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ABSTRACT

Adults with type 2 diabetes mellitus tend to exhibit an increased level of central adiposity, augmenting their risk of further non-communicable diseases (NCDs). Importantly, consistent evidence demonstrates a significant, negative association between cardiorespiratory fitness (CRF) and waist circumference (WC). However, no previous studies have investigated differences in these CRF-related reductions in WC between adults with and without diabetes.

This study used data from the Aerobic Center for Longitudinal Studies, conducted between 1970 and 2006 among predominately Non-Hispanic White, middle-to-upper class adults in Texas. Quantile regression models were used to estimate CRF-related differences in WC between persons with and without diabetes. Age, height, smoking status and birth cohort served as covariates. The analytic sample included 45901 adults.

Significantly larger reductions in WC were observed among adults with diabetes as compared to without diabetes across all WC percentiles. Among males, high CRF levels were associated with significant reductions, as compared to their low-fit counterparts, in WC as large as 21.9 cm for adults without diabetes and as large as 27 cm for adults with diabetes. Among females, high CRF levels were associated with significant reductions, as compared to their low-fit counterparts, in WC as large as 22.3 and 30.0 cm for adults without and with diabetes, respectively.

This study demonstrated that higher CRF is associated with significant reductions in WC, with greater magnitudes found among adults with diabetes, especially among the most centrally obese, highlighting the necessity of exercise prescription in this clinical population potentially leading to lower risks of future NCDs.

1. Introduction

Alarmingly, nearly 10% of the U.S. population suffers from type 2 diabetes mellitus (T2DM) (Bullard and Lessem, 2018; Xu et al., 2018) . T2DM is a chronic disease characterized by central and/or peripheral insulin resistance and eventually leading to deficient secretion of insulin by the pancreatic β-cells (Taylor, 2013). Individuals with T2DM also possess an increased risk of cardiovascular diseases (CVD), the leading cause of death in United States (Low Wang et al., 2016; Xu et al., 2016).

Importantly, central obesity is a ubiquitous comorbidity of T2DM and is strongly associated with several CVD risk factors including but not limited to hypertension and dyslipidemia (Gastaldelli et al., 2007; Nakamura et al., 1994; Fox et al., 2007). Thus, for people with diabetes, the control of central adiposity (i.e. visceral fat) may be particularly important as it is more strongly linked to CVD, as compared to general obesity (Gruzdeva et al., 2018). Studies show that a high proportion of visceral fat contributes to impairment of normal glucose and insulin homeostasis and is associated with hypersecretion of insulin and decreased insulin stimulated-glucose disposal as well as pro-inflammatory

cytokine (e.g., interleukin-6) production leading to chronic systemic inflammation (Gastaldelli et al., 2007; Buse et al., 2007; Barzilai et al., 1999). In general, the benefits and importance of controlling central adiposity through physical activity and/or engaging in chronic exercise (Despres et al., 1991; Donges and Duffield, 2012) is gaining increased acceptance with the endorsement of CRF as a vital sign as well as the prescription of exercise as medicine by clinicians (Kaminsky et al., 2019; Fletcher et al., 2018). However, for persons with T2DM the additional documented benefits of chronic exercise further extend to glucose, lipid and blood pressure homeostasis and lowering chronic systemic inflammation (Boulé et al., 2005; Ghanassia et al., 2006; Kiens, 2006). Specifically, exercise allows for insulin-independent glucose uptake in muscle, which helps to reduce serum glucose levels, subsequently reducing the risk of cardiovascular-related events and mortality (Buse et al., 2007; Blair et al., 1996; Bhati et al., 2018; Richter and Hargreaves, 2013).

