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Daily and Peak Monitor Independent Movement Summary (MIMS) Values Associated With Metabolic Syndrome: NHANES 2011–12 and 2013–14

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ABSTRACT

The U.S. National Health and Nutrition Examination Survey (NHANES) physical activity monitor datasets for 2011–12 and 2013–14 were released in late 2020. To date, there has been limited interpretation of these nationally representative wrist-worn accelerometer data (summarized and reported in Monitor Independent Movement Summary [MIMS] units) and their relationships with health-related outcomes. This study examined the associations between free-living $Daily_{MIMS}$ (volume), Peak 1_{MIMS} and Peak 30_{MIMS} (intensity), and risk of Metabolic Syndrome (MetS). Data from adults (N=3787; 18–80+ years) in the 2011–12 and 2013–14 NHANES cycles with health examination and accelerometry data were included. Accelerometer data were processed into Peak 1_{MIMS} and Peak 30_{MIMS} (MIMS/min), and $Daily_{MIMS}$ (MIMS/day). Design-based generalized linear and logistic regressions, and a sample-weighted decision tree, were used to examine associations between MIMS variables and MetS risk factors. Lower Peak 1_{MIMS}, Peak $30_{MIMS,}$ and $Daily_{MIMS}$ were observed for every one-unit increase in the number of risk factors −3.9 [95% CI: −4.3, −3.4] and −2.3 [−2.6, −2.1] MIMS/min, (−672.1 [−772.7, −571.5] MIMS/day, respectively, all $p<0.001$). The Decision Tree classified individuals ≥46.5 years with a $Daily_{MIMS}$ ≥12 245 MIMS/day and a Peak 30_{MIMS} <45.1 MIMS/min as having MetS (≥3 risk factors). Individuals <46.5 years with a Peak 1_{MIMS} ≥62.9 MIMS/min were classified with 0 risk factors. Higher $Daily_{MIMS}$ and $Peak_{MIMS}$ were associated with an absence of MetS risk factors, with a progressive decline as the number of risk factors increased. These findings may be considered as preliminary benchmarks for $Daily_{MIMS}$ and $Peak_{MIMS}$ associated with cardiometabolic risk.

1 | Introduction

The National Health and Nutrition Examination Survey (NHANES) is a cross-sectional health surveillance system that uses a complex, multi-stage probability design to achieve a US population representative sample. The US Centers for Disease Control and Prevention (CDC) released NHANES Physical Activity monitor (PAM) data from the 2011–12 and 2013–14 cycles in late 2020. In a departure from previous cycles, two major changes were implemented regarding the PAM data. First, accelerometry data were collected on the wrist (instead of the waist location as implemented in prior survey years), and second, instead of processing the data using ActiGraph's proprietary activity count and step algorithms as in previous survey cycles,

the data were processed using the novel Monitor-Independent Movement Summary (MIMS) algorithm [1] and reported in summary files as MIMS/min values accumulated in 1-min epochs, 1-h epochs, and per day. Briefly, the MIMS algorithm is an acceleration summary metric that was developed to address issues relating to wrist-worn placement and universal application of the algorithm across different brands and models of accelerometers [1]. To date, few studies have utilized these relatively newly-released NHANES PAM datasets to examine associations between MIMS-based physical activity (PA) and health-related outcomes.

Belcher et al. [2] were the first group to publish findings from the 2011–12 and 2013–14 NHANES PAM data. Their study reporting population-referenced percentile values for daily MIMS ($Daily_{MIMS}$; MIMS/day), published in 2021, was a critical first step towards understanding the distribution of PA volume when expressed in MIMS units at a population level. Further, we recently published a report on the associations between $Daily_{MIMS}$ and peak MIMS ($Peak_{MIMS}$; MIMS/min, i.e., the highest MIMS values in a given day and across several days, representing best effort or intensity) variables and cognitive function among older adults [3]. Notably, studies examining the relationships between MIMS variables and risk factors more traditionally associated with cardiometabolic health are currently absent from the literature. The lack of such studies makes it difficult to interpret MIMS values in relation to the prevention and/or treatment and management chronic diseases (e.g., how many MIMS/day is enough for disease prevention/management?) [4]. Importantly, this likely has limited further implementation and widespread adoption of MIMS as a PA metric. Collectively, there is currently a general lack of understanding of MIMS variables as PA metrics. Given the importance of NHANES as a national health surveillance system, it is imperative for researchers to examine the relationships between MIMS variables and health outcomes.

