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# Associations of Physical Activity and Lactation Duration With Cardiometabolic Risk Factors:

The CARDIA Study

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# Abstract

**BACKGROUND**—Physical activity (PA) and lactation benefit cardiometabolic health.

**OBJECTIVES**—The purpose of this study was to describe the joint associations of PA and lactation with cardiometabolic risk.

**METHODS**—We averaged PA across exams and summed lifetime lactation in Black and White parous women in the Coronary Artery Risk Development in Young Adults Study. Categories were created for PA (–PA: <median; +PA: median) and lactation (–L: <3 months, +L: 3 months). Participants were assigned to one of 4 groups: –PA/–L, –PA/+L, +PA/–L, and +PA/+L (most favorable). Cardiometabolic risk factors at the year 30 exam were standardized into a risk score. We evaluated associations of groups with risk factors and risk score using linear regression.

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APPENDIX For supplemental tables, please see the online version of this paper.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

Covariates included age, race, study center, parity, education, smoking, medication use, alcohol consumption, and baseline body mass index, and diet quality.

**RESULTS**—The median PA was 256 exercise units and 54% reported lactation duration of 3 months. Of 1,068 participants, 303 were in the -PA/-L category, 231 in -PA/+L, 184 in +PA/-L, and 350 in +PA/+L. +PA/+L participants were older, had more years of education, lower body mass index, gained less weight, and less likely to be Black vs -PA/-L participants. Risk scores differed between categories except -PA/+L and +PA/-L (P=0.08): -PA/-L: 0.23+/-0.04, -PA/+L: 0.08+/-0.04, +PA/-L: -0.02+/-0.05, and +PA/+L: -0.23+/-0.03. After adjustment, +PA/+L was associated with a lower/better risk score ( $\beta = -0.15$ , 95% CI: -0.25 to -0.04).

**CONCLUSIONS**—Above average PA throughout adulthood combined with 3 months of lactation was associated with lower risk scores. Participants with either behavior had lower risk vs those with neither behavior. Attaining these levels of behaviors may reduce cardiometabolic risk in parous women.

#### **Keywords**

cardiometabolic risk; lactation; physical activity

There are many cardiometabolic-related health benefits of physical activity (PA) and lactation for women. Habitual PA has a beneficial effect on lowering fasting glucose and insulin levels, and PA reduces the long-term risk of hypertension, type 2 diabetes, the metabolic syndrome, and cardiovascular disease in women.<sup>1</sup> PA also promotes glucose uptake by skeletal muscle, the mobilization of fat stores, more favorable lipid levels, and reduces risk of excessive weight gain over time.<sup>2,3</sup> Higher intensity lactation is also associated with lower fasting blood glucose and insulin concentrations, and longer lactation duration may lower risk of progression to type 2 diabetes, and the metabolic syndrome and lower the prevalence of hypertension, hyperlipidemia, and cardiovascular disease in women.<sup>4–8</sup> Evidence from human and animal studies suggested that extended lactation increases mobilization of adipose tissue stored accumulated during pregnancy in some,<sup>6,9</sup> but not all studies.<sup>10</sup>

During lactation, the mammary glands divert approximately 50 g of glucose per day via a non-insulin-mediated pathway,<sup>11</sup> and insulin secretion rates are lower in lactating women.<sup>12</sup> Breastfeeding also stimulates the hormone prolactin, which is associated with the preservation of pancreatic beta-cell mass and mobilization of adipose tissue stores.<sup>13</sup> Lactating women have a higher maternal basal metabolic rate compared to non-lactating women,<sup>12,14,15</sup> with the lactating breast requiring approximately 25% of the body's daily energy production.<sup>16</sup> However, the additional energy need can be met by dietary intake of 300 kilocalories per day.<sup>12,17,18</sup>

To our knowledge, no studies have examined the joint associations of PA and lactation duration on cardiometabolic risk later in life. Accordingly, our purpose was to evaluate the associations of cumulative, self-reported PA volume and lactation duration, assessed over 30 years of follow-up, with a variety of cardiometabolic risk factors and standardized risk score after pregnancy.<sup>19</sup> We hypothesized that women with a cumulative level of PA

above the median throughout the 30 years of attended exams and at least a moderate duration of lifetime lactation achieved around childbearing would have the most favorable cardiometabolic risk profile. As PA and lactation behaviors tend to be influenced by personal, environmental, and socioeconomic factors,<sup>8,20–22</sup> we conducted our analyses in a well-characterized cohort of racially and socioeconomically diverse women and performed stratified analyses to better account for the influence of unmeasured factors on our findings.

#### **METHODS**

#### THE CORONARY ARTERY RISK DEVELOPMENT IN YOUNG ADULTS STUDY.

The CARDIA (Coronary Artery Risk Development in Young Adults) Study is a longitudinal, multicenter, population-based observational study designed to investigate determinants of coronary heart disease and its risk factors in Black and White men and women. At baseline (Y0) in 1985–1986, 5,115 participants ages 18 to 30 years (53% women and 52% Black adults) were recruited from 4 urban areas in the United States: Birmingham, Alabama; Oakland, California; Chicago, Illinois; and Minneapolis, Minnesota. The CARDIA Study was approved by Institutional Review Boards at each center. All participants signed written, informed consent. Of the 2,787 women initially enrolled in CARDIA, only women who reported at least one post-baseline birth and attended the year 30 exam (Y30) were included in the analyses, for a final analytic sample of 1,068 women.