Previous studies demonstrated that higher levels of cardiorespiratory fitness (CRF), an indicator of habitual exercise, is strongly associated with central adiposity (Blair et al., 1996; McDonald et al., 2016; Earnest et al., 2013). In addition, the magnitude of this association differs across the central adiposity distribution, with the greatest reductions in waist circumference (WC) consequent to higher levels of CRF, occurring at the upper adjusted WC percentiles (i.e., 90th) (McDonald et al., 2016). These studies, however, were conducted in healthier adult populations. Thus, the presence of the CRF-related reductions in central adiposity and its quantile/percentile effect among adults with diabetes is unknown. Therefore, the purpose of this study is to comprehensively assess differences in the association between WC, a measure of central adiposity, and CRF for adults with diabetes as compared to adults without diabetes using quantile regression.

2. Methods

2.1. Study population

The Aerobics Center Longitudinal Study (ACLS) is a prospective observational study of individuals who completed comprehensive medical examinations at the Cooper Clinic in Dallas, Texas (Blair et al., 1989). Study participants came to the clinic for periodic preventive health examinations and for counseling regarding diet, exercise, and other lifestyle factors associated with increased risk of chronic disease. Between 1970 and 2006, participants received at least one comprehensive medical examination and maximal graded treadmill exercise test at the clinic and were enrolled in the ACLS. Most study participants were non-Hispanic whites from middle-to-upper socioeconomic strata and were either referred by their employers, physicians or self-referred. The study was reviewed and approved annually by the Cooper Institute Institutional Review Board, and all participants provided written informed consent. The data set used for this study included 35307 males and 9784 females (total observations 88101, total participants 45091, average number of visits 1.95). Among these subjects, 12951 males and 2069 females had more than one visit.

2.2. Measures

The comprehensive health evaluation is described in detail elsewhere (Blair et al., 1996; Kampert et al., 1996). The outcome of interest in this study was WC. A measuring tape was used to assess WC at the umbilicus. WC values were reported in centimeters (cm) and rounded to the nearest millimeter. Cardiorespiratory fitness was measured by a maximal treadmill exercise test using a modified Balke protocol (Gibbons et al., 1989). The treadmill speed was 88 m*min^{-1} initially, and participants started the test at 0% grade. The grade was increased to 2% for the second minute and was thereafter increased 1% per minute until the 25th minute. After 25 min, the speed was increased 5.4 m*min^{-1} without a grade change until test termination. All

participants were encouraged to give maximal effort during the test. Participants who had the test stopped by a physician for problematic signs and symptoms or failed to reach 85% of age-predicted maximal heart rate, were excluded from the analyses to ensure that near maximal effort was obtained. CRF in maximal METs was estimated from the final treadmill grade and speed using the following equation from the American College of Sports Medicine: [(speed × 0.1) + (speed × grade × 1.8) + 3.5] / 3.5. To estimate CRF, $\dot{V}O_{2max}$ was obtained by multiplying maximal METS by 3.5 ml $O_2 \cdot kg^{-1} \cdot min^{-1}$ and expressed as ml $O_2 \cdot kg^{-1} \cdot min^{-1}$ (Swain and Brawner, 2014). Diabetes status was determined in accordance with the American Diabetes Association guidelines, using either of the following two criteria (American Diabetes Association, 2018). If fasting-plasma glucose $\geq$ 7 mmol/l (126 mg/dl) was reported at a clinical follow-up evaluation or, if a response to a health survey stated that the subject was either currently taking hypoglycemic medication or was diagnosed with T2DM by their personal physician then the observation was classified as having come from a person with diabetes.

2.3. Statistical analysis

Stata (version 12) was used for all statistical analyses. Regression models were stratified by sex with WC treated as the dependent variable. Quantile regression (Koenker, 2005) was used to assess the associations between CRF and WC at the 10th; 25th, 50th, 75th and 90th WC percentiles. Regression models with CRF treated continuously were used to assess differences in the association between WC and CRF between persons with and without diabetes via a two-way interaction term between CRF and diabetes status. To provide easily interpretable estimates of the magnitude of associations between WC and CRF, regression models treating CRF as a categorical predictor stratified by both sex and diabetes status were also used. For analyses where CRF was categorized, $\dot{V}O_{2max}$ was divided into three levels (high, moderate and low) using age and sex-specific cut-points consistent with previous studies using ACLS data (Sui et al., 2007). Additional predictors including smoking status, age (years), height (inches) and birth cohort were adjusted for in all regression models due to an established relationship with central adiposity and/or CRF. Smoking status was obtained from a standardized questionnaire. Participants were classified as a nonsmoker or current smoker at the time of each examination. Birth cohort was based on each participant's year of birth categorized into 4 groups (1930 or earlier, 1931–1940, 1941–1950, after 1950).