A recent study by Karas et al. [5] demonstrated a high correlation between MIMS and other prevalent PA measures (e.g., activity counts). Notably absent from the aforementioned study were any comparisons of intensity-based expressions of MIMS. This is attributable to the fact that, to our knowledge, the relationship between MIMS/min and measured intensity (e.g., oxygen uptake) has not been investigated. In the absence of such information, we may borrow from the step-based metrics literature [6, 7] to construct index variables indicative of total daily and peak (higher intensity) minutes of MIMS activity. Total $Daily_{MIMS}$ (units: MIMS/day) is a simple summation of all MIMS values throughout the day, averaged across all valid wear days. Peak 1_{MIMS} (units: MIMS/min) represents the single highest MIMS/min value within a day, averaged across all valid wear days. Peak 30_{MIMS} (units: MIMS/min) represents the highest 30 (not necessarily consecutive) minutes within a day, averaged across all valid wear days. The post-processing of accelerometry data into these MIMS metrics may provide a more comprehensive evaluation of free-living PA in terms of both volume (Daily MIMS) and intensity (Peak 1_{MIMS} and Peak 30_{MIMS}) levels.

Therefore, the purpose of this study was to examine the relationship between $Daily_{MIMS}$ (PA volume), $Peak_{MIMS}$ (PA intensity), and cardiometabolic risk using the 2011–12 and 2013–14 NHANES dataset. In particular, we sought to obtain values of $Daily_{MIMS}$ and $Peak_{MIMS}$ associated with either absence or presence of metabolic syndrome (MetS) risk factors and overall classification. A secondary purpose was to examine the potential combined and independent associations of $Daily_{MIMS}$, and Peak 1- and Peak 30_{MIMS} on MetS classification. Given the novelty of the MIMS algorithm, and the lack of prior studies examining the association of MIMS metrics with cardiometabolic risk factors, the findings of this study may provide valuable insight on how to interpret the MIMS values and thus establish their clinical relevance.

2 | Materials and Methods

2.1 | Study Design and Sample

This study included data from the 2011–12 and 2013–14 NHANES. A description of data collection procedures and open access to data can be found at https://wwwn.cdc.gov/nchs/nhanes/. All NHANES study procedures were approved by the National Center for Health Statistics ethics review board and participants provided written informed consent. Local Institutional Review Board approval for the analysis conducted herein is not required as NHANES data is publicly available in deidentified format. For the purposes of this analysis, we included data from adults between 18 and 80+ year of age ($n = 11\,977$). After removing those who were pregnant ($n = 122$; due to related impacts on PA and MetS risk factors), those who did not have accelerometry data ($n = 1980$), those who wore the device on their dominant wrist ($n = 108$), those who were non-fasted at the time of their assessment ($n = 5443$; requirement for accurate measurement of blood biomarkers), those who did not have complete MetS risk factor data ($n = 204$), and those who did not have smoking data ($n = 98$), a final eligible sample of 4022 participants remained.

2.2 | Measures

Each participant was fitted with an accelerometer (80 Hz sampling rate; ActiGraph GT3X+, ActiGraph, Pensacola, FL, USA) on their non-dominant wrist. Participants were instructed to wear the device for 24 h for 7 full days and 2 partial days (first and last). As described by Belcher et al. [2] the PAM data were processed using the novel MIMS algorithm. Complete details of the MIMS algorithm can be found in the original report from John and colleagues [1]. Participant-level PAM data were downloaded in 1-min epochs and processed using custom R scripts. As described briefly by Belcher and colleagues [2], and as explained in further detail in the NHANES PAM documentation [8], a machine learning algorithm was used to predict and label each minute as wake wear, sleep wear or non-wear, and also to generate data quality flags. In the present analysis, minutes with data quality flags (PAXQFM) were removed and only wake wear and sleep wear minutes were retained (PAXPREDM). In accordance with the report from Belcher et al. [2], the accelerometer data from the first and last day (partial days) were removed, retaining 7 consecutive days of recording. Further, we adopted the same valid wear time

criteria, whereby a valid day consisted of 1440 min of accelerometer data (i.e., 24 h), < 5% non-wear time (< 72 min; $n = 214$ removed), and < 17 h of sleep wear ($n = 21$ removed). All data from individuals with at least 1 valid day were included in the final data set. As a result, our findings can be interpreted in the context of the population-referenced values reported by Belcher et al.

