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The Protective Role of Physical Activity on Type 2 diabetes: An Analysis of Effect Modification by Race-Ethnicity

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Abstract

Background—It is well known physical activity (PA) plays a role in the prevention of type 2 diabetes (T2D). However, the extent to which PA may impact T2D risk among different raceethnic groups is unknown. Therefore, the purpose of this study was to systematically examine the effect modification of race-ethnicity on PA and T2D.

Methods—PubMed and Embase databases were systematically searched through June 2016. Study assessment for inclusion was conducted in three phases: 1) title review (N= 13,022), 2) abstract review (N=2,200), and 3) full text review (N=265). A total of 27 studies met the inclusion criteria and were used in the analysis. Relative This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/jdb.12574 risks (RRs) and 95% confidence intervals (CIs) were extracted and analyzed using the Comprehensive Meta-Analysis software. All analyses used a random-effects model.

Results—A significant protective summary RR, comparing the most active group to the least active PA group, was found for non-Hispanic White (RR 0.71, 95% CI 0.60–0.85), Asians (RR 0.76, 95% CI 0.67–0.85), Hispanics (RR 0.75, 95% CI 0.64–0.89), and American Indians (RR 0.73, 95% CI 0.60–0.88). The summary effect for non-Hispanic Blacks (RR 0.91, 95% CI 0.76–1.08) was non-significant.

Conclusions—The results of this study indicate that PA (comparing most to least active groups) provides significant protection from T2D with the exception of non-Hispanic Blacks. The results also indicate a need for race-ethnicity specific reporting of RRs in prospective cohort studies that incorporate multi-ethnic samples.

Keywords

Race; ethnicity; diabetes; risk; physical activity

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INTRODUCTION

The prevalence of type 2 diabetes among adults in the United States (U.S.) is estimated to be anywhere from 9.3–14.5%, depending upon the dataset and diagnostic criteria ^{1, 2}. Furthermore, by the year 2050, the type 2 diabetes prevalence in the U.S. is projected to reach upwards of 21–33% ³. However, substantial race-ethnic disparities exist in the prevalence of type 2 diabetes. At 15.9%, American Indian/Alaskan Natives have the highest estimated prevalence of type 2 diabetes ¹. The next highest prevalence rates are found among Non-Hispanic Blacks (NHB, 13.2%), Hispanics (12.8%), Asians (9.0%) and those who are non-Hispanic White (NHW,7.6%)¹. Race-ethnic disparities in the prevalence of type 2 diabetes are expected to persist⁴: the projected 50 year increase in prevalence of type 2 diabetes will be highest among NHBs, followed by Hispanics and other ethnicities compared to NHW.

Physical activity (PA) is an important component of type 2 diabetes prevention initiatives⁵ and has been shown to reduce the risk of type 2 diabetes ⁶. However, the extent of type 2 diabetes protection associated with PA has yet to be fully examined in regards to effect modification by race-ethnicity. A narrative review by Gill et al. ⁷ suggested varying thresholds of PA protection against type 2 diabetes may across race-ethnic groups. Moreover, the authors also suggested that the current U.S. Department of Health and Human Services (DHHS) uniform guideline of 150 min moderate-intensity aerobic PA per wk ⁸ may not provide equal protection against developing type 2 diabetes across race-ethnic groups.

The 2008 Physical Activity Guidelines Committee Report ⁹, indicates significant need to further understand the effects of PA on diabetes risk among ethnically-diverse populations. While meta-analyses have examined and established a clear inverse relationship between PA and type 2 diabetes risk ^{6, 10}, to our knowledge, no meta-analysis has assessed effect modification of this relationship by race-ethnicity. Therefore, the purpose of this systematic review and meta-analysis was to compile the evidence from prospective cohort studies on potential effect modification of the aerobic PA and type 2 diabetes risk relationship by race-ethnic groups.

