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Early Childhood Adversity and HbA1c Levels:
A Study of Puerto Rican Young Adults in Two Sites

By

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Degree to be awarded: Master of Public Health

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Early Childhood Adversity and HbA1c Levels:
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By

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B.S., University of Georgia, 2017

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Abstract

Early Childhood Adversity and HbA1c Levels:
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By Yamamah Nadine Ackleh

Abstract

Background: Adverse childhood experiences have been linked to a variety of poor health outcomes in adulthood, but gaps in the literature exist regarding their association with diabetes. To date few studies have focused on racial and ethnic minorities, have used prospectively collected ACE data as opposed to retrospective self-reporting, or have used laboratory-measured HbA1c data. This study examined the association between both prospectively and retrospectively reported ACEs and HbA1c levels measured in young adulthood. The study population is a sample of Puerto Rican young adults living in either Puerto Rico or the South Bronx.

Methods: The Boricua Youth Study (BYS) is a longitudinal cohort study of Puerto Rican-identifying households living in the South Bronx, New York, and San Juan, Puerto Rico. A follow-up study was conducted on a sample of young adults in this cohort, in which they provided retrospectively collected ACE data and a blood sample to measure HbA1c (BYS-Health Assessment). Unadjusted and adjusted linear regressions were performed for the association between prospective and retrospective ACE score and HbA1c. Separate analyses examined the association between the presence of ACEs in the child maltreatment subgroup only and HbA1c. All models were subsequently stratified by site.

Results: This study found null associations overall between ACE score and HbA1c in young adulthood and between child maltreatment ACEs and HbA1c in both the unstratified and site-stratified analyses in this sample. For example, compared to individuals with 0 ACEs, individuals with 4+ ACEs had an adjusted β=0.04, 95% CI: -0.15 to 0.23 (prospective model) and an adjusted β=0.02, 95% CI: -0.16 to 0.19 (retrospective model).

Conclusion: These results suggest that in this population, both cumulative adversity and child maltreatment do not affect risk of diabetes in young adulthood. Further research is needed to examine this association across different age groups in this population to ascertain the time course of the effect of child adversity on diabetes risk manifestation.

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Introduction

The term "Adverse Childhood Experiences," or ACEs, refers to distressing events that may occur in the life of children from ages 0-17, which may include experiencing or witnessing violence, various forms of abuse or neglect, and living in a household with dysfunction or instability (*Adverse Childhood Experiences (ACEs)*, 2021). The seminal paper on ACEs described a direct correlation between the number of categories of adverse childhood events experienced by participants and the presence of a number of diseases and health-risk behaviors in adulthood, such as coronary artery disease, lung disease, substance use disorders, depression and suicide attempts, smoking, and high-risk sexual practices (Felitti et al., 1998). Subsequent research has documented links between ACEs and a growing number of poor health outcomes in adulthood, including cancer, stroke, and mortality (Basu et al., 2017).

Several possible pathways mediating the association between ACEs and negative health outcomes have been proposed, including biological mechanisms (Danese & McEwen, 2012; Deighton et al., 2018; Herzog & Schmahl, 2018), adverse health behaviors (Suglia et al., 2018), and mental health problems (Suglia et al., 2018).

In addition to being associated with poor health outcomes, ACEs have implications for both the ability of affected individuals to obtain and use healthcare resources and for increased system-wide healthcare costs. First, ACEs are correlated with lower markers of socioeconomic status such as education level and employment, which are all associated with a decreased healthcare access (Alcalá et al., 2018). In the United States, this lack of access manifests as decreased likelihoods of having health insurance, having a primary care provider, and using screening services for certain cancers (Alcalá et al., 2018).

The estimated cost of ACEs is $748 billion annually in North America (Bellis et al., 2019). However, further study is needed to assess the full burden of ACEs in a global context outside North America and Europe. This would include establishing appropriate definitions of ACEs for populations in which children are regularly exposed to large-scale environmental stressors such as political violence, in order to accurately represent the burden of ACEs in these communities (Bellis et al., 2019).

In the United States, pronounced disparities exist in ACE burden by race and socioeconomic status, with Black and Hispanic children having a higher likelihood of exposure to one or more ACEs than non-Hispanic white and Asian children (Suglia et al., 2020). Though research about ACEs outside North America and Europe is relatively lacking, what is known about ACEs in a global context suggests a similar pattern that children in marginalized communities suffer from higher numbers of ACEs (Bellis et al., 2019). Relatedly, children affected by one or more ACEs are also likely to be suffering from adversities related to housing, neighborhood, and school environments, which are stressors that may confer cumulative health risks (Suglia et al., 2020).