#### PHYSICAL ACTIVITY.

Self-reported PA was assessed at each exam using the CARDIA Physical Activity History questionnaire and reported in exercise units as details regarding PA frequency or duration were not assessed directly.<sup>23,24</sup> Participants were asked about participation in 13 different recreational sport, exercise, or leisure activities (8 vigorous intensity activities and 5 moderate intensity activities), and total moderate-vigorous PA was determined by multiplying the number of months the activity was performed by the intensity of the activity.<sup>24</sup> Activities were weighted by frequency and summed across all activities. A score of 300 exercise units is roughly equivalent to meeting PA guidelines.<sup>23</sup> We averaged total exercise units across all attended exams to have a cumulative assessment of total PA. PA was then categorized into 2 groups representing PA below vs equal to or above the median. This average PA score represented PA across all attended exams, encompassing 30 years of data collection.

#### LACTATION DURATION.

Lactation was self-reported for each birth at year 7 for all previous birth(s) and for each new birth at subsequent exams. If women reported breastfeeding their child, they were asked to select from one of the following duration categories: none, >0 but <6 weeks, 6 weeks to 11 weeks, 3 to 6 months, or 6 months or more. To calculate duration in this study, we used the midpoint of each lactation category for each birth: 21 days for <6 weeks, 66 days for 6 to 11 weeks, 135 days for 3 to 6 months, and 210 days as the upper limit for 6 months or more, as previously reported in CARDIA.<sup>8</sup> We then summed lactation duration in days across all births. We examined lactation duration as a continuous measure and categorized

into 2 groups, ie, 0 to 89 days (<3 months) and 90 days (3 months) of cumulative lactation duration. The 3 months of lactation could be achieved across multiple births.

#### PARITY AND PREGNANCY COMPLICATIONS.

Information regarding pregnancies, number of births (parity), birth outcomes, lactation, and pregnancy complications were obtained using questionnaires at each CARDIA exam. Gestational diabetes mellitus (GDM) was self-reported, and a validation study conducted in 165 women that included 200 pregnancies demonstrated high sensitivity (100%) and specificity (92%) for self-reported GDM in CARDIA.<sup>8</sup> We only included parous women in our analyses to account for any effect of childbearing itself on our exposures and outcomes.

#### **BLOOD PRESSURE.**

Blood pressure (BP) was measured in triplicate by a trained technician in the right arm using an oscillometer (HEM907XL Omron Corp) in the seated position after a 5-minute rest. There was a 1-minute break in between measurements. Cuff size was determined by measuring the arm circumference midway between the acromion process and olecranon. The final 2 measurements were averaged for analysis. Self-report of hypertension diagnosis and treatment were noted at each exam using standardized surveys. We defined hypertension as a systolic BP 130 mmHg, diastolic BP 80 mmHg, or current use of antihypertensive medication.

#### CARDIOMETABOLIC RISK FACTORS AND CARDIOMETABOLIC RISK SCORE.

Waist circumference (WC) was measured horizontally at the midpoint between the iliac crest and lowest portion of the ribcage and measured anteriorly at the midpoint between the xiphoid process and the umbilicus. Fasting collection for glucose, insulin, cholesterol, and HDL-C was conducted using standardized CARDIA protocols and serum was processed at central laboratories. Lipid profile was calculated by summing triglycerides and LDL-C and subtracting HDL-C. After an overnight fast of 10 hours, blood was drawn via venipuncture, and glucose concentrations were measured by the hexokinase ultraviolet method at baseline and hexokinase coupled to glucose-6-phosphate dehydrogenase in other CARDIA examinations. Insulin levels were assessed with radioimmunoassay. We calculated the homeostasis model assessment of insulin resistance (HOMA-IR) as previously described to evaluate insulin resistance: HOMA-IR = (fasting glucose  $[mg/dL] \times$  fasting insulin  $[\mu U/mL]$ /405.0.<sup>25</sup> We calculated a cardiometabolic risk score as previously described in the CARDIA study.<sup>26,27</sup> Briefly, the cardiometabolic risk score was determined by standardizing and summing individual risk variables, including WC, average of systolic and diastolic blood pressures (mean BP), fasting blood glucose, insulin, triglycerides, and negative HDL-C, and dividing by 6 to calculate a z-score. Higher scores indicate greater cardiometabolic risk.

#### COVARIATES.

Participants self-reported their race, education, medical history, medication usage, cigarette smoking status, and alcohol consumption at each exam. Using data from an interviewer-administered diet history questionnaire developed for the CARDIA study, an a priori diet

score was developed to quantify overall diet quality in CARDIA.<sup>28</sup> A higher diet score is better and indicates a healthier diet.<sup>28</sup> Body weight was measured without shoes and in light clothing to the nearest 0.2 kg with a calibrated balance beam scale. Height recorded to the nearest 0.5 cm. Body mass index (BMI) was calculated as weight (in kilograms) divided by height in meters squared in each exam.