METHODS

Data sources and searches

Systematic searches of the literature were independently conducted in PubMed and Embase by two authors (W.R.B. and E.C.F.). A modified version of the search criteria employed by Aune et al. ⁶ was used: (physical activity OR exercise OR sports OR walking OR biking OR running OR fitness OR exercise test OR inactivity OR sedentary activity) AND diabetes AND (case–control OR retrospective OR cohort OR cohorts OR prospective OR longitudinal OR follow-up OR cross-sectional OR trial) AND (ethnic OR ethnic group OR race OR racial group). Furthermore studies included in another meta-analysis we screened as well ⁶. Standard guidelines for conducting and reporting meta-analyses were followed ¹¹.

Study Selection

Research articles were examined for the following eligibility criteria: human participants who were without type 2 diabetes at the start of the studies and were adults (18 years) at the time of follow-up; assessed aerobic-based PA; published or available in English; were prospective cohort studies; assessed and reported the race-ethnicity specific relative risks (RR) for type II diabetes; adjusted risk estimates for age; and allowed for the determination of a most versus least physically active group. The article screening process is presented in Figure 1. A total of 27 individual articles met the full eligibility criteria ^{12–38}. Race-ethnic groups identified and used in the analyses were NHW, NHB, Asian, Hispanic, and American Indian.

Data Extraction and Quality Assessment

Relative risks and 95% confidence intervals (CIs) for diabetes were extracted and entered into Comprehensive Meta-Analysis (CMA) software version 3.0 (Biostat, Englewood, NJ, USA, 2014). Random-effects models were used for all analyses, given that true effects are likely to vary across studies (rather than a fixed-model, which assumes the same value or true effect for all studies) ³⁹. In all studies, the RR estimates extracted were those comparing the highest to the lowest level of PA. A second analysis was conducted among studies ^{17, 21, 28, 37, 38} that used the current DHHS moderate-intensity aerobic PA guideline of at least 150 min/wk as their demarcation point for PA ⁸ (i.e., comparing those who met the recommendations to those who did not). Race-ethnic groups utilized in the secondary analysis included all identified previously except American Indians.

Quality assessment was performed using the Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies ⁴⁰ which uses a 14 question scale (higher score corresponding to higher quality) to assess quality. All studies were independently rated by two researchers (W.B. and E.F.); all studies were rated as 'good' (average Quality Assessment score= 10.9, range 10–11). Since the studies were all of good quality, analyses examining the potential impact of differential study quality on the main RR effects were not conducted.

Data Synthesis and Analysis

Data analysis was conducted using CMA software version 3.0. Heterogeneity was quantified using I^2 ; a descriptive index that estimates the ratio of true variation (heterogeneity) to total variation across the observed effect sizes ³⁹. An overall main effect of PA on type 2 diabetes was calculated for each race-ethnic group. A second analysis was conducted to assess the overall effect of meeting the 2008 DHHS moderate-intensity aerobic PA recommendation on type 2 diabetes risk ⁸. Significance for the main effects was set at 0.05. Potential publication bias was examined using a funnel plot.

RESULTS

A total of 1,150,574 participants were identified across all studies meeting the inclusion criteria. Table 1 illustrates the characteristics of the individual studies (N=27). Duration of follow-up ranged from two 30 to twenty-eight years 35 . Studies were conducted in the U.S.

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(n=9) and internationally (n=17), with one study conducted in both the U.S. and Canada ³⁰. The method for identifying cases of type 2 diabetes varied by study and included ascertainment by medical records; report of insulin or medication use; 2 hr oral glucose tolerance tests; fasting plasma glucose, or self-report of a physician diagnosis. Potential publication bias was not detected in the funnel plot (supplemental figure 1 [supp. 1.]).

Figures 2–6 show the results comparing the most active to the least active groups among the race-ethnic groups examined (Figure 2: NHW, Figure 3: Asian, Figure 4: Hispanic, Figure 5: American Indian, Figure 6: NHB). Significant, and similar, summary RRs for PA and type 2 diabetes were found for NHWs (RR 0.71, 95% CI 0.60–0.85), Asians (RR 0.76, 95% CI 0.67–0.85), Hispanics (RR 0.74, 95% CI 0.64–0.84), and American Indians (RR 0.73, 95% CI 0.60–0.88). The summary effect for NHBs (RR 0.91, 95% CI 0.76–1.08) did not attain statistical significance.