Cardiometabolic diseases in adulthood such as coronary artery disease, ischemic heart disease, and stroke confer a significant health burden and have a well-documented association with ACEs (Suglia et al., 2020). However, research investigating the association of ACEs with the specific health outcome of diabetes has yielded mixed results. The original ACEs study found that risk of diabetes increases if the number of reported ACEs was at or above a threshold of four (Felitti et al., 1998). This is in line with the Biological Embedding of Stress model, which describes the idea that disease manifests after a certain threshold of cumulative stress has been met (Huffhines et al., 2016). This is a notable finding in the original ACEs study, because while

associations between ACEs and certain cardiometabolic health measures may be seen lower levels of exposure, the association with diabetes is only seen at relatively higher levels of ACE exposure. This threshold of four ACEs for conferring increased diabetes risk has been supported by other studies, such as one conducted in England which also demonstrated that reporting at least four ACEs increased the odds of diabetes (Bellis et al., 2015), as well as a meta-analysis which found that individuals with at least four reported ACEs had a higher risk of all measured outcomes including diabetes, compared to individuals with exposure to zero ACEs; though notably the association for the outcomes of physical inactivity, obesity, and Type 2 diabetes was relatively weaker than those for the other ACEs measured (Hughes et al., 2017). Another meta-analysis similarly demonstrated a weakly positive association between cumulative exposure to ACEs and the presence of type 2 diabetes (Jakubowski et al., 2018).

However, several meta-analyses exist that do not replicate this finding, such as the meta-analysis by Petruccelli et al. which found no association between ACEs and diabetes in its adjusted model (Petruccelli et al., 2019). Some evidence also suggests that certain component ACEs have stronger associations with diabetes risk. For example, neglect had the strongest association with diabetes in one meta-analysis (Huang et al., 2015). Yet other studies have found that certain, single categories of abuse increase the risk of diabetes, but the studies vary with regard to the type of abuse investigated (Huffhines et al., 2016). Studies which take into account the severity and timing of abuse provide evidence for the idea that cumulative risk, i.e. increased severity of abuse, was associated with a greater risk of diabetes. (Huffhines et al., 2016).

Significant gaps in knowledge about the association between childhood adversity and diabetes exist, including gaps in methodology and study population. To date, most studies investigating the association of ACEs with diabetes have been cross-sectional rather than

longitudinal and have measured ACEs via retrospective reporting; it has been shown that moderate variability exists between prospective and retrospective measures of ACEs, and thus different disease risk may be concluded between groups where ACEs are measured prospectively versus retrospectively (Baldwin et al., 2019; Suglia et al., 2018). Additionally, disparities in cardiometabolic diseases such as obesity, diabetes, and hypertension are known to exist across the life course, with these diseases disproportionately impacting children belonging to racial and ethnic minorities as well as children of lower socioeconomic status (Suglia et al., 2020); however, few studies have been conducted among populations that carry the greatest burden of risk. Furthermore, a correlation between ACEs and cardiovascular disease development has been demonstrated in young adults (Doom et al., 2017). However, further study is needed to elucidate the association between ACEs and diabetes risk young adulthood specifically, as existing meta-analyses have not restricted their included studies to young adult populations (Huang et al., 2015; Jakubowski et al., 2018) or have not included age as a variable (Petruccelli et al., 2019).

This study will examine the association of ACEs on young adult HbA1c levels in a prospective cohort of Latinx youth in Puerto Rico and the South Bronx (specifically, the Health Assessment sub-study of the Boricua Youth Study). Understanding this relationship will add to existing knowledge about health disparities which Puerto Rican minority youth populations face as well as help elucidate how diabetes risk may manifest in this population. The multi-site nature of the study (Puerto Rican youth based in the South Bronx as well as in Puerto Rico) also has the potential to reveal differentials in health risks among youth who do or do not exist as an ethnic minority where they live and have or have not impacted by immigration.

This knowledge will also support the development of interventions that are both targeted to Puerto Rican communities and timed to intervene during periods of vulnerability, with the goal of reducing the morbidity and mortality associated with diabetes.

Methods

BYS And BYS-HA Study Overview

The Boricua Youth Study (BYS) is a longitudinal, multisite cohort study of multistage probability samples of households representing the South Bronx, New York, and the Standard Metropolitan Area of San Juan, Puerto Rico. The sampling methodology used has been outlined in detail (Bird et al., 2006). Briefly, households were eligible to participate if they had one or more children aged 5-13 years old of Puerto Rican background and if one or more of the children's parents or guardians in the home also identified themselves as being of Puerto Rican background. Up to three eligible children per household could participate (three were selected at random if more than three were eligible). After providing parental consent (and child assent if over the age of 7), participating families completed a questionnaire and were followed annually for three years (assessment waves 1-3) from 2001-2004 (N = 2,491).

A young adult follow-up (wave 4) took place from 2013-2017 with a retention rate of over 80% of the original cohort (N=2,004) (Duarte et al., n.d.). Young adults who completed this follow-up who were between ages 5-9 at baseline in 2001 (N=1119) were asked to complete an interview, health assessment, and provide a blood sample for the Boricua Youth Health Assessment sub-study (BYS-HA). A total of 823 participants completed the BYS-HA. The baseline age range of 5-9 years old was chosen for recruitment of BYS-HA participants to ensure that the prospectively assessed ACE in this sample occurred in early childhood (before age 10)

as opposed to in adolescence. Of these 823 participants who completed the BYS-HA, 707 provided a blood sample for a cardiometabolic assessment, which was used to measure HbA1c. This sample (N = 707) was subsetted on participants who had no missing data for the exposure variables, i.e., no missing data or responses of "do not know" or "decline to respond" for any of the prospectively or retrospectively collected ACE measures (N=597). The sample was further subsetted on participants who had no missing data for any of the additional predictor variables (age at the time of BYS-HA, sex, site, maternal education level, and public assistance) (N=592) (Figure 1).

