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# Journal of Diabetes and Its Complications

journal homepage: WWW.JDCJOURNAL.COM



# The differential impact of adverse childhood experiences in the development of pre-diabetes in a longitudinal cohort of US adults



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#### ARTICLE INFO

Article history: Received 3 July 2018 Received in revised form 17 August 2018 Accepted 9 September 2018 Available online 15 September 2018

Keywords: Adverse childhood experiences Insulin resistance Pre-diabetes Body Mass Index Longitudinal

## ABSTRACT

*Background:* ACEs have a dose-response relationship with diabetes. The relationship between ACEs and prediabetes is not well known and may represent an effective area for prevention efforts.

*Methods:* Data from 1054 participants from two waves of the longitudinal MIDUS study were used. Multivariate general linear regression models assessed the relationship between ACEs and biomarker outcomes. Correlation tests and mediation models investigated the relationship between ACE and pre-diabetes.

*Results:* Individuals reporting ACEs were statistically significantly more likely to have higher BMI (1.13 (0.34–1.92)), higher waist circumference (2.74 (0.72–4.76)), elevated blood fasting insulin levels (2.36 (0.71–4.02)) and higher insulin resistance (HOMA-IR (0.57 (0.08–1.06)). BMI/waist circumference and insulin resistance did not maintain independent relationships with ACEs once HOMA-IR was included in the dichotomized ACE model (p = 0.05 and p = 0.06, respectively), suggesting the relationship between BMI and ACEs may be mediated by insulin resistance.

*Conclusions:* These results represent one of the first studies to examine the differential impact of ACEs on a diverse set of clinical pre-diabetes measures. Findings suggest sexual and physical abuse, and financial strain during childhood are important factors associated with higher risk for pre-diabetes, and should be considered during intervention development.

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#### 1. Introduction

Adverse childhood experiences (ACEs) represent a broad cascade of events occurring before the age of 18, such as abuse, neglect, and family instability, that produce a state of chronic stress throughout childhood and confer risk for poor health in adulthood.<sup>1–3</sup> Well documented as being predictors of adult morbidity and mortality,<sup>4–8</sup> a single endorsement of an ACE significantly increases risk for diabetes in adulthood, with risk increasing as number of reported ACEs increases.<sup>1,9,10</sup> A growing body of evidence supports the relationship between overall ACEs and diabetes,<sup>9,11,12</sup> the cumulative impact of ACEs and diabetes,<sup>13</sup> and the differential impact of specific ACEs and diabetes.<sup>12,14,15</sup> However, less is known about the mechanisms of influence, and how best to intervene to disrupt the impact of ACEs on developing diabetes.<sup>9</sup> The ACE literature suggests that lifestyle, such as physical activity and nutrition,

play an important role in leading to adult morbidity.<sup>16</sup> Specifically, obesity has been suggested as a pathway between ACEs and diabetes.<sup>15</sup> However, this has not been examined in a pre-diabetic population. Additionally, little has been done to provide clinicians with a model for treating patients who have ACEs and are at risk for developing diabetes.<sup>9</sup>

Pre-diabetes is a widely unexplored area in the literature for understanding the impact of ACEs on diabetes and may be an important area of emphasis for intervention in individuals exposed to ACEs.<sup>17</sup> Prediabetes is characterized by elevated glucose levels and is consistent with a Hemoglobin A1c (HbA1c) ranging from 5.7–6.4%, fasting plasma glucose (FPG) of 100 mg/dL to 125 mg/dL, or oral glucose tolerance test (OGTT) of 140 mg/dL to 199 mg/dL.<sup>18</sup> Additional risk factors for prediabetes include being overweight, being over the age of 45, and family history of diabetes.<sup>19</sup> While designation of pre-diabetes does not necessarily determine a future diagnosis of diabetes, risk increases significantly, and little is known as to whether ACEs serve to compound risk for pre-diabetes, ultimately leading to diabetes. Li and colleagues recently examined whether exposure to ACEs significantly predicts insulin sensitivity and glucose intolerance in a sample of adults and found that among adults endorsing ACEs, greater insulin sensitivity was

Conflict of interest: Authors report no conflict of interest.

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demonstrated among those with ACEs compared to those without as measured by an OGTT, however individual ACE categories were not explored.  $^{\rm 17}$ 

As diabetes remains the 7th leading cause of death in the US, representing significant economic burden and hospitalization, <sup>19</sup> two important gaps in the literature warrant greater attention: 1) the biological pathways and the latency period between exposure to ACEs and diabetes development, and 2) the differential impact that individual ACEs have on insulin sensitivity and diabetes related outcomes, i.e. are certain ACEs more detrimental to the development of diabetes compared to others. Addressing these gaps will provide clinicians and researchers with evidence to guide screening and response to ACEs in the healthcare setting. Given the growing focus on trauma informed care, <sup>20</sup> new information is needed to structure screening and treatment for individuals who experiences ACEs. Using a longitudinal cohort of US adults, this study aimed to examine the impact of six ACE categories on the development of pre-diabetes as measured by glycemic control, glucose measures, insulin measures, and obesity markers.

# 2. Material and methods

# 2.1. Sample

Data was obtained from the first two waves of the longitudinal study "Midlife in the United States: A National Longitudinal Study of Health and Well-Being" (MIDUS). MIDUS is funded by the National Institute on Aging and is a publicly available dataset. The first phase of dataset was initiated in 1995–1996. The first wave included 7108 participants between the ages of 25 and 74 who completed telephone interviews and self-administered questionnaires (SAQ). Participants were noninstitutionalized adults from the contiguous US. Surveys included questions that explored a wide range of demographic characteristics, personality traits and behaviors. Participants from the first wave then participated in a second phase of MIDUS from 2002 to 2004 during which biological and neurological data was collected from 1054 participants. Individuals who accepted the invitation for collection of biologic specimens during the second wave spent 24 h in one of three General Clinical Research Centers, received a physical exam, collection of fasting blood samples, and a urinalysis in the morning after an overnight stay. Biological measures collected as part of the MIDUS wave 2 study included height, weight, waist circumference, waist to hip ratio, blood pressure, hemoglobin A1c, blood fasting glucose levels, and blood fasting insulin levels. Details of recruitment strategy, data collection methods, and detailed sample description have been described elsewhere.<sup>23</sup> MIDUS replaced missing values with respondents mean value. When valid responses were not available responses were recorded as missing and, in some cases, responses were imputed for missing data.<sup>24</sup> The Institutional Review Board provides a waiver to conduct this secondary data analysis using publicly available data.

### 2.2. Measures

#### 2.2.1. Adverse childhood experiences

The ACE Study Questionnaire<sup>1</sup> was used to identify measures of adverse events experienced during childhood. The MIDUS study collected information on a number of possible ACEs included in the Felitti et al definition of ACE, as well as questions categorized by the MIDUS investigators as additional ACEs surrounding family instability and financial strain. Therefore, a combined set of ACE categories was created to include: emotional abuse, physical abuse, sexual abuse, substance abuse by parents during childhood, family instability, and financial strain.

ACE categories included:

 Emotional abuse. This item was derived from childhood family background questions in wave 1 and Childhood Trauma Questionnaire (CTQ) completed by participants at the biomarker collection.

- Physical abuse. This item was derived from childhood family background questions and CTQ, as well questions regarding "ever physically assaulted" before age 18 from wave 2 SAQ.
- Sexual abuse. This item was also derived CTQ, and question regarding "ever sexually assaulted" before age 18 from wave 2 SAQ.
- 4) Parental substance abuse. This item referred to substance abuse from a parent during childhood and was derived from childhood background question "what was the main reason father/mother was not working for pay during most of your childhood years? Alcohol or drug abuse"; additional items assessing this category were derived from the CTQ questions "My parents were too drunk or high to take care of me"; Wave 2 phone interview question "lived with alcoholic during childhood" and "Ever parent drank caused problems" and "Ever parent drugs caused problems".
- 5) Family instability. This item was measured using the following questions: "Did you live with both of your biological parents up till you were 16?"; "Who was the male head of your household for most of your childhood"; "ever parents divorced" before age 18 at wave 2 SAQ.
- 6) Financial strain. This item was derived from childhood background questions regarding receipt of welfare; a mother or father having less than a high school education for father; and; report of being 'worse off' than other families.

Each type of ACE was dichotomized. A count of reported ACEs was additionally created for each individual to indicate the number of ACE categories the individual responded positive, as commonly seen in the ACE literature.<sup>1</sup> Finally, a dichotomized ACE variable was created to indicate yes if an individual responded positive to any of the six categories, and no if they responded negative to all six categories.

#### 2.2.2. Biological measures

Biological markers were taken from the second wave of the MIDUS study. The following markers were selected for analysis and categorized based on national recommendations:

- Body mass index (BMI). BMI was categorized as underweight (<18.5), normal (18.5 to <25), overweight (25.0 to <30), obesity (30.0 or higher), and morbid obesity (40 or higher).<sup>25</sup>
- 2) Waist circumference in centimeters. Waist circumference was categorized by sex. For men: low (<94), high (94–<102), and very high (102 and greater. For women: low (<80), high (80–<88), and very high 88 and greater).
- 3) Waist-to-hip ratio. Waist-to-hip ratio was categorized by sex. For men: ideal-very low risk (<0.90), low risk (0.90–0.95), moderate risk (0.95–1.0), and high risk (1.0 and greater). For women: ideal-very low risk (<0.70), low risk (0.70–0.80), moderate risk (0.80–0.85), and high risk (0.85 and greater).
- 4) Systolic and diastolic blood pressure. Blood pressure was categorized as normal (<120/<80 mm Hg), prehypertension (120-< 140/<80 mm Hg), stage 1 hypertension (140-<160 or 90-100 mm Hg), and stage 2 hypertension (≥160 or ≥100 mm Hg).<sup>26</sup>
- 5) Blood fasting glucose. Blood fasting glucose was categorized as normal (<100), pre-diabetes (100–<126), and diabetes (126+).<sup>27</sup>
- Blood fasting Insulin. Blood fasting insulin was categorized as normal (<8), low risk (8–<12), moderate risk (12–<25), and high risk (25+).<sup>27</sup>
- 7) Insulin resistance. Insulin resistance (IR) was categorized as normal (<2), low IR (2–<3), moderate IR (3–<5), and severe IR (5+).<sup>27</sup> Insulin resistance (IR) was determined using the homeostatic model assessment of insulin resistance = HOMA IR calculated as a product of glucose (G0, mg/dL) and insulin (I0,  $\mu$ U/L) divided by the constant 405: HOMAIR = (G0 × I0) / 405. HOMA-IR was a precalculated variable provided in the publicly available dataset. Details of variable calculations can be found through MIDUS ICPSR Codebook.<sup>21,22</sup>

 Blood hemoglobin A1c. Blood hemoglobin A1c (HbA1c) was categorized as normal (<5.7%), pre-diabetes (5.7%-<6.5%), and diabetes (6.5%+).<sup>27</sup>

## 2.2.3. Covariates

Covariates include gender (male, female), age group (34–49, 50–64, 65–84). Race was self-reported and categorized as white, black, and other for the purposes of this analysis Educational level was dichotomized as high school diploma or less, higher education, and household income (<25K, 25–<75K, 75K+). Marital status was dichotomized as married and not married (included separated, divorced, widowed, never married, living with someone).