In analyses examining the 2008 DHHS moderate-intensity aerobic PA recommendation and diabetes risk by race-ethnicity (data not shown), a suggestion of a significant trend was observed for NHWs (RR 0.75. 95% CI 0.55–1.01, p=0.06) and Asians (RR 0.80, 95% CI 0.64–1.01, p=0.06), but the estimates did not attain statistical significance. The summary effects for meeting the 2008 DHHS moderate-intensity aerobic PA recommendation and diabetes risk among NHBs (RR 1.26, 95% CI 0.84–1.90) and Hispanics (RR 0.95, 95% CI 0.66–1.65) did not attain statistical significance.

Sensitivity analyses were conducted to examine the effect of removing a single study on the overall summary effects by race-ethnic group (data not shown). No significant changes were found to the race-ethnic specific summary RRs with the exception of Hispanics. When removing Hsia et al. ¹⁸ from the Hispanic analysis, statistical significance was lost (RR 0.79, 95% CI 0.60–1.03, p=0.09). Furthermore, when removing Ma et al. ²⁵ from the analysis, similar results were found (RR 0.89, 95% CI 0.65–1.22, p=0.46).

DISCUSSION

This systematic review and meta-analysis provides insight into race-ethnic differences in the effect of aerobic PA on type 2 diabetes risk. With the exception of NHBs, a similar magnitude of protection was found comparing the most active to the least active groups, ranging from 24% (among Asians) to 29% (among NHWs). The summary estimate for NHBs, though protective, did not attain statistical significance. The results of this analysis add to the existing literature on PA and type 2 diabetes ^{6, 10} by demonstrating effect modification by race-ethnicity.

Previous work ^{7, 41–43} has also found that there may be race-ethnicity specific differences in the volume of aerobic PA necessary to elicit protection against type 2 diabetes. Celis-Morales et al. ⁴¹ found that Asian men needed 266 min/wk of moderate aerobic PA in order to achieve similar cardiometabolic profiles (inclusive of fasting glucose and fasting insulin) as NHW men participating in 150 min/wk of moderate aerobic PA. Steinbrecher et al. ⁴², in a study contrasting race-ethnic specific differences of type 2 diabetes risk with PA, found that moderate intensity PA was associated with lower risk for type 2 diabetes only among

NHW males and females. In the same study, Native Hawaiians and Japanese Americans were found to receive no protection from moderate intensity PA. However, vigorous intensity sport activity was associated with lower risk for type 2 diabetes across all race-ethnic groups independent of gender. These results indicate that higher volumes, as well as a higher intensity, may be needed to provide similar protection from type 2 diabetes across various race-ethnic groups.

Among the studies included the current analysis, four studies directly reported the racespecific RRs based upon meeting versus not meeting the current DHHS moderate-intensity aerobic PA recommendation and type 2 diabetes risk. The summary results of these studies suggest a trend towards significant protection against type 2 diabetes for Asians and NHWs, but not NHBs or Hispanics. While these results need to be interpreted with caution, this illustrates a lack of studies specifically examining how meeting the current moderateintensity aerobic PA guideline relates to type 2 diabetes risk. Previous work in the Diabetes Prevention Program ⁵ (designed to examine how lifestyle change inclusive of PA, dietary change and weight loss impacts type 2 diabetes risk) indicated that lifestyle intervention, inclusive of 150 min/wk of moderate aerobic PA, significantly reduced the incidence of type 2 diabetes in NHWs, NHBs, Asians, Hispanics and American Indians. It is possible that meeting the recommendations may not have a significant impact on diabetes risk reduction among NHBs without the addition of weight loss and dietary intervention; however more research is needed.