The blood samples were obtained by trained research assistants, who conducted home visits and collected drops of capillary whole blood from finger sticks (dried blood spots, or DBS). DBS sampling has been demonstrated to be a valid substitute for venipuncture and is valued for its ease of use in the field and cost-effectiveness (Williams & McDade, 2009).

The target population for this analysis is Puerto Ricans living in the United States and Puerto Rico.

Primary Exposure and Outcome Variables

Early childhood exposure to ACEs was assessed both prospectively across waves 1-3 and retrospectively during the BYS-HA health assessment. Prospectively, the ACE exposures assessed included the 10 adversities that were part of the original ACEs study (Felitti et al., 1998). The presence or absence of each ACE was assessed using previously described criteria (Ramos-Olazagasti et al., 2017). Briefly, the ACEs questionnaires used were developed using validated sources including the Parent-Child Conflict Tactics scale (Straus et al., 1998); the Family Psychiatric Screening Instruments for Epidemiologic Studies (Lish et al., 1995); and the Sexual Victimization Scale (Finkelhor & Dziuba-Leatherman, 1994). Exposure was considered

positive if an ACE was present during wave 1, 2, or 3. Retrospectively, ACEs were assessed via young adult self-reporting according to the CDC's ACEs questionnaire (Adverse Childhood Experiences Resources, CDC, 2022).

The ten prospectively assessed ACE exposures were grouped into three types: 1) child maltreatment (encompassing the ACE variables of physical abuse, emotional abuse, sexual abuse, and neglect); 2) parental maladjustment (encompassing the ACE variables parental intimate partner violence, parental substance use problems, parental mental health issues, and parental incarceration; and 3) parental loss (encompassing the ACE variables of parental separation/divorce and parental death). The ten retrospectively collected measures were identical to the prospective measures with two exceptions: the retrospectively collected measures did not include the parental death measure and did include a measure describing the participant's sense of lacking family closeness and support (*Adverse Childhood Experiences Resources, CDC,* 2022).

The primary exposure variable of ACE exposure was examined as a continuous ACE score variable using the total count of endorsed ACEs (0-10). Separate scores were created for the prospectively and retrospectively collected ACE measures. Each ACE score was also divided into four score levels using the following categorical variables: 0 ACEs, 1 ACE, 2-3 ACEs, and 4 or more ACEs. This distribution of score level was chosen based on prior research that has found a threshold effect of adverse health outcomes in adulthood at the level of 4 or more ACEs (Bellis et al., 2015; Hughes et al., 2017). Prospectively collected ACE score and retrospectively collected ACE score were analyzed separately.

In addition, the presence of any of the four ACEs in the maltreatment subgroup was examined as a categorical variable ("yes" if any of the four maltreatment ACEs was present or

"no" if none was present). Each of the component maltreatment ACEs (emotional abuse, physical abuse, sexual abuse, and neglect) was also examined as a categorical variable according to its presence or absence.

The primary outcome variable is hemoglobin A1c (HbA1c) as measured via the blood samples obtained during the BYS-HA. A participant's HbA1c was considered missing if no HbA1c level was recorded.

Additional Predictor Variables

In addition to the primary exposures of prospectively and retrospectively measured ACEs, several other measures collected from the young adult participants in the BYS-HA were used as covariates in some of the adjusted models: the continuous variable of participant age at the time of BYS-HA; and the categorical variables of site (Bronx or Puerto Rico), sex (male or female), maternal education ("less than high school," "high school," or at "least some college"), and use of public assistance ("yes" or "no"). In addition, site (Bronx or Puerto Rico) was considered a potential effect modifier in some of the models.

Statistical Analyses

Descriptive analyses were conducted to summarize the mean and standard deviation of the continuous outcome variable of HbA1c and the continuous predictor variable of young adult age. Descriptive analyses were also conducted to summarize the frequencies of the additional predictor variables of sex, site, maternal education, and public assistance, also collected during the BYS-HA. These analyses summarized the measures in total and also stratified by prospective and retrospective ACE score levels (0, 1, 2-3, and 4 or more).

Unadjusted and adjusted linear regressions were performed for the association between ACE score (both as a continuous score and as categorical score levels) and HbA1c. The

covariates in the adjusted regressions were age, sex, site, maternal education level, and public assistance. A sensitivity analysis was conducted which examined the association between the presence of ACEs in the maltreatment subgroup only and HbA1c. For all analyses, separate models were conducted using the ACE score for prospectively vs. retrospectively collected ACEs. All models were subsequently stratified by site.

Another sensitivity analysis was conducted which examined the association between ACE score (both as a continuous score and as categorical score levels) and log transformed HbA1c. Separate models were conducted using the ACE score for prospectively collected ACEs and the ACE score for retrospectively collected ACEs.

IRB approval was given by the Institutional Review Board at Emory University. Data were analyzed from February 2022-April 2022 using SAS 9.4.