#### 2.3. Statistical analysis

Multivariate general linear regression models were used for each multiple correlated dependent variable to assess the relationship between ACEs and the dependent variables (biomarker outcomes). Each outcome was investigated relative to three ACE definitions: first treating ACE as dichotomous; second as a continuous count of six ACE situations, grouped it into 0, 1, 2, 3, and 4+; and, third treating ACE as 6 separate category variables: emotional abuse, physical abuse, sexual abuse, substance abuse, family instability and financial strain. Univariate and multivariate GLM models were developed to test the unadjusted and adjusted associations for ACEs on each outcome (BMI, waist circumference, waist to hip ratio, systolic blood pressure, diastolic blood pressure, HbA1c, blood fasting glucose levels, blood fasting insulin levels, HOMA-IR insulin resistance). The multivariate tests of the model included ANOVA test for each outcome, MANOVA test for overall effect (all related outcomes as a vector). Finally, we ran a series of correlation tests and mediation models (following steps outlined by Baron and Kenny for mediation)<sup>28</sup> for outcomes found to be significant after fully adjusting for demographics, to investigate the relationship between ACE and these outcomes with other biologic measures taken into account. All analyses were performed using SAS version 9.4 (SAS Institute, Cary NC) with p < 0.05 was considered statistically significant.

# 3. Results

Table 1 displays sample demographics. The cohort for this study was 1054 individuals who completed the initial wave of MIDUS, as well as the biological measures during the second wave. ACE prevalence was high in this cohort with 68.1% endorsing at least one ACE. The majority of the sample was women (54.7%), and most of the population was aged 50–64 (41.3%). This was a very homogenous sample with approximately 93% being White.

Table 2 displays unadjusted comparisons of biological markers. Mean BMI with no ACEs was  $28.33 \pm 5.36$  (18.63-45.80), with ACEs the mean BMI had a significant increase to  $29.57 \pm 6.26$  (14.99-60.39) p = 0.0017. When examining BMI category by no ACEs versus with ACEs, comparisons were statistically significant, p = 0.0131. Specifically, Obesity increased from 28% among those with no ACEs to 35.4% with ACEs. Similarly, waist circumference category Very High was statistically significant, no ACE was 47.16%, with ACE 56.82%; p = 0.0133. Mean blood fasting insulin levels ( $\mu$ IU/mL) without ACE was 11.09  $\pm$  8.56 (1-74), with ACE 13.57  $\pm$  13.65 (1-231); p = 0.0025. Blood Fasting Insulin Levels category categorized as High Risk (25+) was 6.97% with No ACE, 11.28% with ACE, p = 0.0051. Mean HOMA-IR Insulin Resistance without ACE was 2.92  $\pm$  2.94 (0.04-26.93), with ACE 3.52  $\pm$  3.93 (0.18-53.73); p = 0.0129.

In the adjusted analysis (Table 3), the presence of an ACE was associated with an increase in BMI ( $\beta = 1.13, 95\%$  CI 0.34–1.92), increase in Waist circumference ( $\beta = 2.74, 95\%$  CI 0.72–4.76), increase in Blood Fasting Insulin ( $\beta = 2.36, 95\%$  CI 0.71–4.02) and increase in HOMA-IR Insulin Resistance ( $\beta = 0.57, 95\%$  CI 0.08–1.06). When including categories of ACEs in the model, physical abuse was associated with an

Sample demographics.

Cohort count         1054           Gender         477 (45.26%)           Female         577 (54.74%)           Age in years at interview         55.26 $\pm$ 11.78 (34–84)           Median (IQR)         54 (46–64)           Age group         34–49 yrs           30–64 yrs         355 (41.27%)           65–84 yrs         244 (23.15%)           Back         32 (3.04%)           Other         981 (93.07%)           Black         32 (3.04%)           Other         40 (3.80%)           Education level         High school diploma or less           High school diploma or less         254 (24.10%)           Highs school diploma or less         254 (24.10%)           Highs school diploma or less         254 (24.10%)           Highs school diploma or less         254 (24.10%)           Higher education         797 (75.62%)           Married         738 (70.02%)           Household total income category         62,500 (35,000–101,250)           Household total income category         25k           <25k         159 (15.09%)           25k         159 (15.09%)           25k         258           Stak-<75k         454 (43.07%)           75k+	Variables	
Gender	Cohort count	1054
Male         477 (45.26%)           Female         577 (54.74%)           Age in years at interview         55.26 ± 11.78 (34-84)           Median (IQR)         54 (46-64)           Age group         375 (35.58%)           34-49 yrs         375 (35.58%)           50-64 yrs         435 (41.27%)           65-84 yrs         244 (23.15%)           Race         White           White         981 (93.07%)           Black         32 (3.04%)           Other         40 (3.80%)           Education level         Highs chool diploma or less           High school diploma or less         254 (24.10%)           Higher education         797 (75.62%)           Marital status         Marital status           Marited         738 (70.02%)           Household total income         62.500 (35,000-101,250)           Household total income category         62.500 (35,000-101,250)           Household total income category         225k           25k-         75k           25k-         75k           75k +         419 (39.7%)           Childhood adversity         336 (31.88%)           1         312 (29.60%)           2         233 (30.40%)     <	Gender	
Female         577 (54.74%)           Age in years at interview         55.26 ± 11.78 (34-84)           Median (IQR)         54 (46-64)           Age group         34-49 yrs           30-64 yrs         435 (41.27%)           65-84 yrs         244 (23.15%)           Back         32 (3.04%)           Other         91 (9.3.07%)           Black         32 (3.04%)           Other         40 (3.80%)           Education level         40 (3.80%)           Education level         11           Highs chool diploma or less         254 (24.10%)           Higher education         797 (75.62%)           Marited         788 (70.02%)           Household total income         783 (70.02%)           Household total income category         -25k           <25k < 75k	Male	477 (45.26%)
Age in years at interview       Mean $\pm$ dev (min-max)       55.26 $\pm$ 11.78 (34-84)         Median (IQR)       54.46-64)         Age group       375 (35.58%)         34-49 yrs       375 (35.58%)         50-64 yrs       435 (41.27%)         65-84 yrs       244 (23.15%)         Race       White         White       981 (93.07%)         Black       32 (3.04%)         Other       40 (3.80%)         Education level	Female	577 (54.74%)
Mean $\pm$ dev (min-max)       55.26 $\pm$ 11.78 (34-84)         Median (IQR)       54 (46-64)         Age group       34-49 yrs         34-49 yrs       375 (35.58%)         50-64 yrs       435 (41.27%)         65-84 yrs       244 (23.15%)         Race       White         White       981 (93.07%)         Black       32 (3.04%)         Other       40 (3.80%)         Education level       High school diploma or less         High school diploma or less       254 (24.10%)         Higher education       797 (75.62%)         Married       738 (70.02%)         Household total income       (6,572 $\pm$ 60,409 (0-300,000)         Median (IQR)       62,500 (35.000-101,250)         Household total income category       -25k         <25k	Age in years at interview	
Median (IQR)         54 (46-64)           Age group         375 (35.58%)           34-49 yrs         375 (35.58%)           50-64 yrs         435 (41.27%)           65-84 yrs         244 (23.15%)           Race         White           White         981 (93.07%)           Black         32 (3.04%)           Other         40 (3.80%)           Education level         Higher education           Higher education         797 (75.62%)           Marital status         738 (70.02%)           Household total income         62,500 (35.000-101,250)           Household total income category         25k (24.10%)           <25k	Mean $\pm$ dev (min-max)	55.26 ± 11.78 (34-84)
Age group         34-49 yrs         375 (35.58%)           30-64 yrs         375 (35.58%)           50-64 yrs         244 (23.15%)           Race         White         981 (93.07%)           Black         32 (3.04%)         Other           Other         40 (3.80%)         Education level           High school diploma or less         254 (24.10%)         Higher education           Married         738 (70.02%)         Marital status           Married         738 (70.02%)         Household total income           Mean ± dev (min-max)         76.672 ± 60.409 (0-300.000)         Median (1QR)         62.500 (35.000-101.250)           Household total income category         -         -         -         -           <25k	Median (IQR)	54 (46-64)
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Race           White         981 (93.07%)           Black         32 (3.04%)           Other         40 (3.80%)           Education level	65-84 yrs	244 (23.15%)
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Married         738 (70.02%)           Household total income	Marital status	
Household total income         Mean $\pm$ dev (min-max)       76,672 $\pm$ 60,409 (0-300,000)         Median (IQR)       62,500 (35,000-101,250)         Household total income category       25k         <25k	Married	738 (70.02%)
Mean $\pm$ dev (min-max)       76,672 $\pm$ 60,409 (0-300,000)         Median (IQR)       62,500 (35,000-101,250)         Household total income category       25k $<25k$ 159 (15,09%) $25k-       454 (43,07%)         75k+       419 (39,75%)         Childhood adversity       with ACE         Vith ACE       718 (68,12%)         Childhood adversity count category       336 (31,88%)         1       312 (29,60%)         2       203 (19,26%)         3       104 (9.87%)         4+       99 (9,39%)         Emotional abuse       265 (25,14%)         With physical abuse       212 (20,11%)         Sexual abuse       169 (16.03%)         Substance abuse       253 (24,00%)         With mental illness       0 (0.00%)         With mental illness       0 (0.00%)         Family instability       234 (22,20%)         With family instability       234 (22,20%)   $	Household total income	
Median (IQR)         62,500 (35,000-101,250)           Household total income category         75           <25k	Mean $\pm$ dev (min-max)	76,672 ± 60,409 (0-300,000)
Household total income category $<25k$ 159 (15.09%) $25k-<75k$ 454 (43.07%) $75k+$ 419 (39.75%)Childhood adversity $With ACE$ $Nith ACE$ 718 (68.12%)Childhood adversity count category $0$ $0$ 336 (31.88%) $1$ 312 (29.60%) $2$ 203 (19.26%) $3$ 104 (9.87%) $4+$ 99 (9.39%)Emotional abuse265 (25.14%)Physical abuse212 (20.11%)Sexual abuse169 (16.03%)Substance abuse253 (24.00%)Mith sexual abuse253 (24.00%)Mental illness0 (0.00%)Family instability234 (22.20%)Financial strain234 (22.20%)	Median (IQR)	62,500 (35,000–101,250)
25k       159 (15.09%) $25k$ -<75k	Household total income category	
25k-<75k $454 (43.07%)$ $75k+$ $419 (39.75%)$ Childhood adversity $With ACE$ $With ACE$ $718 (68.12%)$ Childhood adversity count category $0$ $0$ $336 (31.88%)$ $1$ $312 (29.60%)$ $2$ $203 (19.26%)$ $3$ $104 (9.87%)$ $4+$ $99 (9.39%)$ Emotional abuse $265 (25.14%)$ Physical abuse $212 (20.11%)$ Sexual abuse $169 (16.03%)$ Substance abuse $253 (24.00%)$ Mith sexual abuse $253 (24.00%)$ Mental illness $0 (0.00%)$ Family instability $234 (22.20%)$ Financial strain $234 (22.20%)$	<25k	159 (15.09%)
75k+       419 (39.75%)         Childhood adversity $1$ With ACE $718$ (68.12%)         Childhood adversity count category $0$ $0$ $336$ (31.88%) $1$ $312$ (29.60%) $2$ $203$ (19.26%) $3$ $104$ (9.87%) $4+$ $99$ (9.39%)         Emotional abuse $265$ (25.14%)         Physical abuse $265$ (25.14%)         Physical abuse $212$ (20.11%)         Sexual abuse $169$ (16.03%)         Substance abuse $253$ (24.00%)         Mental illness $0$ (0.00%)         Family instability $234$ (22.20%)         Financial strain $234$ (22.20%)	25k-<75k	454 (43.07%)
Childhood adversity       718 (68.12%)         With ACE       718 (68.12%)         Childhood adversity count category       336 (31.88%)         0       336 (31.88%)         1       312 (29.60%)         2       203 (19.26%)         3       104 (9.87%)         4+       99 (9.39%)         Emotional abuse       265 (25.14%)         Physical abuse       212 (20.11%)         Sexual abuse       212 (20.11%)         Sexual abuse       169 (16.03%)         Substance abuse       253 (24.00%)         Mental illness       0 (0.00%)         Family instability       234 (22.20%)         Financial strain       234 (22.20%)	75k+	419 (39.75%)
With ACE     718 (68.12%)       Childhood adversity count category     336 (31.88%)       0     336 (31.88%)       1     312 (29.60%)       2     203 (19.26%)       3     104 (9.87%)       4+     99 (9.39%)       Emotional abuse     265 (25.14%)       Physical abuse     212 (20.11%)       Sexual abuse     169 (16.03%)       Substance abuse     253 (24.00%)       Mental illness     0 (0.00%)       Family instability     234 (22.20%)       Financial strain     234 (22.20%)	Childhood adversity	= 10 (00 100)
0       336 (31.88%)         1       312 (29.60%)         2       203 (19.26%)         3       104 (9.87%)         4+       99 (9.39%)         Emotional abuse       265 (25.14%)         Physical abuse       212 (20.11%)         Sexual abuse       169 (16.03%)         Substance abuse       253 (24.00%)         With mental illness       0 (0.00%)         Family instability       234 (22.20%)         Financial strain       234 (22.20%)	With ACE	718 (68.12%)
0       336 (31.88%)         1       312 (29.60%)         2       203 (19.26%)         3       104 (9.87%)         4+       99 (9.39%)         Emotional abuse       265 (25.14%)         Physical abuse       212 (20.11%)         Sexual abuse       212 (20.11%)         Sexual abuse       169 (16.03%)         Substance abuse       253 (24.00%)         With substance abuse       0 (0.00%)         Family instability       234 (22.20%)         Financial strain       234 (22.20%)	Childhood adversity count category	226 (24 200)
1312 (29,60%)2203 (19,26%)3104 (9,87%)4+99 (9,39%)Emotional abuse265 (25,14%)Physical abuse265 (25,14%)With physical abuse212 (20,11%)Sexual abuse169 (16,03%)Substance abuse169 (16,03%)Substance abuse253 (24,00%)Mental illness0 (0,00%)Family instability234 (22,20%)Financial strain234 (22,20%)	0	336 (31.88%)
2203 (19.26%)3104 (9.87%)4+99 (9.39%)Emotional abuse265 (25.14%)Physical abuse265 (25.14%)With emotional abuse212 (20.11%)Sexual abuse169 (16.03%)Substance abuse169 (16.03%)Substance abuse253 (24.00%)Mental illness0 (0.00%)Family instability234 (22.20%)Financial strain234 (22.20%)	1	312 (29.60%)
5104 (9.37%)4+99 (9.39%)Emotional abuse265 (25.14%)With emotional abuse265 (25.14%)Physical abuse212 (20.11%)Sexual abuse169 (16.03%)Substance abuse169 (16.03%)With substance abuse253 (24.00%)Mental illness0 (0.00%)Family instability234 (22.20%)Financial strain234 (22.20%)	2	203 (19.26%)
4+     59 (9.39%)       Emotional abuse     265 (25.14%)       With emotional abuse     265 (25.14%)       Physical abuse     212 (20.11%)       Sexual abuse     169 (16.03%)       Substance abuse     253 (24.00%)       With substance abuse     253 (24.00%)       Mental illness     0 (0.00%)       Family instability     234 (22.20%)       Financial strain     234 (22.20%)	3	104(9.87%)
EnvironmentWith emotional abuse265 (25.14%)Physical abuse212 (20.11%)Sexual abuse169 (16.03%)Substance abuse169 (16.03%)Substance abuse253 (24.00%)Mental illness0 (0.00%)Family instability234 (22.20%)Financial strain234 (22.20%)	4+ Emotional abuse	99 (9.39%)
With enfortunal abuse265 (25.14%)Physical abuse212 (20.11%)Sexual abuse169 (16.03%)Substance abuse169 (16.03%)With substance abuse253 (24.00%)Mental illness0 (0.00%)Family instability234 (22.20%)Financial strain234 (22.20%)	With emotional abuse	265 (25 14%)
With physical abuse     212 (20.11%)       Sexual abuse     212 (20.11%)       With sexual abuse     169 (16.03%)       Substance abuse     253 (24.00%)       With substance abuse     253 (24.00%)       With mental illness     0 (0.00%)       Family instability     234 (22.20%)       Financial strain     234 (22.20%)	Physical abuse	203 (23.14%)
With physical abuse     212 (20.11%)       Sexual abuse     169 (16.03%)       Substance abuse     253 (24.00%)       With substance abuse     253 (24.00%)       Mental illness     0 (0.00%)       Family instability     234 (22.20%)       Financial strain     234 (22.20%)	Mith physical abuse	212(20.11%)
Section abuse169 (16.03%)With sexual abuse169 (16.03%)Substance abuse253 (24.00%)Mental illness0 (0.00%)Family instability0 (0.00%)Financial strain234 (22.20%)		212 (20.11%)
Substance abuse     105 (1003%)       Substance abuse     253 (24.00%)       Mental illness     0 (0.00%)       Family instability     234 (22.20%)       Financial strain     234 (22.20%)	With sexual abuse	169 (16.03%)
With substance abuse     253 (24.00%)       Mental illness     0 (0.00%)       Family instability     234 (22.20%)       Financial strain     234 (22.20%)	Substance abuse	105 (10.05%)
Mental illness     0 (0.00%)       Family instability     234 (22.20%)       Financial strain     234 (22.20%)	With substance abuse	253 (24 00%)
With mental illness0 (0.00%)Family instability234 (22.20%)With family instability234 (22.20%)Financial strain234 (22.20%)	Mental illness	233 (24.00%)
Family instability With family instability 234 (22.20%) Financial strain	With mental illness	0 (0 00%)
With family instability234 (22.20%)Financial strain	Family instability	0 (0.000)
Financial strain	With family instability	234 (22.20%)
	Financial strain	
With financial strain 341 (32.35%)	With financial strain	341 (32.35%)