The discussion above, in addition to the results of the current meta-analysis, prompted the current authors to examine/review possible underlying physiological mechanisms that explain the race-ethnic differences in the protective role of PA. Further, the current results warranted specific focus on these mechanisms in NHBs.

Mechanisms proposed

There are several physiological mechanisms proposed that could explain the lack of significance found for NHBs in the current analysis. These include: 1) genetic predisposition, 2) compromised hepatic suppression of endogenous glucose production (EGP) in response to insulin, 3) lower insulin sensitivity (S_i) in the peripheral tissues (specifically skeletal muscle) despite similar volumes of aerobic PA, 4) a down regulation of insulin receptors driven by hyperinsulinemia and decreased hepatic insulin clearance, 5) increases in intramuscular adipose tissue (IMAT) and intra-myocellular lipid content (IMCL) deposits, and 6) skeletal muscle fiber type differences.

It is well known that decreases in S_i are related to an increased risk for type 2 diabetes ^{44, 45}. Lakoski and colleagues ⁴⁶, when comparing NHBs to NHWs, found similar changes in the homeostatic model assessment of insulin resistance (HOMA-IR) for every 10 minute increase in MVPA, moderate PA, or vigorous PA. Among NHB and NHW women, Irwin and colleagues ⁴⁷ reported similar decreases in fasting insulin levels for every 90 MET-min/d change. Another study conducted by Hasson et al. ⁴⁸ found no differences in the acute improvements in whole-body S_i comparing NHBs to NHWs following a single 75 minute bout of exercise at 75% VO₂ max. The results of these studies indicate that NHBs and NHW have similar physiological responses in the change in S_i from PA. However, similar levels of

 S_i among NHWs and NHBs may not be indicative of similar risk profiles for type 2 diabetes as other factors may contribute.

1. Genetic predisposition—Despite the similar changes in S_i in response to PA, NHBs tend to have lower initial S; compared to NHWs ⁴⁹⁻⁵¹; which may contribute to the lack of significance found in the current study. Further explanation of this potential increased susceptibility to diabetes is associated with the relationship between whole-body S_i and insulin response in NHBs compared to NHW and Asians. In a recent systematic review, Kodama et al. ⁵⁰ calculated and illustrated the relationship between whole-body S_i and the acute-insulin response to glucose (AIRg). Specifically in NHBs with normal glucose tolerance (NGT), the authors concluded that due to the relationship found between S_i and AIRg, even the slightest decrease in S_i results in large nonlinear increases in AIRg which plays a role in the progression towards type 2 diabetes. In contrast, these changes in S_i among NHWs and Asians result in a vastly lower magnitude of changes in AIRg. In other words, among NHBs, the slightest decrease in S_i results in a large increase in the volume of insulin needed to maintain normal blood glucose. Furthermore, NHBs with similar Si values had significantly higher AIRg compared to NHWs. This relationship was further confirmed in a study by Albu et al. ⁵² which found higher AIRg in NHBs during an intravenousglucose-tolerance test independent of Si, visceral adipose tissue, intramuscular adipose tissue (IMAT), subcutaneous adipose tissue, and skeletal muscle mass. Thus Kodama et al. ⁵⁰ and Albu et al. ⁵² conclude there is underlying genetic phenotype in NHBs that may predispose them to increased risk to type 2 diabetes reflected by this relationship.

2. Hepatic influence—Previous research examining the potential mechanism behind why NHBs are at a higher risk for type 2 diabetes has focused on the contributions of hepatic glycemic function. Insulin acts primarily on the peripheral tissues but also has inhibitory effects on hepatic endogenous glucose production (EGP) $^{53, 54}$. EGP has been shown to be the primary determinant of glucose tolerance 55 as well as a contributor to the development of type 2 diabetes 56 . The aforementioned mechanisms may contribute to the lack of significant findings for NHBs in the current meta-analysis. While still controversial, a review by Gaillard et al. 57 suggested that impaired EGP may be a contributing factor to the increased susceptibility of NHBs to type 2 diabetes compared to NHWs. Moreover, in studies that showed similar EGP between NHBs and NHWs, AIRg tended to be higher in NHBs which is indicative of the increased compensation of the pancreatic β -cells to secrete more insulin. Thus, while EGP is linked to increased risk for type 2 diabetes, this proposed mechanism may not be a driving factor as results are equivocal.