#### STATISTICAL ANALYSES.

After assessing normality, differences in participant characteristics and cardiometabolic risk factors were evaluated with Kruskal-Wallis and chi-square tests with nonpara-metric post hoc corrections (Dunn's test) applied if the main analysis was significant. Multivariable linear regression models were used to evaluate the joint associations of cumulative PA (2 categories: above and below the median) and cumulative lactation duration (2 categories: 0 to <3 months vs 3 months or more) with the cardiometabolic risk score and with each cardiometabolic risk factor, including: WC, lipid profiles (described above), glucose, insulin, 2-hour oral glucose tolerance test results, HOMA-IR, percent of glycated hemoglobin (HBA1c), and mean BP. All models adjusted for Y30 study center, race, age, education, parity, medication use for diabetes, cholesterol, and hypertension, current hormone replacement therapy use, alcohol consumption, smoking status, baseline (Y0) diet quality, and baseline BMI. The baseline (Y0) cardiometabolic risk factor of interest was added to the model for risk factor outcomes when available (eg, model examining year 30 WC adjusted for baseline (Y0) WC). The baseline value was available for all individual risk factors except HbA1c and the 2-hour oral glucose tolerance test. BMI change from baseline to Y30 was added to the final model (model 2) to assess its role in the mediation of the associations between PA/lactation and metabolic risk factors. A change in beta 20% indicated a potential confounding effect of BMI change over follow-up on the association. Analyses were conducted in the total sample and stratified by race and history of GDM given the strong association of GDM with the cardiometabolic risk factors we included as outcomes<sup>29</sup> and associations of lactation with lower cardiometabolic risk after GDM.<sup>8,30</sup> In a sensitivity analysis, we added the baseline (Y0) cardiometabolic risk score to the risk score models to account for any baseline differences in risk scores between groups.

#### RESULTS

#### PARTICIPANTS.

Our final sample included 1,068 women, and 1,047 of these participants had the complete risk factor data needed to calculate the risk score. A total of 303 women (28.4%) reported low PA, ie, mean exercise units below the median and <3 months of lactation (–PA/–L), 231 (21.6%) reported low PA, ie, exercise units below the median and at least 3 months of lactation (–PA/+L), 184 (17.4%) reported high PA and <3 months of lactation (+PA/–L), and 350 (32.6%) women reported high PA and at least 3 months of lactation (+PA/+L). Age, race, education, smoking status, and baseline diet quality differed between categories. Proportion of participants using diabetes, cholesterol, and hyper-tension medications was higher in the –PA/–L category. Participant characteristics at Y30 by joint PA and lactation categories are shown in Table 1; characteristics at baseline (Y0) are found in Supplemental Table 1.

#### PHYSICAL ACTIVITY.

Mean PA across attended exams was  $293 \pm 178$  exercise units, and median PA was 256 (IQR: 168–379) exercise units. Women in the +PA groups performed a median of 379 (95% CI: 310–506) exercise units while women in the –PA groups performed a median of 168 (95% CI: 113–204) exercise units across attended exams. Group means are shown in Table 1.

#### LACTATION DURATION.

Of the 1,068 women, 766 (71.7%) reported any history of lactation. A total of 581 women (54.3%) reported a cumulative lactation duration of at least 3 months, and 447 women (41.9%) reported cumulative lactation duration of at least 6 months. Median lactation duration was 4.5 months, and multiparas made up 77.3% of the sample. Group means for lactation in days are shown in Table 1.

#### CARDIOMETABOLIC RISK FACTORS AND RISK SCORE.

Cardiometabolic risk factors and risk scores differed by joint lactation and PA categories, though there was no significant difference in cardiometabolic risk between -PA/+L and +PA/-L categories, P = 0.08. In general, women in the -PA/-L category had the most adverse and women in the +PA/+L category had the most favorable levels of individual cardiometabolic variables and cardiometabolic risk scores (Table 1, Figure 1).

#### **REGRESSION.**

Assignment to the +PA/+L category was associated with lower WC, insulin, HOMA, and HbA1c, but only the association for WC persisted after adjustment for 30-year BMI change. The change in beta coefficient exceeded 20% after accounting for BMI change for almost every individual cardiometabolic risk factor.

Assignment to the +PA/+L category was associated with better cardiometabolic risk score in adjusted analyses (Tables 2 and 3). When we included change in BMI from Y0-Y30, the beta coefficient for the association was reduced by almost 70% and was no longer significant.

The race by group interaction term was nonsignificant for the cardiometabolic risk score, P = 0.22, but we performed analyses stratified by race to account for significant differences in the proportion of Black and White women across exposure groups. The association of assignment to the +PA/+L group with a more favorable cardiometabolic risk score only reached significance in Black women (Supplemental Table 2). The beta coefficient was attenuated more than 20% and the significant association was lost after adjustment for 30-year BMI change, though the association of category assignment with a lower cardiometabolic risk score remained significant in Black women. After accounting for BMI change, a significant direct association of -PA/+L and +PA/+L category with less favorable cardiometabolic risk score was observed in White women.

Of the 1,068 participants, 126 (11.8%) reported ever having GDM. There were no significant associations of exposure categories with cardiometabolic outcomes in women with a history of GDM (Supplemental Table 3).

### SENSITIVITY ANALYSES.

When we adjusted for the baseline (Y0) cardiometabolic risk score in our sensitivity analyses, results were significant and similar in direction and magnitude for the association of + PA/+L category with Y30 cardiometabolic risk score in the whole cohort: b = 0.13, 95% CI: -0.23 to -0.03. As in the main analyses, significance was lost after adjustment for change in BMI, and no other associations by group were significant. Results in Black women were significant and similar in direction and magnitude (b = 0.18, 95% CI: -0.34to -0.03) for the association of +PA/+L category with the Y30 cardiometabolic risk score with Y0 risk score in the model after initial adjustment, though the association of increasing category lost significance after adjustment for change in BMI: (b = 0.03, 95% CI: -0.07 to 0.01). A direct association of -PA/+L with Y30 car diometabolic risk score was detected in White women: b = 0.18, 95% CI: 0.02 to 0.35 with the Y0 cardiometabolic risk score included in the model after initial adjustment. All other associations were similar in direction and strength in White women before and after accounting for BMI change. Results by GDM status were maintained in sensitivity analyses. In sum, results were substantially maintained after adjustment for the baseline (Y0) cardiometabolic risk score.