Results

Of the final study population of 592 participants, 42.74% were from the Bronx and 57.26% were from Puerto Rico. 46.28% of the participants were male and 53.72% were female, and the mean age of the participants at the time the BYS-HA was conducted was 22.66 (SD 1.92). The mean HbA1c for the sample was 5.30% (SD 0.65). 24.83% of the cohort reported a maternal education level of "less than high school;" 33.61% reported "high school;" and 41.55% "at least some college." 29.90% of participants reported having utilized public assistance. Using the prospectively collected ACE measures, 14.19% of participants had an ACE score of 0; 25.17% had an ACE score of 1; 38.51% had an ACE score of 2 or 3; and 22.13% had an ACE score of 4 or greater. Using the retrospectively collected ACE measures, 29.05% had an ACE

score of 0; 32.94% had an ACE score of 1; 22.47% had an ACE score or 2 or 3; and 15.54% had an ACE score of 4 or greater.

In the adjusted and unadjusted regressions, cumulative prospective ACE score was not associated with HbA1c (adjusted β=0.00, 95% CI: -0.04 to 0.03); nor was cumulative retrospective ACE score (adjusted β=0.00, 95% CI: -0.03 to 0.03). When ACE score was subdivided into categorical score levels (0 ACEs, 1 ACE, 2-3 ACEs, or 4+ ACEs), score level was also not associated with HbA1c for either prospective or retrospective ACE measures. Compared to individuals with no ACEs, individuals with a score level of 4+ prospectively reported ACEs had an adjusted β=0.04, 95% CI: -0.15 to 0.23. Individuals with 4+ retrospectively reported ACEs had an adjusted β=0.02, 95% CI: -0.16 to 0.19.

In the sensitivity analysis which used only child maltreatment ACEs, the presence of any type of maltreatment was not associated with HbA1c in adjusted and unadjusted analyses for either prospectively reported ACEs (adjusted β= -0.04, 95% CI: -0.15 to 0.07) or retrospectively reported ACEs (adjusted β=0.10, 95% CI: -0.03 to 0.23). Analyzing each type of maltreatment (emotional abuse, physical abuse, sexual abuse, and neglect) separately also did not reveal an association in either the adjusted or unadjusted regressions for prospectively or retrospectively collected ACEs.

In the site-stratified analysis of participants in the Bronx (N=253), cumulative ACE score was not associated with HbA1c in either the adjusted or unadjusted regression for prospectively reported ACEs (adjusted β=0.00, 95% CI: -0.06 to 0.07) or retrospectively reported ACEs (adjusted β=0 -0.01, 95% CI: -0.22 to 0.20). Categorical ACE score levels were also not associated with HbA1c in either the adjusted or unadjusted regression for prospective or retrospective ACE measures. Compared to individuals in the Bronx with no ACEs, individuals

with a score level of 4+ prospectively reported ACEs had an adjusted β=0.25, 95% CI: -0.21 to 0.72 and an unadjusted β=0.24 95% CI: -0.22 to 0.70. Those with 4+ retrospectively reported ACEs had an adjusted β=0.17, 95% CI: -0.15 to 0.49.

In the site-stratified analysis of participants located in Puerto Rico (N=339), cumulative ACE score was not associated with HbA1c in either the adjusted or unadjusted regression for prospectively reported ACEs (adjusted β= -0.01, 95% CI: -0.04 to 0.02) or retrospectively reported ACEs (adjusted β= -0.02, 95% CI: -0.05 to 0.02). Categorical ACE score levels were also not associated with HbA1c in either the adjusted or unadjusted regression for prospective or retrospective ACE measures. Compared to individuals in Puerto Rico with no ACEs, individuals in the Bronx with a score level of 4+ prospectively reported ACEs had an adjusted β= -0.04, 95% CI: -0.21 to 0.13. Those with 4+ retrospectively reported ACEs had an adjusted β= -0.06 95% CI: -0.25 to 0.13.

Site-stratified sensitivity analyses in which only child maltreatment ACEs were analyzed. For the participants located in the Bronx, using prospective ACE measures, the presence of any maltreatment ACE was not associated with HbA1c (adjusted β= -0.04, 95% CI: -0.26 to 0.17). However, using retrospective ACE measures, the presence of any maltreatment ACE had a positive association in the adjusted and unadjusted regression (adjusted β=0.26, 95% CI: 0.05 to 0.48). Analyzing each component maltreatment ACE as a separate exposure variable did not reveal a similar association in the models for either prospective ACEs or retrospective ACEs. For the participants located in Puerto Rico, the presence of any maltreatment ACEs was not associated with HbA1c using prospective ACE measures (adjusted β= -0.04, 95% CI: -0.215 to 0.06) or retrospective ACE measures (adjusted β= -0.08, 95% CI: -0.23 to 0.07). Analyzing each

component maltreatment ACE as a separate exposure variable also did not reveal an association in either model.

An additional unstratified sensitivity analyses was conducted in which the HbA1c variable was log transformed. Continuous ACE score was not associated with HbA1c in using either prospective ACE measures (adjusted β=0.01, 95% CI: -0.01 to 0.04) or retrospective ACE measures (adjusted β=0.01, 95% CI: -0.01 to 0.04). Categorical ACE score levels were also not associated with HbA1c in either model. Compared to individuals with no ACEs, individuals with a score level of 4+ prospectively reported ACEs had an adjusted β= 0.01, 95% CI: -0.03 to 0.05. Those with 4+ retrospectively reported ACEs had an adjusted β= 0.00, 95% CI: -0.04 to 0.04.