Multiple observations on the same subject may not be independent. The quantile regression estimator is consistent when the data are not independent (Parente Paulo, 2016; Jung, 1996) and the method of Parente and Silva (Parente Paulo, 2016) was used to account for this potential non-independence for standard error and confidence interval estimation. Quantile regression coefficients are interpreted similarly to those of ordinary linear regression coefficients except that a quantile regression coefficient indicates the change in the value at the modeled percentile, not the mean, of the dependent variable. For example, consider the categorical predictor for CRF status with three levels; high, moderate and low (referent level). A coefficient estimate of −5 for moderate fitness in the quantile regression model for the 75th percentile would indicate the 75th percentile of WC is estimated to be 5 cm less for people of a moderate fitness level as compared to those with a low fitness level after controlling for other covariates in the model.

3. Results

Descriptive statistics, based on the number of observations, for the study participants are presented in Table 1. For both male and female adults, across unadjusted quartiles, persons with diabetes were significantly older, had lower CRF and had larger WC as compared to persons without diabetes. For males, the proportion of observations for people with diabetes in the 1930 or earlier birth cohort was

Table 1

Sample characteristics showing mean or number (%) of observations comparing people with and without diabetes stratified by sex. ACLS data collected in the U.S. from 1970 to 2006.

	Males (n = 74144)			Females (n = 13957)		
	No Diabetes	Diabetes	p-value	No Diabetes	Diabetes	p-value
Waist Circumference (cm)						
25th Percentile	86.0	90.2	0.00	66.5	68.0	0.02
50th Percentile	92.0	98.0	0.00	71.0	75.0	0.00
75th Percentile	98.0	107.0	0.00	78.0	86.0	0.00
$\dot{V}O_2max$ (ml/min/kg)						
25th Percentile	37.8	31.5	0.00	29.9	28.3	0.00
50th Percentile	42.6	36.2	0.00	34.6	31.5	0.00
75th Percentile	47.4	42.6	0.00	39.4	36.2	0.00
Age (y)						
25th Percentile	40.0	45.0	0.00	39.0	40.0	0.04
50th Percentile	47.0	52.0	0.00	46.0	47.0	0.13
75th Percentile	55.0	58.0	0.00	54.0	56.0	0.08
Birth Cohort						
< 1931 (ref)	11,045 (95%)	537 (5%)	–	1322 (97%)	41 (3%)	–
1931–1940	18,346 (96%)	716 (4%)	0.00	2676 (97%)	84 (3%)	0.93
1941–1950	23,558 (97%)	812 (3%)	0.00	4212 (97%)	113 (3%)	0.43
> 1950	18,422 (96%)	708 (4%)	0.00	5268 (96%)	241 (4%)	0.07
Smoke						
No (ref)	62,240 (96%)	2391 (4%)	–	12,507 (96%)	455 (4%)	–
Yes	9131 (96%)	382 (4%)	0.84	971 (98%)	24 (2%)	0.06
Fitness Levels						
Low	4929 (89.9%)	551 (10.1%)	–	996 (94.4%)	57 (5.6%)	–
Moderate	21,469 (95.1%)	1115 (4.9%)	0.00	3771 (95.9%)	161 (4.1%)	0.07
High	44,973 (97.6%)	1107 (2.4%)	0.00	8741 (97.1%)	261 (2.9%)	0.00

Note: Differences across percentiles for continuous variables were tested via quantile regression with robust standard errors. Differences in the proportion of people with/without diabetes were tested via logistic regression using clustered robust standard errors with all comparisons made to the referent level.

significantly greater than the proportion in the other birth cohorts.