2.2.1 | Physical Activity Metrics

MIMS data were processed into PA variables that represent average daily volume and peak intensity. Specifically, Peak 1_{MIMS} (units: MIMS/min) was calculated by: (1) rank-ordering all 1440 MIMS/min values within each day in order of highest to lowest; (2) selecting the single highest MIMS/min values for each day; and (3) taking the average across all valid wear days. Similarly, Peak 30_{MIMS} was calculated by: (1) rank-ordering all 1440 MIMS/min values within each day in order of highest to lowest; (2) selecting the highest 30 (not necessarily consecutive) MIMS/min values for each day; (3) taking the average of the highest 30 MIMS/min, and (4) averaging across all valid wear days. Finally, $Daily_{MIMS}$ (units: MIMS/Day) was calculated by: (1) summing all MIMS/min values within each day; (2) taking the average across all valid wear days. We recently published a report with a supplemental file visually demonstrating the data processing steps for Peak 30_{MIMS} to facilitate understanding of how the variable is computed [3]. In addition, we have provided pseudo-code outlining the key steps for computing MIMS metrics in Data S1.

2.2.2 | Metabolic Syndrome Risk Factors

MetS is a cluster of five cardiometabolic risk factors, including elevated waist circumference, elevated triglycerides, elevated blood pressure, elevated fasting glucose, and low high-density lipoprotein cholesterol (HDL-C) [9]. Clinical diagnosis of MetS requires adverse levels for at least 3 of the 5 risk factors. MetS was defined using a harmonized definition [9], including: waist circumference ≥ 88 cm (female) or ≥ 102 cm (male) [US reference values]; triglycerides > 150 mg/dL; HDL-C < 50 mg/dL (female) or < 40 mg/dL (male); systolic blood pressure ≥ 130 and/or diastolic blood pressure ≥ 85 mmHg; and fasting blood glucose ≥ 100 mg/dL. Individuals were classified with MetS if they had aberrant levels according to the criteria above, or if they indicated that they were currently taking medication to control levels (NHANES variable names: hypertension—BPQ050A; dyslipidemia—BPQ100D, hyperglycemia—DIQ070) for at least 3 of the five risk factors.

2.2.3 | Statistical Analyses

Descriptive characteristics of the sample were computed using sample-weighted mean (standard error [S.E.]) for continuous variables and count (%) for categorical variables. Design-based independent *t*-tests (accounting for sample weights) were used to examine the levels of MIMS metrics corresponding to absence or presence of each of the MetS risk factors. Cohen's *d* effect sizes were calculated and interpreted as following: small = 0.2, medium = 0.5, large = 0.8. Design-based multivariable linear regression (Survey Generalized Linear Models) was used to determine the relationship between the number of MetS risk factors and each MIMS metric. A primary model was first constructed to examine the bivariate relationship between each MIMS metrics and increasing number of MetS risk factors. A second model was constructed which adjusted for several a priori defined covariates including age (continuous), sex, race/ethnicity, smoking status (smoked at least 100 cigarettes before: Yes/No). A third model was constructed for both the Peak 1_{MIMS} and Peak 30_{MIMS} metrics to examine the independent association with MetS risk when controlled for $Daily_{MIMS}$ and covariates. The impacts of multicollinearity between Peak and Daily MIMS on the models were assessed by examining the S.E. inflation when $Daily_{MIMS}$ was added to the $Peak_{MIMS}$ models. If the magnitude of change in the S.E. was small (i.e., models had similar S.E. for the β estimates), we retained both $Peak_{MIMS}$ and $Daily_{MIMS}$ variables in the final models. Adjusted regression coefficients (β), 95% confidence intervals (CIs), and *p*-values were extracted. Analyses were performed using the "*Survey*" package [10] in R version 4.1.0 [11], accounting for sample weights, with a two-sided alpha level of 0.05 set for all analyses. In addition, we also developed a Decision Tree model using the "*rpart*" [12] package in R (an implementation of the Classification and Regression Trees [CART] Model), to provide a visual and algorithmic representation of how levels of each MIMS metric (and aforementioned covariates) were associated with classification of none, or presence of 1 or more MetS risk factors. Sample weights were accounted for in the Decision Tree model. Finally, we developed a R Shiny app (https://ua-cv-health-and-physical-activity-lab.shinyapps.io/metabolic_syndrome_risk_viewer/) which allows for interactive use of the underlying dataset to visually examine risk of MetS based on end user input values for PA and several covariates (age, sex, race/ethnicity, smoking). We employed design-based logistic regression models to determine probability of MetS (i.e., ≥ 3 risk factors) for each MIMS metric, controlled for the covariates. We constructed additional models that included: (1) Peak 1_{MIMS} and $Daily_{MIMS}$; and (2) Peak 30_{MIMS} and $Daily_{MIMS}$, to examine the relationships between peak intensity, volume metrics and probability of MetS ($\alpha = 0.05$).