3. Peripheral S_i—A review by Gaillard et al. ⁵⁷ showed that while hepatic S_i differences between NHBs and NHWs remains uncertain, peripheral S_i tends to be lower among NHBs. With the established association between type 2 diabetes risk and peripheral S_i; another mechanism to describe the findings of the current study is a diminished response of the skeletal muscle to changes in peripheral S_i. Delany et al. ⁴³ revealed that participation in similar volumes of objectively measured PA (via upper extremity activity monitors), peripheral S_i (calculated by dividing the rate of glucose disposal by the plasma insulin concentration) was 26% lower in NHBs compared to NHWs in the absence of obesity.

Furthermore, hepatic S_i as well as EGP was similar between groups. Haffner et al. ⁵⁸ found lower peripheral S_i (quantified by insulin-mediated glucose-disposal) independent of aerobic PA. The results of these studies indicate that aerobic PA may not affect peripheral S_i in the same manner that it affects hepatic S_i , especially in NHBs, which could explain the lack of significance found in the current analysis. However, more research is warranted to confirm.

4. Hepatic Insulin Clearance—The consistent findings ^{50, 57} that show NHBs have higher AIRg compared to NHWs even with similar values of S_i could also explain the differences seen in peripheral S_i . Higher AIRg is related to decreases in hepatic insulin clearance ^{50, 59}. Gaillard et al. ⁵⁷ suggested that the compensatory hyperinsulinemic response to a diminished hepatic insulin clearance may contribute to the down-regulation of the skeletal muscle insulin receptors. This would directly lead to decreases in peripheral S_i . It can also be postulated that this mechanism would manifest independent of aerobic PA as aerobic PA does not seem to impact AIRg in the same way as is does hepatic S_i . However, as stated by Gaillard et al. ⁵⁷ this needs further exploration.

5. Skeletal muscle adiposity—One mechanism that may influence the decreased peripheral S_i in NHBs is IMAT and intra-myocellular lipid content (IMCL). IMAT, defined as the adipose tissue found within the muscle fascia, has been linked to a decrease in S_i through inhibition of the insulin signaling pathway ⁶⁰ leading to compromised insulinstimulated glucose uptake and decreased S_i. A recent study by Goedecke et al. ⁶¹ showed that, in NHB women, increased IMCL defined as the accumulation of lipid particles within the muscle cell, and muscle fat % (IMAT) in the soleus were significantly correlated with lower S_i. NHW women had no relationship between IMCL and S_i. It is important to note that dietary habits and PA volume were similar between groups. Albu et al. ⁵² showed that despite similar overall associations, NHB women had significantly lower S_i across volumes of IMAT compared to NHWs. Furthermore, the study participants had similar PA volumes. The results of these studies indicate that independent of PA, the increase in skeletal muscle lipid content may play a role in the decreased peripheral S_i observed in NHBs. However, Ingram et al. ⁶² found conflicting evidence in NHB participants who had no significant correlation between IMCL and decreased peripheral S_i; but NHWs did. Study participants were sedentary and no differences were found in regards to PA between groups. While this mechanism may explain differences in peripheral S_i and perhaps the lack of significance in the current study, more research is needed to isolate the true effects of skeletal muscle lipid accumulation on S_i and type 2 diabetes risk.