Table 2 shows the adjusted quantile regression estimates, stratified by sex, for the association between CRF, treated as a continuous predictor, at the 10th, 25th, 50th, 75th and 90th WC percentiles for people with and without diabetes, as well as the difference between them (i.e. the interaction term). Similarly, Table 3 shows the adjusted quantile regression estimates from the models treating CRF as a categorical predictor stratified by both sex and diabetes status.

3.1. Males

With CRF treated as a continuous predictor, after adjusting for age, height, smoking status and birth cohort, CRF was significantly associated with a decrease in WC for people both with and without diabetes across all WC percentiles with the magnitude of the association increasing uniformly with increasing WC percentiles. The estimated reductions in WC associated with an increase in CRF was significantly

greater for adults with diabetes as compared to adults without diabetes across all WC percentiles (i.e. interaction terms were significant across all percentiles) with the magnitude of this difference increasing with increasing WC percentiles.

With CRF treated categorically, after adjusting for age, height, smoking status and birth cohort, in the stratified analyses for males both with and without diabetes, higher levels of CRF were significantly associated with reductions in WC across all percentiles with the magnitude of the estimates increasing uniformly with increasing WC percentiles. Specifically, for males without diabetes both moderate and high CRF levels were associated with reductions in WC ranging from 4.1 cm to 13.1 cm among moderately-fit and 9.6 cm to 21.9 cm for high-fit males as compared to their low fit counterparts. Similarly, for males with diabetes, both moderate and high CRF levels were associated with reductions in WC ranging from 7.5 cm to 15.7 cm among moderately-fit and 14.3 cm to 27.0 cm for high-fit males as compared to their low fit counterparts. A graphical representation of these regression

Table 2

Adjusted estimated differences in WC (Est.) and 95% confidence intervals (CI) for select WC percentiles stratified by sex. ACLS data collected in the U.S. from 1970 to 2006.

Percentiles										
	10th		25th		50th		75th		90th	
Males	Est.	95% CI	Est.	95% CI	Est.	95% CI	Est.	95% CI	Est.	95% CI
CRF (No Diabetes)	−0.43	(−0.45, −0.41)	−0.51	(−0.53, −0.50)	−0.60	(−0.62, −0.59)	−0.71	(−0.73, −0.70)	−0.82	(−0.84, −0.80)
CRF (Diabetes)	−0.68	(−0.74, −0.62)	−0.82	(−0.88, −0.76)	−0.93	(−1.00, −0.86)	−1.04	(−1.11, −0.97)	−1.17	(−1.25, −1.09)
CRF*Diabetes	−0.25	(−0.31, −0.18)	−0.31	(−0.37, −0.25)	−0.33	(−0.40, −0.25)	−0.32	(−0.40, −0.25)	−0.35	(−0.43, −0.27)
Females										
CRF (No Diabetes)	−0.23	(−0.26, −0.21)	−0.34	(−0.36, −0.31)	−0.49	(−0.53, −0.46)	−0.69	(−0.73, −0.65)	−0.85	(−0.91, −0.80)
CRF (Diabetes)	−0.35	(−0.45, −0.26)	−0.63	(−0.87, −0.39)	−0.92	(−1.15, −0.70)	−1.26	(−1.38, −1.15)	−1.35	(−1.72, −0.97)
CRF*Diabetes	−0.12	(−0.22, −0.02)	−0.29	(−0.53, −0.05)	−0.43	(−0.66, −0.21)	−0.58	(−0.70, −0.46)	−0.49	(−0.87, −0.12)

Note: Coefficients in **bold** indicate significant findings at $p < 0.05$. WC is measured in centimeters. Each of the quantile regression models were stratified by sex and include diabetes (yes/no), smoking (yes/no), height (in), birth cohort (1930 or earlier, 1931–1940, 1941–1950, 1951 or later), age (years) and CRF (ml $O_2 \cdot kg^{-1} \cdot min^{-1}$) and a two-way interaction between diabetes and CRF (diabetes*CRF) as predictors. The referent level for birth cohort is the group born 1930 or earlier.