3 | Results

3.1 | Characteristics of the Sample

The final analytical sample comprised $n = 3787$ individuals with an average (± SD) wear-time of 24.00 ± 0.03 h/day across 6.0 ± 1.6 days of recording. A total of 235 individuals were excluded from the analysis due to not meeting valid wear-time criteria. Individuals excluded from the analysis were, on average, younger (mean difference −0.8 [95% CI: −1.6, −0.1] years, $p = 0.02$), and more likely to be "Non-Hispanic Black" (test for proportions excluded vs. included: 0.25 vs. 0.21; $p < 0.001$) or "Other" race (0.03 vs. 0.02; $p < 0.01$), and less likely to the white (0.39 vs. 0.43; $p < 0.001$). Sample-weight adjusted characteristics are presented in Table 1. For reference, average [S.E.] peak intensity was 59.6 [17.5] and 42.5 [10.5] MIMS/min for Peak 1_{MIMS} and Peak 30_{MIMS}, respectively, while $Daily_{MIMS}$

TABLE 1 | Sample characteristics.

Variable	Mean (S.E.) or median [IQR]	Min–Max
Age (years)	48.7 (17.8)	18.0–80.0
Height (cm)	168.0 (9.9)	134.0–200.0
Mass (kg)	78.6 [66.4, 92.8]	32.3–194.0
BMI (kg/m^2)	27.8 [24.0, 32.3]	15.4–70.1
MetS risk factors		
Waist circumference (cm)	98.9 (16.7)	63.1–176.0
Triglycerides (mg/dL)	98.0 [68.0, 146.0]	16.0–4233.0
HDL-C (mg/dL)	53.2 (15.0)	10.0–150.0
Systolic blood pressure (mm HG)	120.0 [110.0, 132.0]	64.7–235.0
Diastolic blood pressure (mm HG)	69.1 (12.3)	0.0–117.0
Fasting glucose (mg/dL)	99.0 [93.0, 109.0]	47.0–405.0
Physical activity (MIMS units)		
Peak 1_{MIMS} (MIMS/min)	56.6 [48.9, 66.4]	15.3–218.0
Peak 30_{MIMS} (MIMS/min)	41.5 [36.7, 46.9]	11.0–202.0
$Daily_{MIMS}$ (MIMS/day)	13 327 (3901)	1411–36 507
	n	**%**
Sex		
Male	1856	49.0
Female	1931	51.0
Race/ethnicity		
Mexican American	462	12.2
Non-Hispanic Asian	451	11.9
Non-Hispanic Black	791	20.9
Non-Hispanic White	1613	42.6
Other hispanic	379	10.0
Other race	91	2.4
Smoking status		
Yes	1608	42.5
No	2179	57.5

Note: All values presented are adjusted for sample weighting. Metabolic Syndrome risk factor thresholds as defined in the harmonized definition for metabolic syndrome [9]: waist circumference ≥ 88 cm (Female) or ≥ 102 cm (Male) [US reference values]; triglycerides > 150 mg/dL or on medication; HDL-C < 50 mg/dL (female) or < 40 mg/dL (male) or on medication; systolic blood pressure ≥ 130 and/or diastolic blood pressure ≥ 85 mmHg or on medication; and fasting blood glucose: ≥ 100 mg/dL or on medication. Abbreviations: BMI = Body Mass Index; DailyMIMS = MIMS per day (i.e., summation of MIMS/min values within a day, averaged across valid wear days); MIMS = Monitor independent movement summary; Peak 1_{MIMS} = peak 1-min MIMS (i.e., the highest MIMS min value within a day, averaged across valid wear days); Peak 30_{MIMS} = peak 30-min MIMS (i.e., the average of the 30 highest MIMS within a day, averaged across valid wear days); S.E. = standard error.

was 13 327 [3901] MIMS/day. Spearman correlation between the MIMS metrics was as follows: $Daily_{MIMS}$ and Peak 1_{MIMS}, $r_s = 0.49$; $Daily_{MIMS}$ and Peak 30_{MIMS}, $r_s = 0.61$; Peak 1_{MIMS} and Peak 30_{MIMS}, $r_s = 0.89$.