# DISCUSSION

Parous women who maintained above average levels of PA across adulthood and had lactated for 3 months or more after giving birth had the most favorable levels of cardiometabolic risk factors after 30 years of follow-up. PA and cumulative lactation duration were associated with some individual cardiometabolic risk factors and a combined cardiometabolic risk score after initial adjustment for biological and social factors (Central Illustration). The cardiometabolic benefit associated with higher PA and lactation appeared to be explained, at least in part, by less weight gain over time as most associations were attenuated and nonsignificant after adjustment for BMI change. Although higher PA or lactation alone was each associated with a cardiometabolic benefit, the benefit was highest for the group with both behaviors.

Earlier investigations found dose-response relationships between PA, fitness, and cardiometabolic risk factors.<sup>31,32</sup> Another CARDIA investigation used an isotemporal substitution analysis to determine the hypothetical effect of replacing sedentary time with light or moderate-vigorous PA on the cardiometabolic risk score over 10 years.<sup>19</sup> The authors found that theoretically replacing 30 minutes of sedentary time with light or moderate-vigorous PA was associated with a decrease in cardiometabolic risk score 10 years later.<sup>19</sup> Other CARDIA investigations found protective effects of lactation on cardiometabolic risk factors, development of the metabolic syndrome, and incident diabetes.<sup>8,30,33</sup> The authors demonstrated a graded, dose-response relationship between lactation and these outcomes with the lowest hazards associated with the longest cumulative duration of lactation.<sup>8</sup>

Visceral adiposity is also strongly linked with cardiometabolic risk.<sup>34</sup> Lactation history has an unclear relationship with overall and abdominal adiposity, with some research reporting an inverse relationship with visceral adipose tissue and other research finding a direct relationship with WC.<sup>35</sup> Another study found that exclusively breastfeeding vs nonbreastfeeding women lost 1 to 2 kg more fat mass after pregnancy, but this difference was not statistically significant.<sup>36</sup> We observed a smaller WC, a proxy for visceral adiposity, in all women who were not in the –PA/–L category, and assignment to the +PA/–L or +PA/+L category was associated with lower WC after adjustment for potential confounders. Our findings suggest that lifelong PA, vs lactation, may be a more important determinant of WC in parous women in late midlife.

Our study unifies these bodies of work relating PA or lactation to cardiometabolic health and approaches the relationship from the life-course perspective. The women in the +PA/+L category had the lowest (most favorable) cardiometabolic risk factor score, so the data suggest that effects of PA and lactation on cardiometabolic risk could be additive. Importantly, the threshold dose of lactation that was associated with lower cardiometabolic risk in our study could realistically be attained, and our +PA cutoff was just below the amount of PA recommended in national guidelines.<sup>37</sup> However, as the median PA score was 168 (95% CI: 113–204) exercise units in –PA and 379 (95% CI: 310–506) exercise units in +PA groups, the –PA and +PA groups represent participants who generally did not meet vs did meet national PA guidelines.

Attaining an extended period of lactation depends on multiple medical and social factors, and new mothers who experience serious medical complications around childbirth, who must use contra-indicated medications soon after delivery, lack social or family support, must return to work soon after delivery, or have newborns admitted to a neonatal intensive care unit might find it difficult to initiate and maintain lactation.<sup>38</sup> In this study, a 6-month cutoff for +L assignment was initially examined, but we observed a similarly protective association when a 3-month cutoff was selected. We chose to evaluate and report associations using the 3-month cutoff as we believed understanding whether a smaller lactation dose was associated with outcomes had significant public health relevance. Similarly, the barriers associated with maintaining PA have been well-documented and include personal, social, and environmental factors.<sup>20–22</sup> Although attaining both behaviors is ideal, our data showed that either behavior was linked to a more favorable level of cardiometabolic risk, ie, lower risk score vs women with below median levels of both behaviors. Our results indicate that encouraging adequate PA could help attenuate cardiometabolic risk in women who did not lactate or lactated for <3 months.

Black women were disproportionately over-represented in the –PA/–L category and underrepresented in the +PA/+L category. However, stratified analyses revealed a stronger association of higher PA and lactation with cardiometabolic risk scores on Black women, even after controlling for BMI change. Thus, supporting lactation and PA might be especially important strategies for reducing cardiometabolic risk in Black women. However, the interaction term for the race by group interaction was not significant. There were no significant associations for exposure categories and cardiometabolic risk scores for women

with a history of GDM, but the absolute number of women with GDM was low and the confidence intervals were wide.