Table 3

Adjusted estimated differences in WC (Est.) and 95% confidence intervals (CI) for fitness categories across select WC percentiles stratified by sex and diabetes status. ACLS data collected in the U.S. from 1970 to 2006.

Percentiles	10th		25th		50th		75th		90th	
Males	Est.	95% CI	Est.	95% CI	Est.	95% CI	Est.	95% CI	Est.	95% CI
Fitness Level (No Diabetes)										
Moderate	−4.1	(−4.6, −3.5)	−5.4	(−5.8, −4.9)	−7.3	(−7.8, −6.8)	−9.9	(−10.4, −9.3)	−13.1	(−14.0, −12.2)
High	−9.6	(−10.2, −9.1)	−11.7	(−12.1, −11.2)	−14.3	(−14.8, −13.8)	−17.6	(−18.2, −17.0)	−21.9	(−22.8, −21.0)
Fitness Level (Diabetes)										
Moderate	−7.5	(−9.7, −5.3)	−9.6	(−11.6, −7.6)	−10.2	(−11.7, −8.7)	−12.6	(−14.3, −10.3)	−15.7	(−18.1, −13.3)
High	−14.3	(−16.5, −12.1)	−17.8	(−19.8, −15.8)	−19.1	(−20.5, −17.7)	−22.3	(−24.4, −20.1)	−27.0	(−29.5, −24.5)
Females										
Fitness Level (No Diabetes)										
Moderate	−2.7	(−3.5, −2.0)	−4.7	(−5.6, −3.8)	−7.4	(−8.5, −6.4)	−10.6	(−12.0, −9.3)	−13.0	(−14.6, −11.4)
High	−4.8	(−5.6, −4.1)	−7.8	(−8.6, −6.9)	−12.3	(−13.3, −11.3)	−17.9	(−19.1, −16.6)	−22.3	(−23.7, −20.8)
Fitness Level (Diabetes)										
Moderate	−3.5	(−9.9, 2.8)	−11.2	(−16.0, −6.4)	−13.8	(−19.3, −8.3)	−12.5	(−17.1, −8.0)	−18.2	(−27.8, −8.6)
High	−7.9	(−13.9, −2.0)	−17.3	(−21.7, −12.8)	−22.5	(−27.1, −17.9)	−23.4	(−27.5, −19.2)	−30.0	(−39.1, −21.0)

Note: Coefficients in **bold** indicate significant findings at p < 0.05. WC is measured in centimeters. Each of the quantile regression models were stratified by sex and diabetes status and include smoking (yes/no), birth cohort (1930 or earlier, 1931–1940, 1941–1950, 1951 or later), age (years), height (inches) and CRF (low, moderate, high). The referent level for birth cohort is the group born 1930 or earlier. The referent level for CRF is the low fitness group.
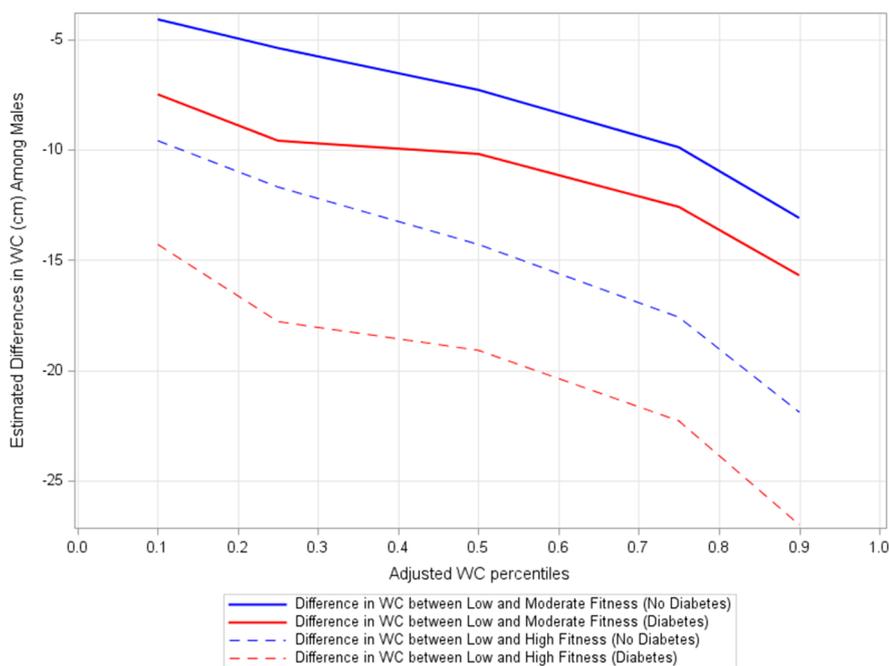

