinsights, Cambridgeshire, UK) and self-reported sleep duration and variability (surveys and diary),[66] quality,[67,68] and napping[69] • Self-reported morningness and eveningness,[66,70] insomnia,[67,68] daytime dysfunction,[71] and sleep apnea symptoms[66]
	Dietary intake: • Dietary intake in the past year[92,93]
	COVID-19-related behaviors
Psychosocial factors	Psychological symptoms: • Depressive symptoms[27,72] • Anxiety symptoms[73] • PTSD symptoms[74] • Experience of 'ataque de nervios'[75] Stress variables: • Perceived stress[76] • Chronic stressors[77] • Traumatic stress from natural disasters[78] • Discrimination and unfair treatment[79] • Loneliness[80] • Caregiving for a sick or frail relative or friend[81] • Beliefs about obligations to care for others[57]
	Individual resources:

	• Coping[82] • Optimism[83] • Religiosity[84] • Spirituality[85,86] • Social support and strain from partner, family, and friends[87] • Life satisfaction[57] • Trust in others[57] • Pet ownership and type[88]
Neighborhood and contextual factors	Neighborhood conditions:[89] • Neighborhood violence and safety • Neighborhood integration • Social cohesion • Social interactions with neighbors • Aesthetic quality • Walking environment • Availability of healthy foods
	Contextual factors: • Social and political participation[57] • Social relations, support, and reciprocity systems[57]
Outcome measures	Primary outcomes[6] • Overall CVH metric score • Diet quality metric score

	• Physical activity metric score • Nicotine exposure metric score • Sleep health metric score • BMI metric score • Non-HDL-cholesterol metric score • Blood glucose metric score • Blood pressure metric score Secondary outcomes (traditional risk factors):[1] • Current smoking • Physical inactivity • Unhealthy diet • Overweight or obesity • Hypertension • Dyslipidemia • Diabetes mellitus

Table 2. Specimens in the PR-OUTLOOK biorepository*

Specimen	Amount
Fasting blood	Whole blood: six 0.5 mL cryovials Plasma: six 0.5 mL cryovials Serum: six 0.5 mL cryovials Buffy coat: 1 mL cryovial PaxGene RNA: 2.5 mL Paxgene DNA: 2.5 mL
Saliva	Two 2-mL cryovials
Spot urine	Six 1.5-mL cryovials
Stool	2.2 tablespoons stored in 20 mL containers
Hair	1-3 cm

*All specimens are stored at -80°C.

Table 3. Comparison of baseline characteristics of the first 2,744 PR-OUTLOOK respondents with the 2021 Puerto Rico Community Survey one-year sample estimates for the population aged 18-29 in Puerto Rico.

Sociodemographic characteristics	PR-OUTLOOK (n=2,744) n (%)	Puerto Rico (n=516,047) n (%)
Age group (years)		
18-24	1,990 (72.5)	311,747 (60.4)
25-29	754 (27.5)	204,300 (39.6)
Sex at birth		
Male	1,059 (38.6%)	259,472 (50.3)
Female	1,685 (61.4%)	256,575 (49.7)
Educational attainment		
High school or less	991 (36.1)	162,838 (31.6)
More than high school	1,751 (63.9)	353,209 (68.4)
Missing	2 (-)	
Marital status		
Married/Living with a partner	364 (13.3)	34,901 (6.8)
Widowed/Divorced/Separated	15 (0.5)	6,326 (1.2)
Never married	2,365 (86.2)	474,820 (92.0)
Health care coverage		
Private	1,629 (59.4)	217,356 (42.1)

Government programs	1,025 (37.4)	260,101 (50.4)
None	75 (2.7)	38,590 (7.5)
Missing	15 (0.5)	
Municipality of residence		
San Juan	412 (15.0)	53,669 (10.4)
Other	2,332 (85.0)	462,378 (89.6)

Source: US Census Bureau. Puerto Rico Community Survey 2021 One-Year PUMS File.

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