Discussion

Overall, this study reveals a null association between cumulative ACE score and HbA1c in young adulthood in this sample. Our finding of no association overall is an important addition to the literature because a) this study focuses on Puerto Rican young adults, whereas most similar studies to date have not focused on Latinx populations specifically; b) this study uses the objective measure of HbA1c as the outcome variable, as opposed to the more commonly used self-reported measure of diabetes; and c) the longitudinal nature of the BYS study allowed for both the prospective and retrospective collection of ACEs data and thus mitigates the potential effects of information bias, both in the form of recall bias (retrospectively collected measures) or social desirability bias (prospectively collected measures).

This finding is similar to that in the meta-analysis by Petruccelli et al., who found no association between the highest reported ACE score and Type 2 diabetes overall in a group of 96 studies (Petruccelli et al., 2019). Another important source of agreement with our null finding

was present in the meta-analysis by Jakubowski et al., in which a null association was found in four out of the five studies whose methodologies involved both prospectively collected ACE measures and objective metabolic measures, as our study did; though the meta-analysis as a whole found a positive association between cumulative ACE burden (retrospectively assessed in the majority of studies) and diabetes (assessed via either self-report, evidence in the medical record, or a combination) (Jakubowski et al., 2018).

We also found a null relationship overall between the child maltreatment ACEs of emotional abuse, physical abuse, sexual abuse, and neglect and HbA1c in all but one model. The exception was the model using retrospectively collected ACEs in the site-stratified analysis examining participants only in the Bronx, which found a weak association between the presence of any maltreatment type and HbA1c. This association was not apparent for the presence of any single component maltreatment ACE. It is possible that this isolated positive association reflects multiple testing and type I error, especially since the association observed is weak; however, it is also possible that there is Type 2 error elsewhere in the site-stratified analysis due to lack of statistical power. Our overall finding of a null association between maltreatment exposure and HbA1c contrasts with the conclusion reached in the meta-analysis by Huang et al., which found a weak overall association between cumulative exposure to abuse and neglect and type 2 diabetes in adulthood in the seven included studies (Huang et al., 2015).

There are several key factors that could contribute to the observed difference between our overall finding of a null association across analyses and the positive associations found in the Jakubowski and Huang meta-analyses. First, many of the included studies were conducted in older age groups than our sample. It is possible that our young adult participants were too young overall for HbA1c to reflect an association; for example, the prevalence of diabetes in the meta-

analysis by Huang et al. was 6.74%, while in our sample it was 1.52% (Huang et al., 2015). Additionally, the diabetes outcome as measured as a self-report in most of the included studies, as opposed to a laboratory measure of HbA1c. Furthermore, the overall demographics of the participants in the included studies were notably different than our sample; for example the majority of the participants included in the Jakubowski meta-analysis were non-Hispanic white females (Jakubowski et al., 2018), and the studies in the Huang meta-analysis included studies from the USA, Finland, and New Zealand but not Latinx populations specifically (Huang et al., 2015).

Our study has several strengths. First, the use of both prospectively collected and retrospectively collected ACE measures mitigates the effects of either recall bias in the retrospective ACE measures or social desirability bias of ACEs in prospective measures. Second, our study focuses on a young adult cohort of Puerto Rican descent, which is an identity group that comprises a significant portion of the Latinx population in the United States and [also is a community that experiences significant health disparities at the systemic level – citation]; thus, this community is an important target population for health research in order to evaluate the need for and efficacy of targeted health interventions. Third, our study participants are part of a multi-site cohort, which improves the generalizability of our findings. The multi-site nature of the study also allows for potential effect modification by site to be analyzed, which could be significant since important social determinants of health such as access to healthcare vary by site. Fourth, our study focuses on the effects of early childhood adversities occurring when participants are under the age of ten. This allows for more robust comparisons to be made with other studies that also examine ACEs occurring in this age range; it also emphasizes the importance of conducting research that focuses on this developmentally vulnerable period. Fifth,

our study uses an objective laboratory measurement of the HbA1c outcome, as opposed to a self-reported diagnosis of diabetes, which increases the validity of our results and contributes to precise understanding of the biologically recognizable effects of adversity. Additionally, because HbA1C is a commonly measured laboratory value in primary care health visits, its use in the literature as an indicator of diabetes risk can inform targeted cardiometabolic health screening efforts at the community level. Finally, our study focuses on the association between ACEs on HbA1c as measured in young adulthood as opposed to at any point in adulthood. This is a strength because it can provide more detailed information regarding what age certain cardiometabolic diseases may start to manifest in communities with high ACE exposure. This knowledge has implications for the development of early prevention and secondary intervention efforts to reduce potential consequences of disease.