Fig. 1. Adjusted quantile regression estimated differences in WC for high and moderately fit as compared to low-fit male adults with and without diabetes across selected WC percentiles. Estimates were stratified by sex and diabetes status and adjusted for smoking status (yes/no), birth cohort (1930 or earlier, 1931–1940, 1941–1950, 1951 or later), age (years) and height (inches). ACLS data collected in the U.S. from 1970 to 2006.

coefficients are presented in Fig. 1.

3.2. Females

With CRF treated as a continuous predictor, after adjusting for age, height, smoking status and birth cohort, CRF was significantly associated with a decrease in WC for persons both with and without diabetes across all WC percentiles with the magnitude of the association increasing uniformly with increasing WC percentiles. The estimated reductions in WC associated with an increase in CRF was significantly greater for adults with diabetes as compared to adults without diabetes across all WC percentiles (i.e. interaction terms were significant across all percentiles).

With CRF treated categorically, after adjusting for age, height, smoking status and birth cohort, in the stratified analyses for female adults both with and without diabetes, higher levels of CRF were significantly associated with reductions in WC across all percentiles with

the exception of the 10th percentile for the moderate fitness group among adults with diabetes. Specifically, for females without diabetes both moderate and high CRF levels were associated with significant reductions in WC across all percentiles with the magnitude of the reductions increasing with increasing WC percentiles and estimates ranging from 2.7 cm to 13.0 cm among moderately-fit and 4.8 cm to 22.3 cm for high-fit females as compared to their low fit counterparts. Similarly, for females with diabetes, a high CRF level was associated with reductions in WC across all WC percentiles with the magnitude of the estimates increasing with increasing percentiles and reductions ranging from 7.9 cm to 30.0 cm when compared to their low fit counterparts. For females with diabetes, a moderate CRF level was associated with significant reductions in WC across all WC percentiles except the 10th percentile with estimated reductions ranging from 11.2 cm at the 25th percentile to 18.2 cm at the 90th percentile when compared to their low fit counterparts. A graphical representation of these regression coefficients are presented in Fig. 2 (appendix).
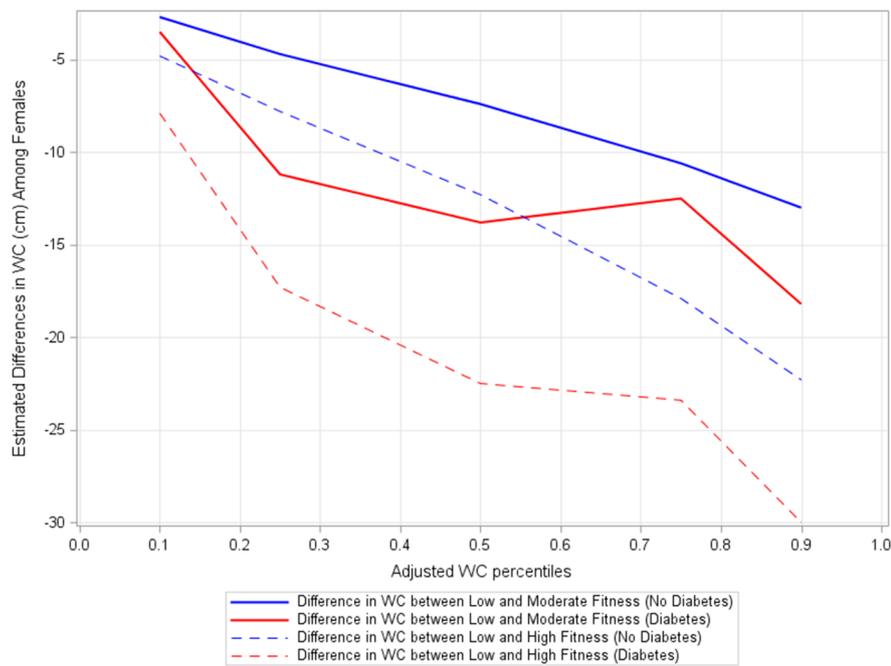
Fig. 2. Adjusted quantile regression estimated differences in WC for high and moderately fit as compared to low-fit female adults with and without diabetes across selected WC percentiles. Estimates were stratified by sex and diabetes status and adjusted for smoking status (yes/no), birth cohort (1930 or earlier, 1931–1940, 1941–1950, 1951 or later), age (years) and height (inches). ACLS data collected in the U.S. from 1970 to 2006.