Our study has limitations. First, the CARDIA Study questionnaire that was used to determine lactation duration did not include a measure of lactation intensity, ie, proportion of feeding that occurred via breastfeeding vs formula feeding. Lactation intensity was associated with cardiometabolic outcomes in an earlier investigation,<sup>33</sup> but we were unable to differentiate between women who exclusively breastfed for at least 3 months vs women who used a combination of breastmilk and formula for 3 months or more as this information was not collected in CARDIA. Self-report of PA is also prone to error. We did not account for use of assistive reproductive technology or hypertensive disorders of pregnancy as assistive reproductive technology use was not determined and hypertensive disorders of pregnancy were not accurately recalled in CARDIA. We acknowledge the potential for residual confounding by unmeasured factors, such as genetics or neighborhood characteristics, however, we adjusted for education, smoking, and diet quality, traits which likely cluster with other social determinants of health and health behaviors, and we performed analyses stratified by race. Strengths of the study include the longitudinal data that encompassed childbearing years in Black and White women. Lactation duration for each birth was obtained at regular intervals that ranged from 3 months to 4 years after delivery, and self-report of GDM was very precise in CARDIA women.8

# CONCLUSIONS

We found that attaining above average PA and 3 months of lactation in adulthood was associated with a lower cardiometabolic risk score in Black and White women. Participants who achieved either one of these behaviors had a lower risk score vs those with neither behavior. Attaining realistic levels of PA and/or lactation, ie, PA just below the level prescribed in national guidelines and a total lactation duration that is half the amount recommended by the American Academy of Pediatrics for a single birth,<sup>39</sup> might help parous women attain lower levels of cardiometabolic risk in late midlife.

#### Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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## ABBREVIATIONS

BP	blood pressure	
GDM	gestational diabetes	
HBA1c	glycated hemoglobin	
HOMA	homeostatic model of insulin resistance	
PA	physical activity	
WC	waist circumference	

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#### PERSPECTIVES

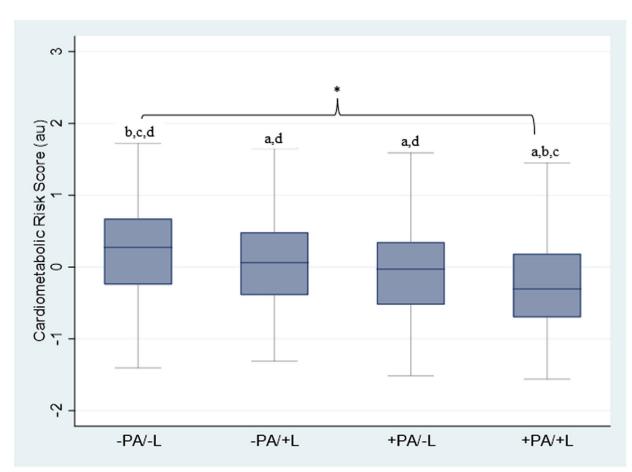
#### COMPETENCY IN MEDICAL KNOWLEDGE:

Parous women who achieved above average physical activity and moderate lactation duration had lower cardiometabolic risk than those with neither behavior. Achieving either behavior was better than neither behavior.

#### TRANSLATIONAL OUTLOOK:

Healthcare providers can encourage lactation after delivery and physical activity throughout adulthood to support cardiometabolic health.

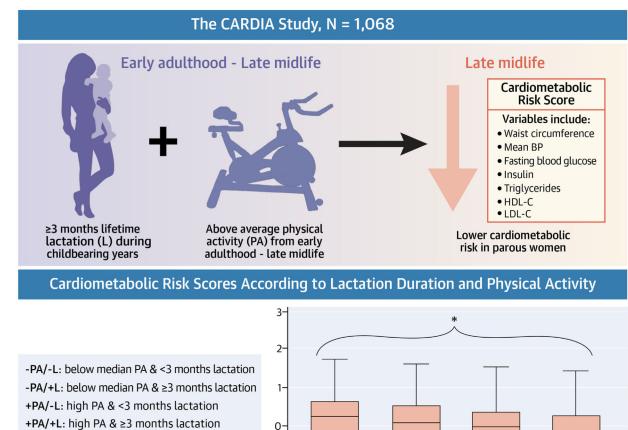
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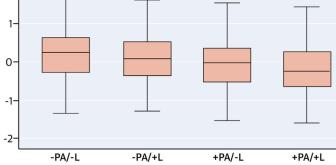
#### FIGURE 1.

Box and Whisker Plot of Unadjusted Cardiometabolic Risk Scores by Physical Activity and Lactation Duration Categories

-PA/-L: below median PA and <3 months cumulative lactation duration; -PA/+L: below median PA and 3 months cumulative lactation duration; +PA/-L: high PA and <3 months cumulative lactation duration; +PA/+L: high PA and 3 months cumulative lactation duration. The box represents median and interquartile range (25th-75th percentile); whiskers represent 5th to 95th percentiles. Outliers not shown. \*Significant effect of exposure categories; <sup>a</sup>significant difference from -PA/-L; <sup>b</sup>significant difference from -PA/+L; <sup>c</sup>significant difference from +PA/-L; <sup>d</sup>significant difference from +PA/+L, all at P < 0.05.