Our study also has several limitations. First there is the possibility of information bias. It is possible that ACE exposure was intentionally or accidentally mis-reported, due to either parental fear of reporting ACEs in the prospective collection or young adult reluctance to share this information in the retrospective collection. More research is needed to assess the concordance between each component ACE at the two collection points; however, our results did not show a difference in association with HbA1c in any prospective-ACE vs. retrospective-ACE models in any of the models except that in Table 3A-S. Second, there is the possibility of selection bias, as the individuals who participated in the BYS-HA study could be overall different from the ones who were not recruited, who were lost to follow-up, or who were recruited and chose not to participate. Third, there is some inherent weaknesses to the ACEs scoring system used in that a) it does not necessarily capture the frequency, severity, or chronology of exposure to component ACEs and b) it does not capture other dimensions of

adversity faced by the study population that could affect health outcomes in adulthood. However, the sources of the questionnaires used have been previously validated in other contexts.

Our findings highlight the need for future research that can examine not only the presence or absence of individual component ACEs but also examine in more detail the severity and frequency of said ACEs. Additionally, further research is needed which both utilizes objective measures of diabetes such as HbA1c and examines the time course of the manifestation of diabetes risk in this population compared to relative ACE burden

Overall, our study finds a null association between cumulative ACE score and HbA1c in young adulthood in this sample as well as a null association between the presence of maltreatment ACEs and HbA1c. These null associations were not modified by site and were overall consistent between models that used prospectively or retrospectively collected ACEs. This knowledge contributes to our understanding of relationship between ACEs and diabetes risk in Puerto Rican young adults, which has important implications for future targeted cardiometabolic health interventions at the community level and public health resource allocation at the legislative level.

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Tables & Figures

Figure 1. Flow diagram for sampling methods.

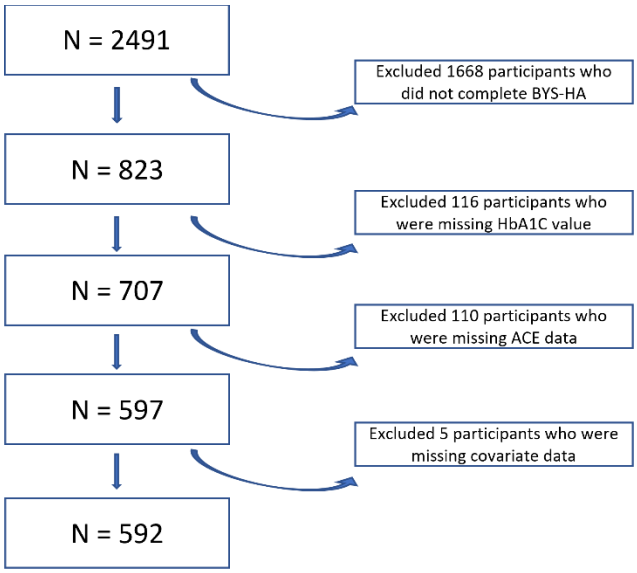

Table 1. Descriptive Statistics of Study Sample, Stratified by Prospectively and Retrospectively Collected ACEs

	Total	Prospective ACEs Score Level				Retrospective ACEs Score Level			
		0 (None)	1 (Low)	2 or 3 (Moderate)	4+ (High)	0 (None)	1 (Low)	2 or 3 (Moderate)	4+ (High)
	N=592 (100%)	N=84 (14.19%)	N=149 (25.17%)	N=228 (38.51%)	N=131 (22.13%)	N=172 (29.05%)	N=195 (32.94%)	N=133 (22.47%)	N=92 (15.54%)
Site, N (%)									
Bronx	253 (42.74%)	15 (17.86%)	60 (40.27%)	106 (46.49%)	72 (54.96%)	48 (27.91%)	80 (41.03%)	65 (48.87%)	60 (65.22%)
Puerto Rico	339 (57.26%)	69 (82.14%)	89 (59.73%)	122 (53.51%)	59 (45.04%)	124 (72.09%)	115 (58.97%)	68 (51.13%)	32 (34.78%)
Sex, N (%)									
Male	274 (46.28%)	33 (39.29%)	62 (41.61%)	109 (47.81%	70 (53.44%)	85 (49.42%)	97 (49.74%)	60 (45.11%)	32 (34.78%)
Female	318 (53.72%)	51 (60.71%)	87 (58.39%)	119 (52.19%)	61 (46.56%)	87 (50.58%)	98 (50.26%)	73 (54.89%)	60 (65.22%)
Age, Mean (SD)	22.66 (1.92)	22.54 (1.73)	22.91 (1.80)	22.59 (2.00)	22.59 (2.05)	22.62 (2.06)	22.54 (1.87)	22.53 (1.95)	23.21 (1.69)
HbA1c, Mean (SD)	5.30 (0.65)	5.25 (0.36)	5.32 (0.75)	5.30 (0.62)	5.32 (0.74)	5.27 (0.44)	5.32 (0.61)	5.32 (0.83)	5.30 (0.79)
Maternal education, N (%)									
less than high school	147 (24.83%)	28 (33.33%)	33 (22.15%)	60 (26.32%)	26 (19.85%)	36 (20.93%)	57 (29.23%)	34 (25.56%)	20 (21.74%)
high school	199 (33.61%)	23 (27.38%)	51 (34.23%)	81 (35.53%)	44 (33.59%)	58 (33.72%)	70 (35.90%)	41 (30.83%)	30 (32.61%)
at least some college	246 (41.55%)	33 (39.29%)	65 (43.62%)	87 (38.16%)	61 (46.56%)	78 (45.35%)	68 (34.87%)	58 (43.61%)	42 (45.65%)
Public assistance, N (%)									
No	415 (70.10%)	60 (71.43%)	99 (66.44%)	158 (69.30%)	98 (74.81%)	116 (67.44%)	143 (73.33%)	90 (67.67%)	66 (71.74%)
Yes	177 (29.90%)	24 (28.57%)	50 (33.56%)	70 (30.70%)	33 (25.19%)	56 (32.56%)	52 (26.67%)	43 (32.33%)	26 (28.26%)