increase in waist circumference ( $\beta = 2.78, 95\%$  CI 0.04–5.52) and increase in blood fasting insulin levels ( $\beta = 2.52, 95\%$  CI 0.25–4.79). Sexual Abuse was associated with an increase in BMI ( $\beta = 1.06, \text{CI } 95\%$  0.00–2.12). Financial Strain was associated with an increase in BMI ( $\beta = 0.97, 95\%$  CI 0.15–1.79), Blood Fasting Glucose levels ( $\beta = 3.50, 95\%$  CI 0.05–6.95), Blood Fasting Insulin levels ( $\beta = 2.00, 95\%$  CI 0.27–3.74) and HOMA-IR Insulin Resistance ( $\beta = 0.67, 95\%$  CI 0.15–1.18).

When investigating ACEs by count per individual, those with one ACE compared to those with none was associated with an increase in BMI of 0.97 (95% CI 0.04–1.90) and increase in Waist circumference of 2.62 (95% CI 0.24–5.00). Reporting two ACEs was associated with an increase in Blood Fasting Insulin levels of 3.56 (95% CI 0.34–5.77) and increase in HOMA-IR Insulin Resistance of 0.73 (95% CI 0.07–1.38), but no significant increase with BMI. Reporting three ACEs was associated with an increase in BMI of 1.87 (95% CI 0.54–3.20) and increase in Waist circumference of 3.67 (95% CI 0.28–7.06). Reporting four or more ACEs was associated with an increase in Waist circumference of 3.86 (95% CI 0.32–7.39), an increase in Blood Fasting Insulin levels of 4.13 (95% CI 0.32–7.04), and an increase in HOMA-IR Insulin Resistance of 1.17 (95% CI 0.31–2.03).

### Table 2

Unadjusted comparisons for outcomes by presence of ACE.