6. Skeletal muscle fiber type—Another mechanism that could contribute to lower S_i and compromised glucose control ⁶³, is a higher percentage of type II skeletal muscle fibers that can be found among NHBs compared to NHWs. Previous research contrasting race-ethnic groups has suggested a potential predisposition to an increased risk for type 2 diabetes with higher percentages of type II fibers ^{63, 64}. More specifically, among lean, obese or participants with type 2 diabetes, type I fibers have been shown to have a higher expression of GLUT4, a greater insulin-stimulate glucose disposal rate, higher glucose oxidation rates and higher nonoxidative glucose metabolism compared to type II fibers ⁶⁵. Interestingly, the expression of proteins specific to the effects of insulin were similar across fiber types i.e.

phosphoregulation. However, the study suggests that there needs to be more research to examine how phosphoregulation itself relates to glucose uptake and similar phosphoregulation might not mediate S_i differences between fiber types. These results were futher confirmed by Daugaard et al. ⁶⁶ who showed that only type I fibers had a significant increase in the expression of GLUT4 compared to both IIa and IIx fibers following two weeks of one-leg knee extensor training at 65% of maximum workload. The authors also conclude that increasing the intensity of the activity could have led to different findings i.e. changes in GLUT4 expression among Type II fibers. Thus, PA at higher intensities may be necessary to elicit the same benefits as those with higher percentages of type I fibers ⁶⁴. However, more research is needed to confirm this hypothesis especially among NHBs. Nevertheless, among NHBs there is evidence to suggest that the biochemical differences between type I and type II fibers coupled with a higher percentage of type II fibers may help partially explain the findings of the current study.

Limitations

This study is not without limitations. First, all meta-analyses are subject to potential publication bias ³⁹. We attempted to examine potential bias using a funnel plot procedure. which revealed no issues in regards to potential publication bias. Nonetheless, this issue is inherent to the systematic review process. Another limitation is that PA was self-reported in the studies used with the exception of one which used pedometers. Previous literature has shown limitations to using self-reported PA measures which may overestimate time spent in MVPA as well as failure to capture other intensities or sporadic activity ^{67, 68}. Also, the lack of studies specifically examining the relationship between PA and type 2 diabetes using the current DHHS aerobic PA recommendation does not provide enough evidence to clearly draw conclusions. The final limitation relates to inherent issues regarding the definitions of race-ethnicity ⁶⁹. More specifically, only four of the definitions we used are considered to be race (NHB, NHW, Asian, and American Indian) and one is considered to be ethnicity (Hispanic) ⁷⁰. Furthermore, there were semi-heterogeneous definitions of "race" and "ethnicity" used across the studies in this analysis. The authors of the current study elected to group study participants into five common race-ethnic groups found in the literature to provide the best insight into the race-ethnic specific relationship between aerobic PA and type 2 diabetes risk.

Future Directions

In the current meta-analysis, there was an evident paucity of prospective cohort studies reporting race-ethnic specific RRs, specifically in NHBs (N=5), Hispanics (N=3), and American Indians (N=5). Sensitivity analyses revealed a complete loss of statistical significance when Hsia et al. ¹⁸ or Ma et al. ²⁵ were removed from the model; thus the interpretability of the summary RR for Hispanics is drastically limited by the available literature. Therefore, priorities for future research in this area should include prospective cohort studies examining PA and type 2 diabetes among multi-ethnic cohorts to examine and report risk across race-ethnic groups (rather than using race-ethnicity as a confounding variable). Furthermore, due to the mechanisms discussed previously, it is also evident that specific intensities should be examined as intensity may play a role in reducing risk for type 2 diabetes in NHBs.

Conclusion

In conclusion, with the exception of NHBs, PA plays a significant role in reducing the risk for type 2 diabetes across race-ethnic groups. Furthermore, the current study illustrates the need to continue investigating effect modification of relationship by race-ethnicity, as well as the need to examine the effect modification between the current aerobic PA guideline and type 2 diabetes risk by race-ethnicity. There are several complex, physiological mechanisms that may explain the findings of the current study, which suggest there may be different race-specific thresholds in regards to the minimum aerobic PA needed to significantly reduce the risk for type 2 diabetes. Future studies may lead to a re-examination of the current aerobic PA guideline for potential changes specific to race-ethnicity.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

There is a significant and similar risk reduction associated with physical activity across race-ethnicity with the exception of non-Hispanic blacks

There are several physiological mechanisms that may explain this finding that are in need of further exploration in the context of physical activity



Figure 1. Prisma Flow Chart



Figure 2.