3.2 | MIMS Values Associated With Absence/Presence of MetS Risk Factors

Table 2 presents mean [S.E.] values for each of the MIMS metrics separated by absence (no) or presence (yes) of each MetS risk factor. Design-based independent *t*-tests indicated significant (all $p < 0.001$) differences between individuals with/without each risk factor for all of the MIMS metrics, with effect sizes ranging from small ($d = 0.24$) to medium ($d = 0.62$). Collectively, a Peak 1_{MIMS} of approximately 64 MIMS/min, Peak 30_{MIMS} of 45 MIMS/min, and a $Daily_{MIMS}$ 14 000 MIMS/day, were associated with the absence of MetS risk factors.

3.3 | Design-Based Generalized Linear Models

We observed strong inverse relationships between each MIMS metric and the number of MetS risk factors (Table 3, Models 1, 4, 7; all $p < 0.001$). Starting from 0 risk factors (reference group), each additional risk factor was associated with lower MIMS values for Peak 1_{MIMS} (−3.8 [95% CI: −4.3, −3.4] MIMS/min), Peak 30_{MIMS} (−2.3 [−2.6, −2.1] MIMS/min), and $Daily_{MIMS}$ (−671.5 [−772.1, −570.7] MIMS/day). A visual representation of this inverse relationship between each of the MIMS metrics and number of MetS risk factors is shown in Figure 1. Notably, the peak intensity variables displayed a relatively uniform inverse linear relationship, whereas $Daily_{MIMS}$ displayed an inverse curvilinear relationship, with a less steep decline between 0 and 3 risk factors, followed by a steeper decline between 3 and 5 risk factors. After adjusting for covariates (age, sex, race/ethnicity, and smoking), the main effects for each of the MIMS metrics remained significant (Models 2, 5, 8; all $p < 0.001$). Furthermore, the relationships between peak intensity metrics (Peak 1_{MIMS} and Peak 30_{MIMS}) and the number of MetS risk factors remained significant when controlled for PA volume ($Daily_{MIMS}$) and covariates (Models 3 and 6; both $p < 0.001$, respectively).

3.4 | Decision Tree Analysis

The Decision Tree model is displayed in Figure 2. Starting at the root node (top of the tree), the primary splitting criteria was age ≥ 46.5 years. When following the path left or right, different levels of each of the MIMS metrics resulted in classification of the number of MetS risk factors ranging from 0 to 5. Two paths classified individuals as having 0 risk factors: (1) individuals < 46.5 years with a Peak $1_{MIMS} \geq 62.9$ MIMS/min; and (2) individuals < 31.5 years with a Peak $1_{MIMS} < 62.9$ MIMS/min. Individuals ≥ 46.5 years with a $Daily_{MIMS} \geq 12\,245$ and a Peak $30_{MIMS} < 45.1$ MIMS/min were classified as having 3 risk factors. Finally, the Decision Tree classified individuals ≥ 46.5 years with a $Daily_{MIMS}$ of < 10 699 MIMS/day as having all 5 risk factors. Notably, aside from age, other covariates (sex, race/ethnicity and smoking status) were not selected by

TABLE 2 | Mean [S.E.] Daily and Peak MIMS levels based on absence or presence of metabolic syndromic risk factors.

MetS risk factor	Peak 1_{MIMS}				Peak 30_{MIMS}				$Daily_{MIMS}$			
	No	Yes	*p*	*d*	No	Yes	*p*	*d*	No	Yes	*p*	*d*
Waist circumference (cm)	64.6 [0.7]	56.6 [0.5]	< 0.001	0.47	45.4 [0.4]	41.1 [0.3]	< 0.001	0.41	13 834 [147]	12 917 [99]	< 0.001	0.24
Triglycerides (mg/dL)	63.1 [0.6]	55.5 [0.5]	< 0.001	0.44	44.9 [0.3]	39.9 [0.3]	< 0.001	0.47	14 031 [119]	12 224 [94]	< 0.001	0.48
HDL-C (mg/dL)	63.8 [0.6]	55.4 [0.4]	< 0.001	0.49	45.3 [0.3]	40.1 [0.3]	< 0.001	0.49	14 080 [101]	12 353 [95]	< 0.001	0.46
Blood pressure (mm HG)	64.7 [0.7]	54.0 [0.4]	< 0.001	0.62	45.7 [0.4]	39.3 [0.3]	< 0.001	0.60	13 986 [116]	12 410 [87]	< 0.001	0.42
Fasting glucose (mg/dL)	63.6 [0.6]	55.4 [0.6]	< 0.001	0.47	45.2 [0.4]	39.9 [0.3]	< 0.001	0.51	13 944 [122]	12 474 [136]	< 0.001	0.39