\*significant effect of exposure categories, *P* < 0.05



#### CENTRAL ILLUSTRATION.

Achieving at Least 3 Months of Lactation and Above Average Physical Activity Was Associated With Lower Cardiometabolic Disease Risk in Parous Participants **TABLE 1** 

4	•	)		
	-PA/-L (n = 303)	-PA/+L (n = 231)	+PA/-L (n = 184)	+PA/+L (n = 350)
Age (y) $b$	53 (51–57) <sup>e</sup> .£	55 $(52-58)^{d,f}$	54 (51–57) <sup>e,g</sup>	55 $(52-58)^{d,f}$
Black race $b$	224 (74) <sup>C</sup>	103 (46)	92 (50)	87 (24) <sup>C</sup>
Education $(\mathbf{y})^{b}$	$14~(12-16)^{e,f,\mathcal{B}}$	$16(14-18)^{d,g}$	$15(14{-}17)d_{\mathcal{B}}$	$16(15{-}18)d\!,e\!,f$
Smoking status $b$				
Former	62 (21)	44 (20)	41 (22)	97 (28)
Current	54 (18) <sup>C</sup>	15 (7) <sup>C</sup>	31 (17) <sup>C</sup>	23 (6) <sup>C</sup>
Parity				
1	70 (23)	41 (18)	56 (30)	75 (21)
2	133 (44)	95 (42)	74 (39)	165 (48)
3	100 (33)	95 (41)	54 (31)	110 (31)
WC (cm)b	97 (86–108) $^{e,f,g}$	93 (82–105) $^{g}$	90 (82–101) $d_{,\mathcal{B}}$	84 (75–94) $d$ ,e,f
Y0 diet score b	56 $(49-64)^{e,f,g}$	64 (56-74) d.g	$65 (56-74)^{d,g}$	72 (63–82) $d$ ,e, $f$
Y0 BMI (kg/m <sup>2</sup> ) $b$	$23.4~(20.5-27.8)f_{\mathcal{S}}$	22.6 $(20.3-25.5)^g$	22.5 $(20.6-24.9)^{d,g}$	21.7 (20.5-23.8) def
Y30 BMI (kg/m <sup>2</sup> ) $b$	$32.3~(27.1–38.0)^{e,f,g}$	30.6(25.1-35.9)dg	29.5 $(24.9-35.2)^{d,\mathcal{B}}$	$26.3 (23.1 - 30.5)^{e,f}$
BMI change $(kg/m^2)b$	$8.3~(3.9{-}12.3)f_{c}$	7.2 (3.3–10.8) ${\cal B}$	$6.3 (3.5 - 10.5) d_{,\mathcal{B}}$	4.2 $(1.1–7.S)^{d,e,f}$
Hypertension $b$	203 (67) <sup>C</sup>	113 (49)	96 (51)	123 (35) <sup>C</sup>
Diabetes b	66 (22) <sup>C</sup>	32 (14) <sup>C</sup>	$15(8)^{\mathcal{C}}$	29 (8) <sup>C</sup>
SBP (mm Hg) $b$	$120~(109-134)^{e,g}$	$116(107-127)^d$	$116(107{-}129)^{\mathcal{B}}$	115 (105–125) $d_i f$
DBP (mm Hg) $^b$	75 (68–84) $^{e,f,\mathcal{B}}$	71 (65–80) <i>d</i>	72 (65–82) $d_{c}g$	71 (63–78) $^{d,f}$
TC (mg/dL)b	192 (167–215) $^{e,g}$	$196(176-220)^{d,f}$	$190~(168-210)^{{\cal C},{\cal G}}$	201 (180–224) $d_{*}^{f}$
HDL-C $(mg/dL)^b$	59 (50–71) $^{g}$	$60 (52-71)1^g$	62 $(52-74)^{g}$	69 (56–82) $d,e,f$
LDL-C $(mg/dL)^b$	$109~(88-129)^{e}$	$115~(95-134)^{d,e}$	$106 \ (86-126)^{{\cal C},{\cal B}}$	$112~(92-131)^{f}$
Triglycerides $(mg/dL)^b$	86 (63–116) $^{g}$	83 (65–115) <sup>g</sup>	81 (51–107)	77 $(57-108)^{d,e}$
Insulin ( $\mu$ U/mL) $b$	$12.5~(7.5{-}19)^{e,f,g}$	$10.9 \; (7-16.3)^{d,f,g}$	$8.8(5.8-14.3)^{d,e,g}$	7.7 $(5.2-12)def$

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	-PA/-L (n = 303)	-PA/+L $(n = 231)$	+PA/-L (n = 184)	+PA/+L (n = 350)
Glucose $(mg/dL)b$	95 (85–105) $^{e,f,\mathcal{G}}$	93 (88–102) $^{d,f,\mathcal{G}}$	92 (86–99) $d,e$	91 (86–98) <i>d,e</i>
HOMA-IR <sup>b</sup>	$3.0~(1.7-4.8)^{e,f,g}$	$2.5(1.6-4.1)^{d,f,g}$	2.0(1.3-3.4)d,e,g	1.7~(1.2-2.9)d,e,f
$\mathrm{HbA1c}~(\%)^{a,b}$	$5.7~(5.4{-}6.0)^f$	$5.6(5.4-5.8)^{d,f,g}$	5.5 (5.3–5.7)d,e	5.5 (5.2–5.7) <i>d</i> ,e
PA (exercise units) $b$	$152(101{-}199)^{e,f,g}$	$177 \ (129-217)^{d,f,g}$	$360~(307-444)^{d,e}$	389 (313–534) <i>d,e</i>
Cumulative breastfeeding duration $(d)^b$	$0~(0-21)^{\mathcal{G}\mathcal{B}}$	270 (201–420) $d_{r}f$	$0 \; (0{-}21)^{\mathcal{C},\mathcal{G}}$	$210(201-405)^{d,f}$

Values are median (IQR) or n (%).