Relative risks for diabetes by aerobic physical activity (most vs. least): NHW adults. N = 238,719. RR: Relative Risk. LCL: Low 95% Confidence Limit. UCL: Upper 95% Confidence Limit. WGHT: Weight



Figure 3.

Relative risks for diabetes by aerobic physical activity (most vs. least): Asian adults. N = 928,319. RR: Relative Risk. LCL: Low 95% Confidence Limit. UCL: Upper 95% Confidence Limit. WGHT: Weight



Figure 4.

Relative risks for diabetes by aerobic physical activity (most vs. least): Hispanic adults. N = 10,817. RR: Relative Risk. LCL: Low 95% Confidence Limit. UCL: Upper 95% Confidence Limit. WGHT: Weight



Figure 5.

Relative risks for diabetes by aerobic physical activity (most vs. least): American Indian adults.

N = 7,022. RR: Relative Risk. LCL: Low 95% Confidence Limit. UCL: Upper 95% Confidence Limit. WGHT: Weight



Figure 6.

Relative risks for diabetes by aerobic physical activity (most vs. least): Non-Hispanic Black adults

N = 30,452. RR: Relative Risk. LCL: Low 95% Confidence Limit. UCL: Upper 95% Confidence Limit. WGHT: Weight

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Table 1

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Author (ref)	Race	Country	Gender	Age(years)	z	Physical activity measure	Follow-up (years)	Adjustments
Burchfield, 1995	Asian	U.S.	W	45 – 68	6,815	hrs x estimated O ₂ consumption	Q	age, BMI, subscapular/ triceps skinfold ratio, systolic blood pressure, triglycerides, glucose, hematocrit, parental history of diabetes
Burke, 2007	MHN	Australia	M/F	15 - 88	514	y/w/p	14	sex, age, BMI, location
Fan, 2015	Asian	China	M/F	35 - 74	6,348	MET-hrs	6.7	age, sex, geographic region (north or south), educational level (0–6, 7– 9, or 10 yr), cigarette smoking (nevet, ever, or current), alcohol consumption (yes or no), BMI, waist circumference
Fretts, 2009	American Indians	U.S.	M/F	45 - 74	1,651	MET-hrs/wk	10	age, study site, sex, education (less than high school, high school, post- high school), cigarette smoking (never, ever, current), alcohol use (never, ever, current), FH of diabetes
Fretts, 2014	American Indians	U.S.	M/F	18 - 74	1,639	Steps/d	8	age, sex, site, education (years), FH of diabetes
Honda, 2015	Asian	Japan	M/F	30 - 64	26,628	MET-hrs	5.2	age, sex, shift work, sleep duration, alcohol consumption, smoking, hyperension, a family history of diabetes, occupational activity, and walking for commuting to and from work
Hsia, 2005	NHW, Asian, Non- Hispanic Black, Hispanic, American Indian	U.S.	ц	No range presented	Total: 86,708 NHW: 74,240 Non- Hispanic 6,465 Asian: 2,445 Hispanic: 3,231	MET-hrs/wk	4 8 - 8	alcohol (past/never vs current drinker), education, smoking, hypertension, hypercholesterolemia, dietary fiber (g), percent energy from carbohydrate