Color cont198718918Body mass ince333 ± 53 (18.07.45.80)23.51 ± 50.2 (14.80-31.00)110Modal (0K)33.3 ± 53 (18.07.45.80)23.51 ± 50.2 (14.80-31.00)110Work ince10.00020.000020.0000110Normal version10.00020.0000110110Normal version10.00020.000020.0000110Overveight15.(40.000)20.000020.0000110Wast incenters11.1.1.80020.0000110110Wast incenters11.1.1.80010.000010.0000110Wast incenters11.1.1.80010.000010.0000110Wast incenters11.1.1.80010.000010.0000110Wast incenters11.1.1.80010.000010.0000110Wast incenters11.1.1.80010.000010.0000110Wast incenters11.1.1.80010.000010.0000110Wast incenters11.1.1.80010.000010.0000110Wast incenters11.1.1.80010.000010.0000110Wast incenters11.1.1.800010.000010.0000110Wast incenters11.1.1.800010.000010.0000110Wast incenters11.1.1.800010.000010.0000110Wast incenters10.000010.000010.0000110110Wast incenters11.1.1.800010.000010.0000110110Wast incenters11.1.1.8000 <t< th=""><th></th><th>No ACE</th><th>With ACE</th><th>p-Value</th></t<>		No ACE	With ACE	p-Value
Body maxim idee (nam)U0001700017Marn i eV (nite)-maxi23.3 ± 3.35 (13.83-45.50)20.57 ± 6.26 (14.95-60.39)100131Mart i eV (nite)-maxi23.3 ± 3.35 (13.83-45.50)20.57 ± 6.26 (14.95-60.39)00131Mart i eV (nite)-maxi95 (23.381)100 (23.541)00131Overweight95 (23.381)249 (14.681)00131Overweight94 (26.057)249 (14.681)00131Overweight94 (26.057)249 (14.681)00131Overweight94 (26.057)249 (14.681)00227Mart i eV (nite-maxi)95 (13.63 (00.1-07.0)95 5 (16.67.61.0-26.0)00237Mart i eV (nite-maxi)96 (23.23 (14.0-16.0)95 5 (16.67.61.0-26.0)00237Water i continever84 (23.53)002 (14.97.0)0033Visite In Irat o (com)84 (23.83)002 (23.97.0)00131Water i continever10.84 (13.01.06.61-16.1)009 (10.62-17.2)007Water i continever10.85 (10.10.66-16.1)009 (10.62-17.2)007Water i contine maxi10.84 (13.01.00.61-16.1)009 (10.23.77.0)0031Water i contine maxi10.12 (13.02.30)207 (23.03.1)10.12Water i contine maxi10.12 (13.23.2)207 (23.03.1)10.12Water i contine maxi10.12 (14.20.10.1)10.11 (23.07.0)20.22Mart i eV (nite-maxi)10.12 (14.20.10.1)10.11 (23.07.1)10.12Water i eV (nite-maxi)10.12 (14.20.10.1)10.11 (23.07.1)10.12Water i eV (nite-maxi)10.12 (14.2	Cohort count	336	718	
Media (QR)         23.3 ± 53.6 (18.63-45.80)         29.57 ± 62.6 (14.99.43)           Media (QR)         23.3 ± 53.6 (18.63-45.80)         20.113           Media (QR)         40.05.03)         20.113           Media (QR)         40.05.03)         20.113           Media (QR)         240 (14.58.3)         20.000           Overweight         13.5 (40.000,         240 (15.38.2)         00.000           Media (QR)         24.000,         24.000,         24.000,         00.000,           Media (QR)         30.2 (44.0-106.0)         90.2 (50.63-40.00)         00.000,         00.000,           Media (QR)         30.2 (44.0-106.0)         90.2 (50.63-40.00)         00.000,         00.000,           With Character Category         19.2 (23.83, 10.00, 66-10, 10.000,         00.000, 60.00,         00.000,         00.000,           With Gramma         19.2 (23.83, 10.00, 66-10, 10.00, 60.00,         00.000, 60.00,         00.000,         00.000,           With Gramma         00.8 (0.80.00, 00, 00, 00, 00, 00, 00, 00, 00, 00	Body mass index (exam)			0.0017
Median (LQA)         AL2 (1209-31.47)         AD30 (LA10-323)           Intervapion         (EGA)         (D111)           Undervapion         (EGA)         (D111)           Normal verifier         95 (23.503)         240 (34.683)         (D111)           Obervarie (Intervance)         240 (35.303)         240 (34.683)         (D111)           Morbid doctary         11 (3.283)         240 (34.683)         (D331)           Morbid doctary         55.3 (8.61.00.0)         65.3 (8.61.00.0)         (D331)           Morbid doctary         55.2 (8.61.00.0)         65.3 (8.61.00.0)         (D331)           Low         55.3 (8.61.00.0)         65.3 (8.61.00.0)         (D331)           Low         55.3 (8.61.00.0)         65.3 (8.61.00.0)         (D331)           Low         15.3 (47.163)         (D311)         (D311)           Waits of partial (caun)         15.3 (47.163)         (D312)         (D311)           Waits of partial (caun)         15.3 (47.163)         (D312)         (D312)           Waits of partial (caun)         15.3 (45.315)         10.0 (45.161)         (D312)         (D311)           Waits of partial (caun)         10.3 (22.31)         0.22.10 (23.31)         (D312)         (D311)           Waits of partial (	Mean $\pm$ dev (min-max)	$28.33 \pm 5.36 (18.63 - 45.80)$	$29.57 \pm 6.26 (14.99 - 60.39)$	
Index         4 (0.50x)         4 (0.50x)           Normal vergint         135 (40.30x)         240 (34.68x)         400 (34.68x)           Overvegint         135 (40.30x)         240 (34.68x)         400 (34.68x)           Math in cliniteners         40 (34.68x)         24 (35.8x)         60.28x           Matri in cliniteners         50 (31.5.2 (50.0.16x)         60.28x         60.28x           Watri in cliniteners         92 (24.44-160.1)         95 (36.2-10.0.1)         60.28x           Watri in cliniteners         90 (22.23x)         142 (17.8x)         60.27x           Watri in cliniteners         90 (22.23x)         142 (17.8x)         60.708           Watri in cliniteners         90 (22.23x)         142 (17.8x)         60.708           Watri in cliniteners         91 (22.5x)         143 (32.7x)         60.708           Watri in cliniteners         91 (22.5x)         211 (23.7x)         10.772           Watri in cliniteners         91 (22.5x)         211 (23.7x)         10.722           Watri in cliniteners         91 (22.5x)         211 (23.7x)         10.722           Modari (100, 100)         10 (12.90x)         211 (23.9x)         211 (23.9x)           Modari (100, 100)         10 (12.90x)         211 (23.9x)           <	Median (IQK)	27.21 (24.69–31.47)	28.56 (25.18-32.92)	0.0121
Normal vergint95 (23.30)109 (23.4%)109 (23.4%)Overvegint135 (40.30)24 (36.38)1Obesing44 (20.03)24 (35.38)1Marbid desity13 (32.8%)42 (36.3%)0.037Marbid functional (min-max)83.2 (34.0-106.0)85.5 (66.3-106.0)0.033Iow85.2 (34.0-106.0)85.5 (66.3-106.0)0.033Iow89.2 (32.53)86.5 (66.3-100.0)0.033Iow89.2 (32.53)86.5 (66.2.3)0.033Iow128 (47.16.5)0.05 (20.2.0)0.05Wilk circumference oregory89.5 (32.0-0.0)0.05Wilk circumference oregory0.05 (20.2.0)0.05 (20.2.0)0.05Wilk cargeory0.05 (20.2.0)0.05 (20.2.0)0.05Wilk cargeory0.05 (89.5%)9.6 (22.3%)0.05Wilk cargeory0.05 (89.5%)9.6 (22.3%)0.05Wilk cargeory0.05 (89.5%)9.6 (22.3%)0.05Wilk cargeory0.10 (41.12.0) (5019)1.00 (1014.1)0.202Wilk cargeory10.4 1.12.0 (5519)1.00 (1014.1)0.202Wind carlel BP (carm)10.4 1.12.0 (5519)1.00 (1014.1)0.202Wilk cargeory10.4 1.12.0 (5519)1.00 (1014.1)0.202Modecare BP (carm)10.4 1.12.0 (5519)1.00 (1016.1)0.202Wilk cargeory10.4 1.12.0 (5519)1.00 (1016.1)0.202Modecare BP (carm)10.4 1.42.0 (57.0)1.00 (1016.1)0.202Modecare BP (carm)10.0 ± 8.5 (	Underweight		4 (0 56%)	0.0151
Overwight         15 (44,00)         249 (38,08)         249 (38,08)           Mothi obesity         14 (280)         24 (5.838)         0.0397           Matt in centimeters         0.0397         0.0397           Marka (10,01)         9.51 ± 15.63 (60.0-187.0)         9.51 ± 16.56 (61.0-266.0)         0.0397           Marka (10,01)         95 (23.583)         0.0397         0.0397           Marka (10,01)         95 (23.583)         0.010 (0.65.100.0)         0.010 (0.65.100.0)           With Info (cson)         0.99 (2.02.097.0)         0.65 (0.00.0)         0.6708           Methan (10,01)         0.99 (0.82-0.097.0)         0.6708         0.6708           Methan (10,02)         0.99 (0.82-0.097.0)         0.0708         0.0708           Methan (10,03)         0.12 (1.0537.0)         0.01087.0         0.01087.0           Methan (10,040.0)         0.12 (1.0537.0)         0.0119.0         0.0129	Normal weight	95 (28 36%)	169 (23 54%)	
Obesing"94 (2008)"24 (25.387)	Overweight	135 (40.30%)	249 (34.68%)	
Module design Water in centures1.288)Use 25.0.0287Mean de (Wint-max)95.12 46.106.0197.53 ± 16.95 (6.10-266.010.0287Median (Q6A)95.2 (24.0106.01168 (23.40%)1.013Water commerce categor0.128.233)1.42 (19.40%)0.039Water commerce categor156 (24.716.01168 (23.40%)0.030Water to fina for cam0.89 (0.29.710168 (23.40%)0.0708Water to fina for cam0.89 (0.29.0710.89 (0.20.7100.0708Median (GN)0.89 (0.29.0710.89 (0.20.1000.0708Median (GN)0.89 (0.29.0710.98 (0.29.0710.0708Moderate risk10 (0.25.31)0.07080.0708Moderate risk10 (23.33)0.0708 (0.29.0710.0708Moderate risk12 (25.10)12 (17.141)12 (17.141)12 (17.141)Median (GN)12 (17.141)12 (17.141)12 (17.141)12 (17.141)Median (GN)74 (64.52.01)12 (17.143)12 (17.143)12 (17.143)Median (GN)12 (17.141)12 (17.143)12 (17.143)12 (17.143)Median (GN)12 (17.143)12 (17.143)12 (17.143)12 (17.143)Med	Obesity	94 (28.06%)	254 (35.38%)	
Waits in continuents:0.023Mean 4 ef (min-max)\$513 + 15.63 (60.0-187.0)\$753 + 16.95 (61.0-260.)Median (1Q8)\$52 (40.0-106.0)\$95 (63.21.00.0)Waits it continuents:\$62 (22.53.3)\$162 (10.63.3)Waits it continuents:\$12 (23.53.3)\$162 (10.62.1.72)Waits it continuents:\$85 - 0.10 (0.66-1.61)\$85 (0.63.2.9.7)Waits it continuents:\$85 - 0.10 (0.66-1.61)\$85 (0.00.00.0.7.72)Mean 4 ef (min-max)\$0.89.2.9.7)\$80 (0.620.7)Mean 4 ef (min-max)\$0.89.2.9.7)\$91 (22.3.33.1)Mean 4 ef (min-max)\$12 (18.2.32)\$21 (23.3.3.1)Mean 4 ef (min-max)\$21 (25.53.1)\$13.1.42 + 17.71 (26.1.53.1)Mean 4 ef (min-max)\$21 (25.53.1)\$13.1.42 + 17.71 (26.1.53.1)Median (1Q8)\$21 (25.53.1)\$13.1.42 + 17.71 (26.1.53.1)Median (1Q8)\$22 (25.54.1)\$13.1.42 + 17.71 (26.1.59.1)Median (1Q8)\$21 (25.63.1)\$13.1.42 + 17.71 (26.1.59.1)Median (1Q8)\$22 (25.43.1)\$13.1.42 + 17.71 (26.1.59.1)Median (1Q8)\$23 (11.71.41)\$23 (11.71.41)Median (1Q8)\$12 (11.71.41)\$23 (11.71.41)Median (1Q8)\$12 (11.71.51)\$23 (11.71.61)Median (1Q8)\$12 (11.71.51)\$23 (11.71.61)Median (1Q8)\$12 (11.71.51)\$23 (11.71.51)Median (1Q8)\$13 (11.71.61)\$23 (11.71.61)Median (1Q8)\$13 (11.71.61)\$14 (20.27.51)Median (1Q8)\$13 (11.71.61)\$14 (20.27.51)Mean (1Q8)\$13 (21	Morbid obesity	11 (3.28%)	42 (5.85%)	