<sup>4</sup>There were 764 women with HbA1c data: 194 –PA/–L, 171 –PA/+L, 141 +PA/–L, and 258 +PA/+L.

 $b_{\rm Significant}$  difference between exposure categories.

 $\overset{\mathcal{C}}{\operatorname{Significant}}$  contribution to rejection of null hypothesis for chi-square test.

 $d_{\rm Significant}$  difference from –PA/–L.

 $^{e}$ Significant difference from –PA/+L.

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 $f_{Significant}$  difference from +PA/–L.

 $^{\mathcal{S}}$ Significant difference from +PA/+L.

months cumulative lactation duration; -PA/+L = below median PA and 3 months cumulative lactation duration; +PA/+L = high PA and <3 months cumulative lactation duration; +PA/+L = high PA and <3 months cumulative lactation duration; +PA/+L = high PA and <3 months cumulative lactation duration; +PA/+L = high PA and <3 months cumulative lactation duration; +PA/+L = high PA and <3 months cumulative lactation duration; +PA/+L = high PA and <3 months cumulative lactation duration; +PA/+L = high PA and <3 months cumulative lactation duration; +PA/+L = high PA and <3 months cumulative lactation duration; +PA/+L = high PA and <3 months cumulative lactation duration; +PA/+L = high PA and <3 months cumulative lactation duration; +PA/+L = high PA and <3 months cumulative lactation duration; +PA/+L = high PA and <3 months cumulative lactation duration; +PA/+L = high PA and <3 months cumulative lactation duration; +PA/+L = high PA and <3 months cumulative lactation duration; +PA/+L = high PA and <3 months cumulative lactation duration; +PA/+L = high PA and <3 months cumulative lactation duration; +PA/+L = high PA and <3 months cumulative lactation duration; +PA/+L = high PA and <3 months cumulative lactation duration; +PA/+L = high PA and <3 months cumulative lactation duration; +PA/+L = high PA and <3 months cumulative lactation duration; +PA/+L = high PA and <3 months cumulative lactation duration; +PA/+L = high PA and <3 months cumulative lactation duration; +PA/+L = high PA and <3 months cumulative lactation duration; +PA/+L = high PA and <3 months cumulative lactation duration; +PA/+L = high PA and <3 months cumulative lactation duration; +PA/+L = high PA and <3 months cumulative lactation duration; +PA/+L = high PA and <3 months cumulative lactation duration; +PA/+L = high PA and <3 months cumulative lactation duration; +PA/+L = high PA and <3 months cumulative lactation duration; +PA/+L = high PA and <3 months cumulative lactation durative lactation; +PA/+L= high density lipoprotein; HOMA-IR = homeostatic model of insulin resistance; LDL = low density lipoprotein; PA = physical activity average across attended exams; <math>PAL = below median PA and <3BMI = body mass index; BMI change = change in BMI from Y0 to Y30 exams; DBP = diastolic blood pressure; diet score = a priori diet quality score; HbA1c = proportion glycated hemoglobin; HDL months cumulative lactation duration; Parity = number of births; SBP = systolic blood pressure; TC = total cholesterol; WC = waist circumference.

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	WC	Insulin	Glucose	Lipid Profile	Mean BP	Risk Score
-PA/-L						
Model 1	Ref	Ref	Ref	Ref	Ref	Ref
Model 2	Ref	Ref	Ref	Ref	Ref	Ref
ß	n/a	n/a	n/a	n/a	n/a	n/a
-PA/+L						
Model 1	0.5 (-1.8 to 2.8)	-0.1 (-1.6 to 1.7)	1.3 (-2.4 to 5.1)	12.1 (-0.4 to 24.7)	-0.0 (-2.3 to 2.4)	0.05 (-0.05 to 0.16)
Model 2	-0.2 (-1.3 to 1.0)	-0.2 (-1.7 to 1.2)	1.2 (-2.5 to 4.9)	11.5 (-0.3 to 23.8)	-0.1 (-2.4 to 2.4)	0.03 (-0.05 to 0.11)
β	>100	75	18	6	>100	40
+PA/-L						
Model 1	$-2.6 (-5.0 \text{ to } 0.1)^{a}$	$-2.0 (-3.7 \text{ to } -0.3)^{a}$	-0.7 (-4.6 to 3.2)	-9.5 (-22.7 to 3.7)	1.5 (-1.0 to 4.0)	-0.09 (-0.20 to 0.02)
Model 2	-1.0 (-2.2 to 0.2)	-1.4 (-2.9 to 0.1)	-0.2 (-4.1 to 3.6)	-5.5 (-18.1 to 7.0)	2.0 (-0.4 to 4.4)	-0.04 (-0.13 to 0.05)
β	61	30	63	44	38	60
+PA/+L						
Model 1	-4.8 (-7.2 to 2.5) <sup>a</sup>	$2.0 (-3.6 \text{ to } -0.3)^{a}$	-1.3 (-5.0 to 2.4)	-9.9 (-22.5 to 2.6)	0.8 (-1.6 to 3.1)	$-0.15 (-0.5 \text{ to } 0.04)^{a}$
Model 2	-1.0 (-2.1 to 0.2)	-0.7 (-2.1 to 0.8)	-0.3 (-4.0 to 3.4)	-1.8 (-13.8 to 10.1)	1.8 (-0.6 to 4.1)	-0.04 (-0.12 to 0.05)
в	60	60	77	81	>100	71
Category assignment	signment					
Model 1	$-1.8 (-2.5 \text{ to } -1.1)^{a}$	$-0.8 (-1.3 \text{ to } -0.3)^{a}$	-0.6 (-1.8 to 0.6)	$-5.3 (-9.3 \text{ to } -1.4)^{a}$ 0.4 (-0.4 to 1.1)	0.4 (-0.4 to 1.1)	$-0.06 (-0.09 \text{ to } -0.03)^2$
Model 2	$-0.4 (-0.7 \text{ to } -0.1)^{21}$	-0.3 (-0.7 to 0.2)	-0.2 (-1.4 to 0.9)	-2.3 (-6.1 to 1.4)	0.7 (0.0 to 1.5)	-0.02 (-0.04 to 0.01)
9	78	63	67	57	75	67