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Author (ref)	Race	Country	Gender	Age(years)	Z	Physical activity measure	Follow-up (years)	Adjustments
					American Indian: 327			
Hu, 2004	MHN	Finland	M/F	45 - 64	4,369	min	9.4	age, sex, study year, systolic blood pressure, smoking status, education, BMI
James, 1998	Non-Hispanic Black	U.S.	M/F	30 - 55	916	Categorized by min into inactive, moderate or strenuous	5	age, sex, education, BMI, WHR
Joseph, 2016	NHW, Asian, Non- Hispanic Black, Hispanic	U.S.	M/F	45 - 84	Total: 5,348 NHW: 2,277 Non- Hispanic Black: 1,293 Asian: 676 Hispanic: 1,102	MET-min/wk	ΓΠ	age, education, sex, study site, race/ethnicity, occupational status, alcohol use, estimated glomerular filtration rate, other cardiovascular health components
Koloverou, 2014	MHN	Greece	M/F	32 – 59	1,485	Total min	10	age
Kriska, 2003	American Indian	U.S.	M/F	15 – 59	1,728	MET-hrs/wk	6	age, BMI
Lee, 2012	Asian	Korea	W	18	675,496	min/wk	7.5	age, smoking status, alcohol intake, hypertension, parental diabetes, baseline glucose, BMI
Ma, 2012	NHW, Asian, Non- Hispanic Black, Hispanic	U.S.	Ľ	50-79	Total: 158,833 NHW: 133,541 Non- Hispanic Black: 14,618 Asian: 4,190 Hispanic: 6,484	MET-hrs/wk	10.4	age, FH of diabetes, hormone therapy use, study arm, each lifestyle risk factor
Nakanishi, 2004	Asian	Japan	W	35 – 59	2,924	Daily energy expenditure (kcals)	7	age, FH of diabetes, alcohol consumption, cigarette smoking, BMI, weekly energy expenditure on physical exercise, systolic blood presure, HDL cholesterol, triglycerides

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Author (ref)	Race	Country	Gender	Age(years)	z	Physical activity measure	Follow-up (years)	Adjustments
Okada, 2000	Asian	Japan	Μ	35 - 60	6,013	d/wk	59,966 person-years	age, BMI, alcohol consumption, smoking habits, blood pressure, parental history of Type 2 diabetes
Panagiotakos, 2008	MHN	Greece	M/F	>18	1,806	MET-min/wk	5	age
Shi, 2013	Asian	China	W	40 - 74	51,464	METS	5.4	age, energy intake, smoking, alcohol consumption, education level, occupation, income FH of diabetes
Tonstad, 2013 (subsample of Non- Hispanic Blacks)	Non-Hispanic Black	U.S. and Canada	M/F	30	7,160	d/wk	2	age
Tsai, 2015	Asian	Taiwan	M/F	53	2,995	d/wk	14	age
Villegas, 2006	Asian	China	Ъ	40 - 70	70,658	METS	4.6	age, kcal/d, education level, income level, occupation, smoking, alcohol, hypertension, chronic diseases
Villegas, 2009	Asian	China	Ч	40 - 70	62,227	METs/d	4.6	age, WHR, BMI, kcal/d, alcohol consumption, smoking, education level, income level, occupation, hypertension
Waki, 2005	Asian	Japan	M/F	40 - 59	28,896	times/wk engaged in activity	10	age
Waller, 2010	MHN	Finland	M/F	18	20,487	MET-hrs/d	28	age, BMI
Wang. 2010	American Indians	U.S.	M/F	45 – 74	1,677	MET-hrs/wk	7.8	age, sex
Xu, 2012	Asian	China	M/F	35	3,031	min/wk	З	age, sex, residence area, educational attainment, BMI category, ciganette smoking, alcohol drinking, TV viewing, vegetables intake, meat intake, diagnosed hypertension
Xu, 2015	Asian	China	M/F	35	4,550	min/wk	ę	age, gender, educational attainment, FH/PA, body weight status, cigarette smoking, alcohol drinking, TV viewing, vegetables intake, meat intake, diagnosed hypertension

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U.S. = United States, M = Male, F = Female, MET = Metabolic Equivalent, hr = Hour, BMI = Body Mass Index, WHR = Waist-to-hip ratio, kcal = Kilocalorie, FH = Family History, TV = Television, HDL = High-density lipoprotein cholesterol