Main 4 dw (min-max)         95.3 ± 15.3 (60.0-187.0)         97.53 ± 16.8 (60.0-87.0)           Wait for (nomference category         0.0130           Low         168 (22.030)         42 (12.030)           Wait for (nomference category         168 (22.030)         42 (12.030)           Wait for higr net (nom -max)         0.89 (10.066-161)         0.89 (10.062-1.72)         60.078           Wait for higr net (nom -max)         0.89 (10.020-1.72)         0.0078         0.0078           Median (100)         0.89 (0.020-1.72)         0.0078         0.0078           Median (100)         0.89 (0.020-1.72)         0.0078         0.0078           Median (100)         0.89 (0.020-1.72)         0.0078         0.0078           Median (100)         0.059 (0.021.02)         0.0078         0.0078           Moderat risk         12 (12.0323)         207 (28.31)         0.0078           Median (100)         10.126.2110         11.02 ± 17.140         0.0078           Median (100)         20.17-141         10.14.2 ± 17.71 (0.2-189)         0.0078           Median (100)         74 (68-23)         75 (68-62)         0.0078           Modian (100)         10.9 ± 450 (1-74)         13.0 ± 17.140         0.0025           Stage 1 hypertension         14 (42.005)	Waist in centimeters			0.0287
Media (10k) Waits (1com/lens category)56 (240-106.0)000000000000000000000000000000000	Mean $\pm$ dev (min-max)	95.13 ± 15.63 (60.0-187.0)	97.53 ± 16.95 (61.0-266.0)	
Mait cruiniterine category00133low98 (23-238)168 (23-403)142 (19.783)High79 (23-586)462 (15.873)462 (15.873)Wery high158 (47.183)088 (65.623)0.8708Werk intit (csam)158 (47.183)0.88 (0.82-0.97)0.88 (0.82-0.97)Wilk orispoy0.89 (0.82-0.97)0.88 (0.82-0.97)0.88 (0.82-0.97)Wilk orispoy0.89 (0.82-0.97)0.88 (0.82-0.97)0.88 (0.82-0.97)Wilk orispoy0.9 (0.835)50 (8.233)0.0678local-very low risk10 (16.233)207 (28.383)1.0000Low risk11 (26.238)207 (28.383)1.0000Average of systolic BYs (exam)13.14 ± 18.20 (85-191)13.14 ± 17.17 (82-189)1.0000Median (100)128 (117-141)13.14 ± 17.162-189)1.00001.0000Average of distolic BYs (exam)128 (117-141)13.14 ± 10.15 (49-114)1.0000Median (100)128 (117-141)13.14 ± 10.15 (49-114)1.00001.0000Median (100)74 (4.969)25 (11.40001.00001.0000Soge of distolic BYs (exam)14 (4.2000)1.00001.00001.0000Soge of distolic Bys (exam)1.00001.00001.00001.0000Soge of distolic Bys (exam)1.00001.00001.00001.0000Soge of distolic Bys (exam)1.00001.00001.00001.0000Soge of distolic Bys (exam)1.00001.00001.00001.0000Soge of distolic Bys (exam)1.00001.	Median (IQR)	95.2 (84.0-106.0)	96.5 (86.8–108.0)	
Date         Starting         Starting         Starting         Starting           Way halp         158 (27,06)         408 (56,25)         0.07,08           Waist thip ratio (can)         0.89 ± 0.10 (0.62-1.72)         0.89 ± 0.10 (0.62-1.72)         0.89 ± 0.10 (0.62-1.72)           Mediatin (QR)         0.89 ± 0.10 (0.62-1.72)         0.89 (0.82-0.97)         0.89 (0.82-0.97)         0.89 (0.82-0.97)           Mediatin (QR)         0.89 (0.898)         50 (6.23)         0.89 (0.82-0.97)         0.89 (0.82-0.97)           Mediatin (QR)         12 (3.52,33)         207 (28,33)         0.89 (0.82-0.97)         0.89 (0.82-0.97)           Mediatin (QR)         12 (3.52,33)         207 (28,33)         0.89 (0.82-0.97)         0.89 (0.82-0.97)           Mediatin (QR)         92 (27,543)         211 (1.52,33)         0.97 (28,33)         0.97 (28,33)           Mediatin (QR)         130 (4 ± 18,20 (55-191)         134 (4 ± 13.20 (55-191)         0.97 (28,43)         0.97 (28,43)           Mediatin (QR)         12 (10,49-110)         10 (9-10)         75 (68-62)         0.247 (78,49)           Normal blood pressure         74 (68-62)         177 (46,653)         0.97 (28,43)         0.97 (28,43)           Starge 1 hypertension         73 (17,98)         10 (9-16,90)         0.97 (28,49)         0.97 (28,49)<	Waist circumference category	00 (20 25%)	169 (22.40%)	0.0133
Very high         158 (47/16)         168 (56.82)         0.65708           Weist to lip ratio (xm)         0.89 ± 0.10 (0.65-1.51)         0.89 (0.82-0.97)         0.65708           Mena ± dev (min-max)         0.89 ± 0.10 (0.65-1.51)         0.89 (0.82-0.97)         0.0578           Media (righ)         0.89 (0.82-0.97)         0.89 (0.82-0.97)         0.0578           Mich createry         0.90 (0.82-0.97)         0.89 (0.82-0.97)         0.0578           Media (righ)         30 (3.938)         20 (3.238)         0.80 (0.82-0.97)         0.0578           Media (righ)         91 (27.253)         211 (28.353)         0.2117         0.2117           Average of systolic B/s (exam)         11 (24.3573)         22417         0.2417           Median (IQR)         128 (17-141)         131 (19-144)         0.322           Median (IQR)         74.64 ± 10.19 (49-107)         75.31 ± 10.15 (48-114)         0.2477           Median (IQR)         74.64 ± 10.19 (49-107)         75.31 ± 10.15 (48-114)         0.2477           Median (IQR)         74.64 ± 10.19 (49-107)         75.31 ± 10.15 (48-114)         0.2477           Median (IQR)         74.64 ± 10.19 (49-107)         75.31 ± 10.15 (48-114)         0.0251           Sigar 1 provension         74 (68-82)         77 (64.53)	LOW High	98 (29.25%) 70 (23.58%)	108 (23.40%)	
Wate to bin ratio (exam)         0.6 (Files)         0.6 (Files)         0.6 (0.62-1.52)         0.6 (0.82-0.57)           Mein di (QR)         0.89 (0.82-0.57)         0.89 (0.82-0.57)         0.80 (0.82-0.57)         0.0678           Milk category         0.0678         0.89 (0.82-0.57)         0.89 (0.82-0.57)         0.0678           Media (VQR)         121 (36.23%)         907 (28.83%)         0.0678           Moderate risk         121 (36.23%)         207 (28.83%)         0.0678           Media (VQR)         127.25%)         211 (33.57%)         0.2317           Meat de (vinim-max)         13.04 ± 18.20 (85-191)         13.14 ± 17.71 (82-189)         0.3242           Median (QR)         128 (17-141)         13.14 ± 17.71 (82-189)         0.3242           Median (QR)         74 (68-82)         75 (68-82)         0.2377           Normal blood pressure         75 (28.928)         77 (24.653)         0.0251           Prehypertension         14 (42.03%)         26 (42.33)         0.0251           Stage 1 hypertension         73 (21.79%)         13.14 (27.03)         0.0251           Stage 1 hypertension         13 (41.823)         13 (42.233)         0.0251           Stage 1 hypertension         13 (41.823)         13 (41.33,53)         0.0251	Very high	158 (47 16%)	408 (56 82%)	
meta         tex         meta         tex         meta           Medan (100)         0.89 (0.82-0.97)         0.89 (0.82-0.97)         0.80 (0.82-0.97)           Wilk category         0.89 (0.82-0.97)         0.80 (0.82-0.97)         0.80 (0.82-0.97)           Milk category         12 (36.23%)         207 (32.33%)         1           Low risk         12 (36.23%)         201 (23.37%)         201 (23.37%)           Average of systolic RFs (exam)         0.2177         0.2187           Medan (100)         128 (17-14)         130 (119-144)         0.2187           Average of systolic RFs (exam)         75.51 ± 10.15 (48-114)         0.2477           Mead = dev (min-max)         130 (14 ± 18.20 (85-191)         132 (15 (48-114))         0.2477           Mead = dev (min-max)         75.13 ± 10.15 (48-114)         0.2477         0.2477           Mead = dev (min-max)         74 (68-82)         75.51 ± 10.15 (48-114)         0.2477           Mead = dev (min-max)         14 (42.03%)         296 (41.23%)         0.2477           Normal blood pressure         75.11 ± 10.5 (16-211)         0.025           Sage 1 hypertension         24 (7.165)         10.57 ± 13.5 (1-231)         0.025           Median (100)         20.55 (1-74)         13.57 ± 13.5 (1-231) <td< td=""><td>Waist to hip ratio (exam)</td><td>156 (11.16.6)</td><td>100 (30.02%)</td><td>0.6708</td></td<>	Waist to hip ratio (exam)	156 (11.16.6)	100 (30.02%)	0.6708
Median (108)         0.89 (0.82-0.97)         0.6678           WHR category         0.6678           Ideal-very low risk         30 (8.983)         99 (0.82-0.97)           Ideal-very low risk         121 (36.23%)         207 (28.83%)           Moderate risk         91 (27.25%)         211 (35.37%)         211 (35.37%)           Moderate risk         92 (27.54%)         214 (33.57%)         28.17           Average of dischole B*s (cram)         13.14 ± 17.71 (82-189)         23.42           Average of dischole B*s (cram)         53.14 ± 17.71 (82-189)         23.42           Average of dischole B*s (cram)         73.14 ± 18.20 (85-191)         13.14 ± 17.71 (82-189)         23.42           Median (108)         126 (117-141)         13.14 ± 17.71 (82-189)         23.42           Median (108)         74 (64 ± 10.19 (49-107)         75 (68-82)         24.71           Median (108)         74 (64 ± 10.19 (49-107)         13.14 ± 17.71 (82-189)         24.717           Normal biolod pressure         70 (28.96%)         71 (74.65%)         24.717           Normal biolod pressure         72 (82.96%)         71 (74.65%)         24.717           Stage 1 hypertension         14 (42.098)         26.758         24.718         24.718           Stage 1 hypertension	Mean $\pm$ dev (min-max)	$0.89 \pm 0.10  (0.66 - 1.61)$	0.89 ± 0.10 (0.62–1.72)	