4. Discussion

The purpose of this study was to comprehensively evaluate differences in the association between CRF and WC for persons both with and without diabetes, using quantile regression. The major findings of this study were, 1) the estimated reductions in WC associated with increased CRF were significantly larger among adults with diabetes as compared to adults without diabetes, 2) a quantile effect was observed showing increased magnitudes of the CRF-related reductions in WC, increasing across the WC distribution, with the largest reductions found at the upper WC percentiles.

Uniquely, the present study showed that reductions in WC consequent to increased CRF among adults with type 2 diabetes were significantly greater than for adults without diabetes (males and females), as evidenced by the significance of all two-way interaction terms from the analyses with CRF treated continuously. From the stratified analyses, the magnitude of the estimated reductions in WC associated with higher levels of CRF for adults with diabetes was between 2.6 cm and 6.1 cm and 0.8 cm and 10.2 cm greater than the corresponding reductions for adults without diabetes, demonstrating the increased strength of the association for adults with diabetes. Because these individuals tend to possess larger amounts of visceral fat (i.e. higher WC) (Gastaldelli et al., 2007), this observation is clinically meaningful as adults with diabetes comprise nearly 10% of the U.S. population and account for $237 billion dollars in direct annual healthcare expenses (Xu et al., 2018; American Diabetes Association. Economic costs of Diabetes in the U.S. in, 2017). Thus, achieving higher levels of CRF for adults with diabetes, via chronic exercise training, may substantially, and positively impact their individual health trajectory by reducing the risk of central obesity-related diseases and effectively managing metabolic health, and decreasing the economic burden within the healthcare system (Blair and Church, 2003; Breneman et al., 2016; Church et al., 2005).

Another unique aspect of this study was the observed quantile effects for CRF-related reductions across the WC distribution for both male and female adults with diabetes (see Table 3 and Fig. 1). This quantile effect is illustrated in Table 3, as well as Figs. 1 and 2. The estimated reductions in WC associated with a moderate or high-fitness level, as compared to a low CRF level, among adults with diabetes were

largest at the highest WC percentiles. For example, the magnitudes of the reduction in WC associated with increased levels of fitness for males with diabetes ranged from minimums of 7.5 cm and 14.3 cm at the 10th percentile to maximums of 15.7 cm and 27.0 cm at the 90th percentiles for moderate and high fit CRF levels respectively. Similar results were observed among females with diabetes and among persons without diabetes (both male and female). Previous studies documented these effects in populations without diabetes and also found that higher levels of CRF were associated with significant reductions in WC which increased in magnitude across the WC distribution (McDonald et al., 2016).