Model 2: adjusted for Model 1 covariates + BMI change from Y0-Y30. B refers to the percent change in beta coefficient between Model 1 and Model 2, ie, change in estimate attributable to weight change consumption, hormone replacement therapy, use of diabetes, cholesterol, and/or hypertension medication, baseline diet quality, baseline BMI, and baseline value of individual risk factor when available. Values are β (95% CD. Category assignment = PA/L exposure categories modeled as continuous (not factor) variables. Model 1: adjusted for age, race, study center, education, parity, smoking, alcohol over follow-up.

<sup>a</sup>Indicates a significant association.

below median PA and 3 months cumulative lactation duration; +PA/-L = high PA and <3 months cumulative lactation duration; risk score lipoprotein cholesterol-high-density lipoprotein cholesterol; mean BP = average of systolic and diastolic blood pressure; -PA/-L = below median PA an-3 months cumulative lactation duration; -PA/+L = -PA/-L = below median PA and PA months cumulative lactation duration PA/+L = -PA/-L = below median PA and PA months cumulative lactation duration PA/+L = -PA/-L = below median PA months cumulative lactation duration PA/+L = -PA/-L = below median PA months cumulative lactation duration PA/+L = -PA/-L = below median PA months cumulative lactation duration PA/+L = -PA/-L = below median PA/+L = below median PHbA1c (n = 728) = percent of glycated hemoglobin; HOMA = homeostatic model of insulin resistance; OGTT (n = 557) = 2-hour oral glucose tolerance test; lipid profile = triglycerides + low-density = standardized cardiometabolic risk score; WC = waist circumference.

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TABLE 2

#### TABLE 3

Associations of Cumulative Lactation Duration and Physical Activity Categories With Additional Indices of Glycemia-Related Cardiometabolic Risk

	HOMA	OGTT	HbA1c
-PA/-L			
Model 1	Ref	Ref	Ref
Model 2	Ref	Ref	Ref
β	n/a	n/a	n/a
-PA/+L			
Model 1	0.1 (-0.4 to 0.6)	-1.4 (-10.8 to 8.0)	0.03 (-0.06 to 0.12)
Model 2	-0.0 (-0.5 to 0.5)	-2.3 (-11.4 to 6.7)	0.03 (-0.06 to 0.12)
β	>100	85	15
+PA/-L			
Model 1	-0.6 (-1.2 to -0.1) <sup>a</sup>	-5.4 (-15.6 to 4.7)	-0.15 (-0.24 to -0.05) <sup>a</sup>
Model 2	-0.4 (-0.9 to 0.1)	-5.2 (-15.0 to 4.6)	-0.14 (-0.23 to -0.05) <sup>a</sup>
β	34	9	7
+PA/+L			
Model 1	$-0.6 (-1.1 \text{ to } -0.1)^a$	-6.4 (-15.9 to 3.1)	-0.08 (-0.17 to 0.02)
Model 2	-0.2 (-0.7 to 0.3)	-3.8 (-13.1 to 5.4)	-0.05 (-0.14 to 0.04)
β	67	37	29
Category assignment			
Model 1	$-0.2 (-0.4 \text{ to } -0.1)^a$	-2.3 (-5.3 to 0.7)	$-0.04 (-0.07 \text{ to } -0.01)^a$
Model 2	- 0.1 (-0.3 to 0.1)	-1.3 (-4.2 to 1.6)	$-0.03 (-0.03 \text{ to } -0.01)^a$
β	50	43	26

Values are b (95% CI). Category assignment = PA/L exposure categories modeled as continuous (not factor) variables. Model 1: adjusted for age, race, study center, education, parity, smoking, alcohol consumption, hormone replacement therapy, use of diabetes, cholesterol, and/or hypertension medication, baseline diet quality, baseline BMI, and baseline value of individual risk factor when available. Model 2: adjusted for Model 1 covariates + BMI change from Y0-Y30.  $\beta$  refers to the percent change in beta coefficient between Model 1 and Model 2, ie, change in estimate attributable to weight change over follow-up.

#### <sup>*a*</sup>Indicates a significant association.

-PA/-L = below median PA and <3 months cumulative lactation duration; -PA/+L = below median PA and 3 months cumulative lactation duration; +PA/-L = high PA and <3 months cumulative lactation duration; +PA/-L = high PA and <3 months cumulative lactation duration; +PA/-L = high PA and 3 months cumulative lactation duration; +PA/-L = high PA and 3 months cumulative lactation duration; +PA/-L = high PA and 3 months cumulative lactation duration; +PA/-L = high PA and 3 months cumulative lactation duration; +PA/-L = high PA and 3 months cumulative lactation duration; +PA/-L = high PA and +PA/-L =