Wilk category0.06 (SMSX)59 (8.22S)0.007 (SMS)I deal-very low risk121 (36.23X)027 (28.33X)112 (35.73X)Moderate risk91 (27.25K)121 (23.57X)211 (23.57X)High risk92 (27.54X)211 (23.57X)22.51XMetar of Systolic BP (exam)130.14 ± 18.20 (Sb-11)1131.42 ± 17.71 (32-189)12.51XMetan d (QR)128 (171-741)130 (119-144)30.112 ± 17.71 (32-189)32.51XMetan d (QR)128 (171-741)130 (119-140)13.014 ± 17.71 (32-189)32.51XMetan d (QR)128 (171-741)130 (119-140)32.51X32.51XMetan d (QR)75.31 ± 10.15 (48-114)13.71X32.51X32.51XModian (QR)76 (8-82)25.51X32.51X32.51X32.51XStage 1 hypertension71 (23.95K)13.57 ± 13.55 (1-231)32.51X32.51X32.51XStage 1 hypertension11.09 ± 8.56 (1-74)13.57 ± 13.55 (1-231)32.51X32.51X32.51XMedian (QR)9 (5-14)10.51X32.51X <td>Median (IQR)</td> <td>0.89 (0.82–0.97)</td> <td>0.89 (0.82-0.97)</td> <td></td>	Median (IQR)	0.89 (0.82–0.97)	0.89 (0.82-0.97)	
Ideal-very low risk30 (898)59 (822s)Low risk12 (3623x)207 (28.33x)	WHR category			0.0678
Low risk         121 (36.23%)         207 (28.33%)           Moderate risk         91 (27.25%)         211 (29.39%)           High risk         202 (75.44%)         211 (29.39%)           Average of systolic BPS (exam)         0.217         0.217           Median (IQR)         120 (157-141)         130 (119-144)         0.237           Median (IQR)         74 (64 ± 10.19 (49-107)         75.31 ± 10.15 (48-114)         0.247           Median (IQR)         74 (66-82)         75 (68-82)         0.247           Median (IQR)         76 (28.96%)         77 (24.65%)         0.247           Stage 1 hypertension         141 (42.05%)         266 (41.23%)         0.0025           Stage 1 hypertension         141 (42.05%)         266 (41.23%)         0.0025           Stage 1 hypertension         141 (42.05%)         267 (41.23%)         0.0025           Stage 1 hypertension         141 (42.05%)         267 (41.23%)         0.0025           Stage 1 hypertension         11.09 ± 8.56 (1-74)         10 (6-16)         0.0025           Moderate risk (1225)         84 (24.83%)         201 (24.44%)         0.0129           Low risk (221)         136 (41.82%)         230 (14.24.28)         0.0129           Moderate risk (1225)         84 (24.53)	Ideal-very low risk	30 (8.98%)	59 (8.22%)	
Moderate risk         91 (27,25%)         21 (23,39%)           High risk         92 (27,54%)         21 (23,57%)         20 (21,77%)           Average of disatolic Brs (exam)         131.42 ± 17.71 (82-189)         20 (11,71,11%)           Average of disatolic Brs (exam)         131.42 ± 17.71 (82-189)         20 (11,71,11%)           Average of disatolic Brs (exam)         0.324 ± 10.01 (94-107)         75.31 ± 10.15 (48-114)         20 (21,71,71,11%)           Median (IQR)         74 (64 ± 10.19 (49-107)         75.18 ± 10.15 (48-114)         20 (21,71,71,11%)           Median (IQR)         74 (64 ± 10.19 (49-107)         75.18 ± 10.15 (48-114)         20 (21,71,71,11%)           Normal blood pressure         77 (28-65%)         75 (68-82)         20 (21,71,71,11%)           Normal blood pressure         70 (28-65%)         10 (21,723,11%)         20 (21,71,71,11%)           Stage 1 hypertension         73 (21,79%)         194 (270,20%)         20 (21,71,71,11%)           Stage 1 hypertension         73 (21,79%)         194 (270,20%)         20 (21,71,71,11%)           Median (IQR)         91 (12,91,71,11%)         10 (5-16)         20 (21,71,71,11%)           Blood Asting insulin levels attegory         10 (5-16,11%)         10 (5,11,11%)         20 (21,21,11,11%)           Normal (24)         10 (21,91,11,11,11,11%)	Low risk	121 (36.23%)	207 (28.83%)	
Hign 1986 $92 (27, 943)$ $24 (33, 5/3)$ Average of systolic BPs (exam)0.28170.2817Median (IQR)120 (117-141)130 (119-144)0.2812Average of diastolic BPs (exam)75.31 ± 0.15 (48-114)0.2812Median (IQR)76.68 + 2075.31 ± 10.15 (48-114)0.2812Median (IQR)76.89 + 2075.31 ± 10.15 (48-114)0.2812Blood pressure0.2895(3)75.01 ± 0.12 (48-52)0.2812Normal blood pressure70 (28.968,1)92.64 (4.233)0.2812Stage 1 hypertension24 (7.163)94 (4.70.23)0.0025Stage 1 hypertension27 (7.163)14 (4.209)0.0015Blood fasting insulin levels µU/mL15.72 + 1.365 (1-231)0.0025Mean ± dev (min-max)1.09 ± 8.56 (1-74)10.66-160.0015Modian (IOR)9 (5-14)10.66-160.0015Iood rasting insulin levels µU/mL55.05 (55.63)18 (12.228)0.0015Modian (IOR)9 (5.5763)18 (12.228)0.0129Ioom rask (3 - 2.12)84 (25.453)230 (12.42.428)0.0129Ioom rask (3 - 2.12)84 (25.453)230 (12.42.428)0.0129Ioom rask (40,12)2.01 (11.9-3.56)2.10 (11.633)0.0129Insulin resistance9.92 ± 2.94 (0.04-2.693)3.25 ± 3.93 (1.8-5.37.31)0.0129Ioom rask (40,12)2.01 (11.9-3.56)2.29 (12.42.42.81)0.0129Ioom rask (41.2-25)62 (42.75%)2.10 (11.63.%)0.0129Ioom rask (41.2-3)2.02 (12.82.%)2.30 (14	Moderate risk	91 (27.25%)	211 (29.39%)	
Average of system is reasonable for the system is a sys	High risk	92 (27.54%)	241 (33.57%)	0.2017
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Moan + doy (min max)	$120.14 \pm 19.20$ (95.101)	$121.42 \pm 17.71.(92.190)$	0.2817
Average of diastolic BPs (exam)Def (11 - 11)0.3242Mean $\pm$ der (min-max)74.64 $\pm$ 10.19 (49-107)75.31 $\pm$ 10.15 (48-114)0.3242Median (UQN)74.668-82)75 (68-82)0.2477Normal blood pressure97 (28.96%)177 (24.65%)0.2477Normal blood pressure97 (28.96%)177 (24.65%)0.2477Normal blood pressure97 (28.96%)194 (27.02%)296 (41.23%)Stage 1 hypetrension32 (17.9%)194 (27.02%)58 (27.0%)Stage 1 hypetrension24 (7.16%)13.57 $\pm$ 13.65 (1-231)0.0025Median (UQN)9 (5-14)13.57 $\pm$ 13.65 (1-231)0.0025Median (UQN)9 (5-14)13.57 $\pm$ 13.65 (1-231)0.0051Normal (-8)138 (41.82%)230 (32.4%)0.0051Low risk (8-12)85 (25.76%)158 (22.28%)0.0051Low risk (8-12)85 (25.76%)101.128%)0.0025Median (UQN)2.92 $\pm$ 2.94 (0.04-26.93)3.52 $\pm$ 3.93 (0.18-53.73)0.1128%HOMA-R1: Insulin resistance0.0040.1128%0.0051Normal (-2)156 (47.27%)288 (40.62%)0.0046Normal (-2,-3)72 (1.82%)130 (18.34%)0.0070Median (UQR)5.99 $\pm$ 0.94 (4.70-15.20)5.99 $\pm$ 0.90 (3.80-13.40)0.9670Median (UQR)5.99 $\pm$ 0.94 (4.70-15.20)5.99 $\pm$ 0.90 (3.80-13.40)0.9670Median (UQR)5.99 $\pm$ 0.94 (4.70-15.20)5.99 $\pm$ 0.90 (3.80-13.40)0.9670Median (UQR)5.99 $\pm$ 0.94 (4.70-15.20)5.99 $\pm$ 0.90 (3.80	Median $\pm$ dev (mm-max)	$130.14 \pm 18.20 (83 - 151)$ 128 (117 - 141)	$131.42 \pm 17.71(82-185)$ 130 (119–144)	
Media (QR)         764 ± 10.19 (49-107)         75.31 ± 10.15 (48-114)           Median (QR)         74 (68-82)         75 (68-82)           Blood pressure         0.2477           Normal blood pressure         97 (28.96%)         177 (24.65%)           Prehypertension         141 (42.09%)         296 (41.23%)           Stage 1 hypertension         73 (21.79%)         194 (27.02%)           Stage 1 hypertension         24 (7.16%)         1100 (6-16)           Blood fasting insulin levels µU/mL         13.57 ± 13.65 (1-231)         0.0051           Median (QR)         9 (5-14)         10 (6-16)         0.0051           Blood fasting insulin levels ategory         100 (6-16)         0.0051           Normal (-8)         138 (41.82%)         241 (33.99%)         0.0051           Low risk (8-r12)         85 (25.76%)         158 (22.88%)         0.0051           Moderate risk (12-r25)         84 (25.45%)         23 (03.2.44%)         10129           Median (QR)         252 ± 2.94 (0.04-26.53)         35.2 ± 3.39 (0.18.5.5.73)         0.129           Median (QR)         126 (47.27%)         28 (40.62%)         0.0496           Normal (-2)         150 (21.16%)         0.0496           Normal (-2,7%)         127 (12.82%)         150 (21.16%) <td>Average of diastolic BPs (exam)</td> <td></td> <td></td> <td>0.3242</td>	Average of diastolic BPs (exam)			0.3242
Median (QR)         74 (68-82)         75 (68-82)           Blood pressure         74 (68-82)         75 (68-82)           Normal blood pressure         97 (28.96%)         177 (24.65%)         0.2477           Normal blood pressure         97 (28.96%)         177 (24.65%)         0.2477           Prehypertension         141 (42.00%)         296 (41.23%)         177 (24.65%)         0.278           Stage 1 hypertension         210 (75%)         194 (27.02%)         177 (24.65%)         0.0025           Stage 1 hypertension         210 (75%)         100 (75%)         100 (75%)         0.0025           Blood fasting insulin levels (ategory         0.0025         0.0025         0.0025           Median (QR)         18 (41.82%)         241 (33.99%)         0.0015           Low risk (8-12)         85 (25.76%)         158 (22.28%)         0.0015           Moderate risk (1225)         84 (25.45%)         230 (24.44%)         0.0129           Median (QR)         2.92 ± 2.94 (0.04-26.93)         3.25 ± 3.93 (0.18-53.73)         0.0129           Median (QR)         2.92 ± 2.94 (0.04-26.93)         2.39 (1.04-2.81)         0.0129           Median (QR)         100 (1.19-3.56)         2.39 (1.04-2.81)         0.0129           Median (QR)         100 (1.1	Mean $\pm$ dev (min-max)	74.64 ± 10.19 (49–107)	75.31 ± 10.15 (48-114)	
Blood pressure0.2477Normal blood pressure97 (28.96%)177 (24.65%)Prehypertension73 (21.79%)296 (41.23%)Stage 1 hypertension24 (7.16%)194 (27.02%)Stage 1 hypertension24 (7.16%)100%)Blood fasting insulin levels µll/mL1.0.9 ± 8.56 (1-74)13.57 ± 13.65 (1-231)Median (0R)1.0.9 ± 8.56 (1-74)13.57 ± 13.65 (1-231)0.0025Blood fasting insulin levels µll/mL0.00160.00160.0016Median (0R)138 (41.82%)241 (33.99%)0.0016Blood fasting insulin levels µll/mL0.00160.00160.0016Normal (-8)23 (52.76%)320 (22.44%)0.0019I hypertension23 (52.76%)320 (22.44%)0.0019Moderat risk (12-<25)	Median (IQR)	74 (68-82)	75 (68–82)	