The quantile effects observed among adults both with and without diabetes demonstrates two important concepts. First, while our study shows that achieving higher (moderate and high) levels of CRF positively impacts WC among individuals with varying amounts of central adiposity, the most centrally obese, both with and without diabetes, may benefit the greatest from attaining higher levels of CRF. In support of this, previous studies reported larger gains in health benefits among the lowest-fit individuals, very likely represented by the most obese given the positive relationship between body weight and energy expenditure (Blair and Church, 2003; Leibel et al., 1995). Importantly, while the amount of central adiposity of individuals at the lower percentiles of the WC distribution is potentially less affected by increases in CRF, these individuals may experience many of the other previously documented benefits including enhanced metabolic health and cardiovascular function (Ferrari et al., 2006; Shojaee-Moradie et al., 2007; Harms and Hickson, 1983; Archer and Blair, 2011).

Second, our study observation of quantile effects establishes, along with other studies (McDonald et al., 2016; Bottai et al., 2014), the importance of utilizing more comprehensive statistical methods to analyze the associations between CRF and health-related outcomes. The ubiquity of employing statistical analyses focused on the center of the distributions (i.e. mean, median) of the outcome interest (e.g., WC) deprives the scientific literature of the differences (e.g., strength or direction) of these important associations potentially existing among various subpopulations. As such, the associations of interest may be under- or overestimated, subsequently affecting the interpretation and conclusions of the data, important "take-home" messages to the general population and misinformation that guides the development of health-

related policies.

There are some strengths and limitations of this study that warrant attention. First, to our knowledge, this is the first study to comprehensively evaluate the association between CRF and central adiposity among persons both with and without diabetes. Using this approach allowed for a thorough investigation of this association providing a more accurate description for several subpopulations across the WC distribution. Second, although $\dot{V}O_{2max}$ was not estimated via indirect calorimetry, CRF was objectively measured with a well-established exercise treadmill protocol providing an accurate assessment of an individual's aerobic capacity and indication of their habitual physical activity. Third, the large sample size adequately powered our study to evaluate our association of interest at several percentiles of the WC distribution. The limitations of this study include limited generalizability. Our study used data from the ACLS database which sampled male and female adults from 1970 to 2006, who were predominantly of the non-Hispanic White race, middle-to-upper class socioeconomic strata and resided in Dallas, Texas. Consequently, the findings of this study are limited to similar individuals. Second, the results of this study are not enough to draw casual inferences. Third, other potentially important extraneous factors were not considered in the analyses including individual dietary patterns and the possible impact of commonly prescribed medications on CRF and/or physical activity (Murlasits and Radak, 2014; Mikus et al., 2013).

In conclusion, our study observations demonstrate that increased CRF is associated with significant reductions in WC for adults both with and without diabetes. Moreover, the study findings show that the magnitude of the reductions in WC are significantly greater for adults with diabetes, emphasizing the necessity of exercise prescription in this clinical population, whom tend to deposit larger amounts of adipose tissue in the abdominal region. Lastly, the observed quantile effects highlight the importance of utilizing comprehensive statistical methods to analyze CRF and health-related associations in future investigations.

Author Contributions

SMM, CS and AO participated in generating the idea for the manuscript. AO and MB conducted the statistical analysis. MDW and XS refined the research idea and provided editorial assistance. All authors were involved in writing/reviewing the paper and had final approval of the submitted version.

CRediT authorship contribution statement

Andrew Ortaglia: Conceptualization, Formal analysis, Supervision, Writing - original draft, Writing - review & editing. **Samantha M. McDonald:** Conceptualization, Writing - original draft, Writing - review & editing. **Christina Supino:** Conceptualization, Visualization, Writing - review & editing. **Michael D. Wirth:** Investigation, Methodology, Supervision, Writing - review & editing. **Xuemei Sui:** Methodology, Visualization, Writing - review & editing. **Matteo Bottai:** Formal analysis, Supervision, Writing - review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

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