Table 2. Adjusted and unadjusted associations of prospective and retrospective ACE score as a continuous and categorical measure with HbA1c.

	Unadjusted regression		**Adjusted regression**	
	Beta coefficient	95% CI	B coefficient	95% CI
Prospectively collected ACEs				
Continuous ACEs score	0.00	(-0.03, 0.03)	0.00	(-0.04, 0.03)
Categorical ACEs Score Level				
ACE score = 0	0	0	0	0
ACE score = 1	0.06	(-0.11, 0.24)	0.05	(-0.13, 0.22)
ACE score = 2-3	0.04	(-0.12, 0.21)	0.02	(-0.14, 0.19)
ACE score = 4+	0.07	(-0.11, 0.25)	0.04	(-0.15, 0.23)
Retrospectively collected ACEs				
Continuous ACEs score	0.00	(-0.02, 0.04)	0.00	(-0.03, 0.03)
Categorical ACEs Score Level				
ACEs = 0	0	0	0	0
ACEs = 1	0.05	(-0.09, 0.18)	0.04	(-0.09. 0.18)
ACEs = 2-3	0.05	(-0.10, 0.20)	0.05	(-0.11, 0.19)
ACEs = 4+	0.03	(-0.13, 0.20)	0.02	(-0.16, 0.19)

Table 2-S1. Adjusted and unadjusted associations of the presence of prospective and retrospective maltreatment ACEs and component maltreatment ACEs with HbA1c.

	Unadjusted regression		Adjusted regression	
	Beta coefficient	95% CI	B coefficient	95% CI
Prospectively collected ACEs				
Any maltreatment ACE present	-0.03	(-0.14, 0.08)	-0.04	(-0.15, 0.07)
Component Maltreatment ACEs				
Emotional abuse	0	(-0.12, 0.12)	-0.01	(-0.13, 0.11)
Physical abuse	-0.07	(-0.18, 0.05)	-0.08	(-0.20, 0.04)
Sexual abuse	0.04	(-0.15, 0.23)	0.02	(-0.17, 0.22)
Neglect	0.01	(-0.11, 0.14)	0.01	(-0.11, 0.14)
Retrospectively collected ACEs				
Any maltreatment ACE present	0.11	(-0.02, 0.23)	0.10	(-0.03, 0.23)
Component Maltreatment ACEs				
Emotional abuse	0.12	(-0.03, 0.27)	0.1	(-0.05, 0.26)
Physical abuse	0.09	(-0.08, 0.27)	0.09	(-0.09, 0.26)
Sexual abuse	0.08	(-0.11, 0.27)	0.09	(-0.11, 0.29)
Neglect	0.01	(-0.30, 0.33)	0.16	(-0.33, 0.32)

Table 2-S2. Adjusted and unadjusted associations of prospective and retrospective ACE score as a continuous and categorical measure with log transformed HbA1c.

	Unadjusted regression		Adjusted regression	
	Beta coefficient	95% CI	B coefficient	95% CI
Prospectively collected ACEs				
Continuous ACEs score	0.00	(-0.02, 0.02)	0.00	(-0.02, 0.02)
Categorical ACEs Score Level				
ACE score = 0	0	0	0	0
ACE score = 1	-0.03	(-0.13, 0.07)	-0.04	(-0.14, 0.06)
ACE score = 2-3	-0.02	(-0.10, 0.08)	-0.01	(-0.11, 0.08)
ACE score = 4+	0	(-0.10, 0.10)	-0.01	(-0.14, 0.06)
Retrospectively collected ACEs				
Continuous ACEs score	0.00	(-0.02, 0.01)	-0.01	(-0.02, 0.01)
Categorical ACEs Score Level				
ACEs = 0	0	0	0	0
ACEs = 1	0.01	(-0.07, 0.09)	0.01	(-0.06, 0.09)
ACEs = 2-3	-0.02	(-0.10, 0.07)	-0.01	(-0.10, 0.07)
ACEs = 4+	-0.02	(-0.11, 0.08)	-0.02	(-0.12, 0.07)

Table 3A. Site-stratified analysis: South Bronx only. Adjusted and unadjusted associations of prospective and retrospective ACE score as a continuous and categorical measure with HbA1c.