Normal blood pressure         97 (28,96%)         177 (24,65%)           Prehypertension         141 (42,09%)         296 (41,23%)         128           Stage 1 hypertension         73 (21,75%)         194 (27,02%)         128           Stage 2 hypertension         24 (7,16%)         151 (7,10%)         0.0025           Blood fasting insulin levels µlU/ml.         1.09 ± 8.56 (1-74)         13.57 ± 13.65 (1-231)         0.0025           Median (UQR)         9 (5-14)         10 (6-16)         0.0051           Normal (-8)         138 (41.82%)         241 (33.99%)         0.0051           Normal (-8)         138 (41.82%)         203 (32.44%)         0.0051           Idev risk (812)         84 (25.45%)         203 (32.44%)         0.0129           Moderate risk (1225)         84 (25.45%)         203 (12.45%)         0.0129           Moderate risk (1225)         84 (26.45%)         203 (12.45%)         0.0129           Median (UQR)         2.09 ± 2.94 (0.04-26.93)         3.52 ± 3.93 (0.18-53.73)         0.019           Median (UQR)         2.06 (47.27%)         203 (1.42-4.28)         0.0496           Median (UQR)         2.06 (45.07%)         130 (13.83%)         2.39 (1.42-4.28)         0.0496           Invulin resistance         6.2 (18.79%)	Blood pressure			0.2477
Prehypertension         141 (42.0%)         296 (41.23%)           Stage 1 hypertension         73 (21.79%)         194 (27.02%)           Stage 1 hypertension         24 (7.16%)         51 (7.10%)           Blood fasting insulin levels µU/mL         1.57 ± 13.65 (1-231)         0.0051           Mean ± dev (min-max)         1.09 ± 8.56 (1-74)         13.57 ± 13.65 (1-231)         0.0051           Blood fasting insulin levels category         0.0051         0.0051         0.0051           Normal (-8)         138 (1.82%)         241 (33.99%)         0.0051           Low risk (812)         85 (25.76%)         158 (22.28%)         0.0051           Moderate risk (1225)         84 (25.45%)         201 (32.44%)         0.0051           Modaret risk (1225)         84 (25.45%)         30 (12.48%)         0.0129           Mean ± dev (min-max)         2.92 ± 2.94 (0.04-26.93)         3.52 ± 3.93 (0.18-53.73)         0.0129           Mean ± dev (min-max)         2.92 ± 2.94 (0.04-26.93)         3.59 ± 3.93 (0.18-53.73)         0.0129           Insulin resistance categor         0.011.93-35         0.01 (1.93.35%)         0.01 (8.34%)         0.0129           Normal (-2)         156 (47.27%)         28 (40.62%)         0.01 (8.34%)         0.0129           Insulin resistance category </td <td>Normal blood pressure</td> <td>97 (28.96%)</td> <td>177 (24.65%)</td> <td></td>	Normal blood pressure	97 (28.96%)	177 (24.65%)	
Stage 1 hypertension         73 (21,79%)         194 (27,02%)           Blood fasting insulin levels µlU/mL         0.0025           Mean ± dev (min-max)         11.09 ± 8.56 (1-74)         13.57 ± 13.65 (1-231)           Median (1QR)         9 (5-14)         10 (6-16)           Blood fasting insulin levels category         0.0051           Normal (<8)	Prehypertension	141 (42.09%)	296 (41.23%)	
Stage 2 hypertension         24 (1.6k)         0.0025           Meah ± dev (min-max)         11.09 ± 8.56 (1-74)         13.57 ± 13.65 (1-231)         0.0025           Median (UQR)         9 (5-14)         10 (6-16)         0.0051           Blood fasting insulin levels category         0.0051         0.0051           Normal (<8)	Stage 1 hypertension	73 (21.79%)	194 (27.02%)	
block lasting insumit evers jut/init.         0.0025           Mean ± dev (min-max)         11.09 ± 8.56 (1-74)         13.57 ± 13.65 (1-231)         0.0051           Medna (10R)         9 (5-14)         10 (6-16)         0.0051           Blood fasting insulin levels category         241 (33.99%)         0.0051           Normal (<3)	Stage 2 hypertension	24 (7.16%)	51 (7.10%)	0.0025
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Mean $\pm dev(min-max)$	$11.09 \pm 8.56(1-74)$	$1357 \pm 1365(1-231)$	0.0025
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Median (IOR)	9(5-14)	10.6-16	
Normal (-3)138 (41.82%)241 (33.99%)Low risk (812)85 (25.76%)156 (22.28%)Moderate risk (1225)84 (25.45%)230 (32.44%)High risk (25+)23 (6.97%)80 (11.28%)HOM-AR: Insulin resistance0.0129Mean $\pm$ dev (min-max)2.92 $\pm$ 2.94 (0.04-26.93)3.52 $\pm$ 3.93 (0.18-53.73)Median (1QR)2.10 (1.19-3.56)2.39 (1.42-4.28)Insulin resistance category0.0496Normal (-2)156 (47.27%)288 (40.62%)Low IR (23)72 (21.82%)150 (21.16%)Moderate IR (35)62 (18.79%)141 (19.89%)Severe IR (5+)40 (12.12%)130 (18.34%)Blood hemoglobin (HbA1c) (%)0.9670Mean $\pm$ dev (min-max)5.99 $\pm$ 0.94 (4.70-15.20)5.99 $\pm$ 0.03 (3.80-13.40)Mean $\pm$ dev (min-max)5.99 $\pm$ 0.94 (4.70-15.20)5.99 $\pm$ 0.03 (3.80-13.40)Median (1QR)5.80 (5.60-6.15)5.80 (5.60-6.12)Blood hemoglobin (HbA1C) category0.9472Normal (-5.7%)111 (33.33%)243 (34.37%)Prediabets (6.5%+)31 (12.51%)90 (12.73%)Blood fasting glucose levels mg/dL0.9114Mean $\pm$ dev (min-max)60 (90-104)96 (89-104)Mean $\pm$ dev (min-max)100.30 $\pm$ 24.96 (5-377)100.48 $\pm$ 24.72 (67-418)Median (QR)60 (90-104)96 (89-104)Blood fasting glucose levels mg/dL0.3497Mean $\pm$ dev (min-max)101.30 $\pm$ 24.96 (5-377)100.48 $\pm$ 24.72 (67-418)Median (QR)60 (90-104)96 (89-104) <td>Blood fasting insulin levels category</td> <td></td> <td></td> <td>0.0051</td>	Blood fasting insulin levels category			0.0051
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Normal (<8)	138 (41.82%)	241 (33.99%)	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Low risk (8–<12)	85 (25.76%)	158 (22.28%)	
High risk (25+)23 (6.97%)80 (11.28%)HOMA-IR: Insulin resistance0.0129Mean $\pm$ dev (min-max)2.92 $\pm$ 2.94 (0.04–26.93) $5.2 \pm$ 3.93 (0.18–53.73)Median (1QR)2.10 (1.19–3.56)2.39 (1.42–4.28)Insulin resistance category0.0496Normal (<2)	Moderate risk (12–<25)	84 (25.45%)	230 (32.44%)	
HOM-IR: Insulin resistance       0.0129         Mean ± dev (min-max)       2.92 ± 2.94 (0.04-26.93)       3.52 ± 3.93 (0.18-53.73)         Median (IQR)       2.10 (1.19-3.56)       2.39 (1.42-4.28)         Insulin resistance category       0.0496         Normal (<2)	High risk (25+)	23 (6.97%)	80 (11.28%)	
$\begin{array}{llllllllllllllllllllllllllllllllllll$	HOMA-IR: Insulin resistance	2.02 + 2.04 (0.04 20.02)		0.0129
$\begin{tabular}{ c c c } & 2.50 (1.19-5.36) & 2.59 (1.42-4.28) & 0.0496 &$	Median $\pm$ dev (min-max)	$2.92 \pm 2.94 (0.04 - 26.93)$	$3.52 \pm 3.93 (0.18 - 53.73)$	
Normal (-2)       156 (47.27%)       288 (40.62%)         Low IR (23)       72 (21.82%)       150 (21.16%)         Moderate IR (35)       62 (18.79%)       141 (19.89%)         Severe IR (5+)       40 (12.12%)       130 (18.34%)         Blood hemoglobin (HbA1c) (%)	Insulin resistance category	2.10 (1.19-5.50)	2.39 (1.42-4.28)	0.0496
Instant (2-3)72 (21.82%)150 (21.16%)Iow IR (2-<3)	Normal (<2)	156 (47.27%)	288 (40.62%)	0.0 150
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Low IR (2–<3)	72 (21.82%)	150 (21.16%)	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Moderate IR (3-<5)	62 (18.79%)	141 (19.89%)	
Blood hemoglobin (HbA1c) (%)         0.9670           Mean ± dev (min-max)         5.99 ± 0.94 (4.70-15.20)         5.99 ± 0.90 (3.80-13.40)           Median (IQR)         5.80 (5.60-6.15)         5.99 ± 0.90 (3.80-13.40)           Blood hemoglobin (HbA1C) category         0.9472           Normal (<5.7%)	Severe IR (5+)	40 (12.12%)	130 (18.34%)	
	Blood hemoglobin (HbA1c) (%)			0.9670
Median (IQR)5.80 (5.60-6.15)5.80 (5.60-6.12)Blood hemoglobin (HbA1C) category0.9472Normal (<5.7%)	Mean $\pm$ dev (min-max)	$5.99 \pm 0.94  (4.70  15.20)$	$5.99 \pm 0.90 \ (3.80 - 13.40)$	
Blood hemoglobin (HbA1C) category         0.9472           Normal (<5.7%)	Median (IQR)	5.80 (5.60-6.15)	5.80 (5.60-6.12)	
Normal (<5.7%)	Blood hemoglobin (HbA1C) category	111 (00 00%)	242 (24 270/)	0.9472
Freduzitetes (17.5~-0.36)     175 (35.73.6)     374 (32.30.6)       Diabetes (6.5%+)     43 (12.91%)     90 (12.73%)       Blod fasting glucose levels mg/dL     0.9114       Mean ± dev (min-max)     100.30 ± 24.96 (5-377)     100.48 ± 24.72 (67-418)       Median (IQR)     96 (90-104)     96 (89-104)       Blood fasting glucose levels category     0.3497       Normal (<100)	NOTITIAL $(<5.7\%)$ Produbotos $(5.7\%) < 6.5\%$	111 (33.33%) 170 (52.75%)	243 (34.37%) 274 (52.00%)	
Blod fasting glucose levels mg/dL       0.9114         Mean ± dev (min-max)       100.30 ± 24.96 (5-377)       100.48 ± 24.72 (67-418)         Median (IQR)       96 (90-104)       96 (89-104)         Blood fasting glucose levels category       0.3497         Normal (<100)	Diabetes $(6.5\%+)$	$A_3(12.91\%)$	90 (12 73%)	
Mean ± dev (min-max)         100.30 ± 24.96 (5-377)         100.48 ± 24.72 (67-418)           Median (IQR)         96 (90-104)         96 (89-104)           Blood fasting glucose levels category         0.3497           Normal (<100)	Blood fasting glucose levels mg/dL	45 (12.51%)	50 (12.75%)	09114
Median (IQR)         96 (90–104)         96 (89–104)           Blood fasting glucose levels category         0.3497           Normal (<100)	Mean $\pm$ dev (min-max)	100.30 ± 24.96 (5-377)	100.48 ± 24.72 (67-418)	0.0111
Blood fasting glucose levels category         0.3497           Normal (<100)	Median (IQR)	96 (90–104)	96 (89–104)	
Normal (<100)         214 (64.85%)         437 (61.64%)           Prediabetes (100-<126)	Blood fasting glucose levels category			0.3497
Prediabetes (100-<126)         92 (27.88%)         228 (32.16%)           Diabetes (126+)         24 (7.27%)         44 (6.21%)	Normal (<100)	214 (64.85%)	437 (61.64%)	
Diabetes (126+) 24 (7.27%) 44 (6.21%)	Prediabetes (100–<126)	92 (27.88%)	228 (32.16%)	
	Diabetes (126+)	24 (7.27%)	44 (6.21%)	

In the follow-up analyses to investigate outcomes significantly associated with ACEs after adjustment for demographics, BMI and waist circumference were no longer significant once HOMA-IR was included in the dichotomized ACE model (p = 0.05 and p = 0.06, respectively). Similar results were seen for ACE count with BMI and waist circumference no longer

significantly associated with ACE after inclusion of HOMA-IR (p = 0.06 and p = 0.27, respectively). While the correlation between BMI and waist circumference was high (0.78) suggesting these outcomes may be similar, the correlation between BMI and HOMA-IR was low (0.38), so loss of significance was not a result of collinearity and instead may suggest mediation.

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 Table 3

 Adjusted analyses for outcomes by three categorization of ACE.

	BMI		WC		W-H Ra	tio	SBP		DBP		HbA1c		BFG		BFI		HOMA	IR
	В	CI	ප	CI	В	CI	б	CI	в	CI	В	CI	б	CI	в	CI	ප	CI
ACE dichotomized ACE	1.13	0.34; 1.92	2.74	0.72; 4.76	0.01	-0.00; 0.02	1.19	-1.07; 3.46	0.81	-0.49; 2.11	-0.02	-0.14; 0.10	-0.00	-3.29; 3.28	2.36	0.71; 4.02	0.57	0.08; 1.06
ACE count 1	0.97	0.04; 1.90	2.62	0.24; 5.00	0.01	-0.00; 0.02	1.54	-1.13; 4.21	0.80	-0.73; 2.33	-0.01	-0.15; 0.13	-0.70	-4.58; 3.17	1.61	-0.34; 3.55	0.43	-0.15; 1.00
2	0.68	-0.38; 1.73	1.98	-0.72; 4.67	0.00	-0.01; 0.01	0.04	-2.98; 3.06	1.23	-0.51; 2.96	-0.03	-0.19; 0.13	-0.72	-5.13; 3.68	3.56	-1.34; 5.77	0.73	0.07; 1.38
c	1.87	0.54; 3.20	3.67	0.28; 7.06	0.01	-0.00; 0.03	2.01	-1.78; 5.81	0.01	-2.17; 2.19	-0.11	-0.31; 0.09	0.66	-4.84; 6.16	0.94	-1.82; 3.71	0.22	-0.60; 1.04
$^{4+}$	1.88	0.50; 3.26	3.86	0.32; 7.39	0.01	-0.01; 0.03	1.61	-2.35; 5.57	0.79	-1.48; 3.07	0.09	-0.12; 0.30	3.48	-2.30; 9.27	4.13	1.23; 7.04	1.17	0.31; 2.03
ACE category																		
Emotional abuse	0.12	-0.88; 1.12	-0.41	-2.97; 2.15	-0.00	-0.01; -0.01	0.56	-2.32; 3.44	1.01	-0.64; 2.66	-0.01	-0.16; 0.14	0.34	-3.87; 4.55	-0.67	-2.79; 1.45	-0.14	-0.77; -0.48
Physical abuse	0.87	-0.20; 1.95	2.78	0.04; 5.52	0.01	-0.01; 0.02	0.34	-2.75; 3.43	-0.84	-2.61; -0.93	0.01	-0.15; 0.18	-1.72	-6.23; 2.79	2.52	0.25; 4.79	0.42	-0.25; 1.09
Sexual abuse	1.06	0.00; 2.12	2.33	-0.38; 5.03	0.01	-0.01; 0.02	-0.36	-3.41; 2.68	-0.84	-2.58; -0.91	-0.09	-0.25; 0.07	0.44	-3.99; 4.88	1.31	-0.92; 3.54	0.35	-0.31; 1.01
Substance abuse	0.05	-0.84; 0.93	-1.06	-3.34; 1.22	-0.01	-0.02; -0.01	-0.71	-3.27; 1.86	0.26	-1.21; 1.73	-0.04	-0.17; 0.10	1.70	-2.01; 5.42	-0.14	-2.00; 1.73	0.06	-0.49;0.61
Family instability	-0.41	-1.32; 0.51	-0.26	-2.60; 2.08	0.00	-0.01; 0.01	1.19	-1.44; 3.83	0.53	-0.98; 2.04	0.01	-0.13; 0.14	-1.27	-5.09; 2.55	0.40	-1.52; 2.32	0.03	-0.54; 0.60
Financial strain	0.97	0.15; 1.79	1.44	-0.66; 3.55	0.00	-0.01; 0.01	0.34	-2.02; 2.71	0.29	-1.07; 1.64	0.07	-0.05; 0.20	3.50	0.05; 6.95	2.00	0.27; 3.74	0.67	0.15; 1.18
Adjusted coefficients	for full r	nodels displaye	1 with 95	i% confidence ir	tervals, t	old indicates p <	0.05. Ad	justed for gende	r, age, ra	ice, educational	level, hou	sehold income,	and mari	tal status.	:			
BMI = body mass in	dex; WC	= waist circun	ference	W-H = waist	to hip: SI	SP = systolic blo	od pressu	ire: DBP = diast	colic bloc	d pressure; BFC	= blood	fasting glucose	: BFI = b	lood fasting ins	ulin.			

### 4. Discussion

Overall, in a longitudinal cohort of US adults, we found that compared to those without ACEs, individuals reporting ACEs were more likely to have higher BMI, higher waist circumference, elevated blood fasting insulin levels, and higher insulin resistance as measured by HOMA-IR. This association was more significant with BMI, waist circumference, and insulin levels than with central/abdominal obesity, blood pressure, or elevated glucose levels. Of interest, BMI/waist circumference and insulin resistance do not maintain independent relationships with ACEs once either factor is accounted for, suggesting the relationship between BMI and ACEs may be mediated by insulin resistance. Finally, among the individual ACE categories, experiences of sexual abuse were associated with higher BMI; experiences of physical abuse was associated with increased fasting insulin as well as waist circumference; and experiences of financial strain was associated with higher BMI, increased fasting glucose, increased fasting insulin, and insulin resistance.

Overall, these results suggest that ACEs increase the risk of prediabetes through increased BMI, increased waist circumference, and increased insulin resistance. These results are consistent with existing literature suggesting obesity as an important factor when looking at ACE exposure and adult morbidity.<sup>29-34</sup> Power and colleagues found that in a longitudinal cohort overtime, not only were ACEs associated with increased BMI in adulthood, but specific ACEs differentially accelerated BMI in adulthood compared to individuals who never experienced ACEs.<sup>31</sup> However, the timing of this relationship, and how it influences outcomes over time is unclear. The current results suggest that the association of ACEs with BMI and insulin resistance are not independent of each other, but rather represent important factors within the pathway between ACEs and pre-diabetes in adulthood. In addition to its association with obesity, chronic exposure to psychosocial stressors has been associated with increased corticotropin-releasing factor (CRH) levels, consistent with chronic activation of the HPA axis known to cause elevated cortisol levels and therefore increased insulin resistance.<sup>35,39</sup>

This is the first study to our knowledge to examine the independent relationship that six ACE categories have on pre-diabetes characteristics, including BMI and waist circumference. These results have important clinical, research, and public health implications. Despite the evidence that the literature has provided on the relationship between ACEs and diabetes, little is being done at the clinical level to provide a mechanism for providers to actively screen and tailor treatment plans for adults with a history of ACEs. This may be due in part to the limited training available for students, residents, and clinicians regarding ACE screening at the clinic level.<sup>36</sup> Existing screening procedures have been developed for primary and secondary prevention and take place at the prenatal and pediatric level.<sup>37,38</sup> While some concern has been raised regarding the lack of evidenced based treatments available for ACE screening efforts,<sup>40</sup> as well as the sensitivity surrounding the discussion of ACEs, as it relates directly to pre-diabetes and diabetes, screening would allow providers to better understand patients who may be at increased risk for diagnosis and complications and tailor existing treatment recommendations around risk. Bethell et al recently reviewed methods for ACE assessment and found that population-based surveillance as well as practice-based assessment is an acceptable method for ACE screening.<sup>41</sup> Glowa and colleagues recently pilot tested ACE screening across 3 primary care clinics and found that screening for ACEs in the clinic setting is feasible and sensitivity to questions was not found to be a barrier.<sup>42</sup> Of note, this study found that ACE scores > 4 were more predominate in patients being seen for chronic illness visits. Recognizing that ACE score and exposure may accelerate the diagnosis of pre-diabetes, screening tools would enable providers to tailor treatment plans to suit patients' needs and minimize risk. In addition, recognizing that specific types of ACEs may have a differential effect on outcomes is important for designing and implementing screening. Dube describes the need for ACE screening at the clinic level as a mechanism for detection that enables informed care, as opposed to diagnosis of traumatic experiences.<sup>43</sup> Utilizing approaches such as detection rather than diagnosis arms clinicians with the proper history and context for developing a health risk profile. This level of comprehensive assessment provides the substrate for tailored treatment plans and informed recommendations for care that may improve health outcomes and lower utilization. This is particularly relevant as the ACE literature provides overwhelming evidence for the dose-response relationship between ACE exposure and diabetes as well as the cost utilization seen among individuals who endorse ACEs compared to those who do not.<sup>38,44</sup> The current study provides new information for clinicians for tertiary prevention by demonstrating the influence of ACEs at the prediabetes state and suggests the need to intervene through screening procedures to actively prevent a diagnosis of diabetes.

Additional research is needed to provide evidence for educating clinicians on screening procedures and developing treatment interventions for adults who have experienced ACEs and are at risk for developing pre-diabetes<sup>36</sup> A significant limitation in the diabetes literature exists for whether individuals who have experienced ACEs differ clinically from individuals who have never experienced ACEs, once diabetes manifests. It is unknown if ACEs accelerate the transition from pre-diabetes to diabetes and whether treatment response varies for those who have a history of ACEs compared to those who do not. Understanding these relationships would allow for the development of evidence-based treatment and would guide screening efforts clinically as well as for public health policy and training curriculum. Additionally, the need for caution and sensitivity is highly warranted when it comes to screening for ACEs at any level, however, there remains a lack of evidence for the patients' perspective on conducting ACE screening during the clinical encounter. These results provide the next step for the literature in recognizing that ACE exposure impacts insulin sensitivity and that ACE categories have a differential impact on pre-diabetic characteristics. However, pathways leading to this relationship need to be further elucidated.

#### 5. Limitations

While this study is strengthened by its longitudinal design and large sample size, there are some limitations that should be considered. First, ACEs are self-report and experiences of abuse were not substantiated; however, the literature has shown that recall bias for certain traumatic and significant life experiences are relatively low.<sup>45,46</sup> Second, this sample represented a largely non-Hispanic white population and for this reason may not be generalizable to other more diverse populations. Thirdly, ACEs represent a broad spectrum of experiences that impact individuals across the life course. This study was limited to 6 categories of ACEs and there may be ACEs that relate to pre-diabetes that are not captured in this dataset. Finally, while the individuals in the dataset were followed longitudinally, the biologic measures were collected at one-time point. Therefore, causation between the biologic measures cannot be supported.

#### 6. Conclusion

These results represent one of the first studies to examine the differential impact of ACEs on a diverse set of clinical pre-diabetes measures. These findings suggest that of the ACE categories, sexual abuse, physical abuse, and financial strain during childhood are important factors when considering risk for pre-diabetes, while overall BMI, waist circumference, and insulin resistance should be a focused for intervention development. BMI and insulin resistance are not independent of each other, but rather represent important factors within the pathway between ACEs and pre-diabetes in adulthood. Screening for ACEs during the clinical encounter may improve detection of individuals at risk for developing diabetes. Additional research is needed to examine the pathways underlying this relationship and to further understand if these associations lead to the development of diabetes.

# Funding

This study was supported by the National Institute of Diabetes and Digestive and Kidney Diseases (Grant K24DK093699, principal investigator Leonard Egede, MD, MS).

#### Authors' contributions

LEE, RJW and JC conceptualized the study. JC was a major contributor in writing and interpreting the manuscript. EG analyzed and interpreted the data in this manuscript. CM and NW were major contributors in writing the manuscript. RW and LE were major contributors in interpreting the data in this manuscript. All authors read and approved the final manuscript.

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