	Unadjusted regression		Adjusted regression	
	Beta coefficient	95% CI	B coefficient	95% CI
Prospectively collected ACEs				
Continuous ACEs score	0.00	(-0.06, 0.07)	0.00	(-0.06, 0.07)
Categorical ACEs Score Level				
ACE score = 0	0	0	0	0
ACE score = 1	0.15	(-0.32, 0.62)	0.17	(-0.30, 0.64)
ACE score = 2-3	0.23	(-0.22, 0.67)	0.26	(-0.19, 0.71)
ACE score = 4+	0.24	(-0.22, 0.70)	0.25	(-0.21, 0.72)
Retrospectively collected ACEs				
Continuous ACEs score	0.02	(-0.03, 0.07)	-0.01	(-0.22, 0.20)
Categorical ACEs Score Level				
ACEs = 0	0	0	0	0
ACEs = 1	0.15	(-0.15, 0.44)	0.15	(-0.15, 0.45)
ACEs = 2-3	0.25	(-0.05, 0.56)	0.26	(-0.05, 0.57)
ACEs = 4+	0.16	(-0.16, 0.47)	0.17	(-0.15, 0.49)

Table 3A-S. Site-stratified analysis: South Bronx only. Adjusted and unadjusted associations of the presence of prospective and retrospective maltreatment ACEs and component maltreatment ACEs with HbA1c.

	Unadjusted regression		Adjusted regression	
	Beta coefficient	95% CI	B coefficient	95% CI
Prospectively collected ACEs				
Any maltreatment ACE present	-0.02	(-0.23, 0.19)	-0.04	(-0.26, 0.17)
Component Maltreatment ACEs				
Emotional abuse	0	(-0.21, 0.21)	-0.02	(-0.24, 0.19)
Physical abuse	-0.04	(-0.25, 0.17)	-0.08	(-0.30, 0.14)
Sexual abuse	0.17	(-0.15, 0.49)	0.13	(-0.20, 0.45)
Neglect	0.04	(-0.20, 0.28)	0.05	(-0.19, 0.29)
Retrospectively collected ACEs				
Any maltreatment ACE present	0.25	(0.04, 0.47)	0.26	(0.05, 0.48)
Component Maltreatment ACEs				
Emotional abuse	0.2	(-0.04, 0.45)	0.21	(-0.04, 0.46)
Physical abuse	0.21	(-0.08, 0.50)	0.21	(-0.09, 0.50)
Sexual abuse	0.21	(-0.11, 0.53)	0.23	(-0.09, 0.56)
Neglect	-0.05	(-0.49, 0.40)	-0.05	(-0.50, 0.40)

Table 3B. Site-stratified analysis: Puerto Rico only. Adjusted and unadjusted associations of prospective and retrospective ACE score as a continuous and categorical measure with HbA1c.

	Unadjusted regression		Adjusted regression	
	Beta coefficient	95% CI	B coefficient	95% CI
Prospectively collected ACEs				
Continuous ACEs score	-0.01	(-0.04, 0.02)	-0.01	(-0.04, 0.02)
Categorical ACEs Score Level				
ACE score = 0	0	0	0	0
ACE score = 1	0.05	(-0.11, 0.21)	0.03	(-0.12, 0.19)
ACE score = 2-3	-0.04	(-0.19, 0.10)	-0.04	(-0.18, 0.11)
ACE score = 4+	0.05	(-0.11, 0.21)	-0.04	(-0.21, 0.13)
Retrospectively collected ACEs				
Continuous ACEs score	-0.02	(-0.06, 0.01)	-0.02	(-0.05, 0.02)
Categorical ACEs Score Level				
ACEs = 0	0	0	0	0
ACEs = 1	0	(-0.13, 0.12)	-0.01	(-0.13, 0.12)
ACEs = 2-3	-0.1	(-0.25, 0.04)	-0.09	(-0.23, 0.06)
ACEs = 4+	-0.09	(-0.28, 0.11)	-0.06	(-0.25, 0.13)

Table 3B-S. Site-stratified analysis: Puerto Rico only. Adjusted and unadjusted associations of the presence of prospective and retrospective maltreatment ACEs and component maltreatment ACEs with HbA1c.

	Unadjusted regression		Adjusted regression	
	Beta coefficient	95% CI	B coefficient	95% CI
Prospectively collected ACEs				
Any maltreatment ACE present	-0.05	(-0.16, 0.05)	-0.04	(-0.15, 0.06)
Component Maltreatment ACEs				
Emotional abuse	-0.02	(-0.15, 0.10)	0	(-0.12, 0.13)
Physical abuse	-0.09	(-0.21, 0.02)	-0.06	(-0.18, 0.05)
Sexual abuse	-0.17	(-0.40, 0.05)	-0.18	(-0.41, 0.03)
Neglect	0	(-0.12, 0.12)	0.01	(-0.12, 0.13)
Retrospectively collected ACEs				
Any maltreatment ACE present	-0.11	(-0.25, 0.04)	-0.08	(-0.23, 0.07)
Component Maltreatment ACEs				
Emotional abuse	-0.05	(-0.23, 0.13)	-0.02	(-0.20, 0.16)
Physical abuse	-0.07	(-0.27, 0.12)	-0.05	(-0.24, 0.15)
Sexual abuse	-0.14	(-0.37, 0.09)	-0.13	(-0.36, 0.10)
Neglect	0.13	(-0.43, 0.70)	0.05	(-0.51, 0.62)