Note: Values are presented as mean and standard error [S.E] and are adjusted for sample weighting. Yes/No above refers to participants categorized with Metabolic Syndrome risk factor values above or below thresholds defined in the harmonized definition for metabolic syndrome [9]: Waist: ≥ 88 cm (Female) or ≥ 102 cm (Male) [US reference values]; Triglycerides: > 150 mg/dL or on medication; HDL-C: < 50 mg/dL (Female) or < 40 mg/dL (Male) or on medication; Blood pressure: Sys ≥ 130 and/or Dias ≥ 85 mmHg or on medication to treat hypertension; Fasting blood glucose: ≥ 100 mg/dL.
Abbreviations: BMI = Body Mass Index; $Daily_{MIMS}$ = MIMS per day (i.e., summation of MIMS/min values within a day, averaged across valid wear days); *d* = Cohen's *d* effect size; MIMS = Monitor independent movement summary; Peak 1_{MIMS} = peak 1-min MIMS (i.e., the highest MIMS min value within a day, averaged across valid wear days); Peak 30_{MIMS} = peak 30-min MIMS (i.e., the average of the 30 highest MIMS within a day, averaged across valid wear days).

TABLE 3 | Sample weight-adjusted multiple regression models describing the relationship between the number of metabolic syndromic risk factors and physical activity (Daily and Peak MIMS variables).

MIMS Variable	Regression output	
	Adjusted β (95% CIs)	*p*
Peak 1_{MIMS} (MIMS/min)		
Model 1	−3.9 (−4.3, −3.4)	< 0.001
Model 2	−2.0 (−2.5, −1.5)	< 0.001
Model 3	−1.2 (−1.6, −0.8)	< 0.001
Peak 30_{MIMS} (MIMS/min)		
Model 4	−2.3 (−2.6, −2.1)	< 0.001
Model 5	−1.3 (−1.6, −1.0)	< 0.001
Model 6	−0.7 (−0.9, −0.4)	< 0.001
$Daily_{MIMS}$ (MIMS/day)		
Model 7	−672.1 (−772.7, −571.5)	< 0.001
Model 8	−441.0 (−569.1, −312.9)	< 0.001

Note: All models were adjusted for sample weighting. Models 1, 4, 7: MIMS metric value (dependent variable) ~ number of MetS Risk factors (independent variable). Models 2, 5, 8: MIMS metric value (dependent variable) ~ number of MetS Risk factors (independent variable) with adjustment for covariates (sex, race/ethnicity and smoking status). Models 3, 6: MIMS metric value (dependent variable) ~ number of MetS Risk factors (independent variable) with adjustment for covariates, and also controlled for $Daily_{MIMS}$.
Abbreviations: $Daily_{MIMS}$ = MIMS per day (i.e., summation of MIMS/min values within a day, averaged across valid wear days); Peak 1_{MIMS} = peak 1-min MIMS (i.e., the highest MIMS min value within a day, averaged across valid wear days); Peak 30_{MIMS} = peak 30-min MIMS (i.e., the average of the 30 highest MIMS within a day, averaged across valid wear days).

the Decision Tree model, suggesting that they had limited discriminatory power for classification of MetS risk factors in the current model.

3.5 | Metabolic Syndrome Risk Prediction Using Logistic Regression (Shiny App)

To facilitate further exploration of the final dataset, we developed a R Shiny app (https://ua-cv-health-and-physical-activity-lab.shinyapps.io/metabolic_syndrome_risk_viewer/) which allows end-users to interact with the underlying data in several ways. First, considering each of the MIMS metrics separately (Tabs 1–3), individuals can obtain the probability (from 0.0 to 1.0; obtained from logistic regression models, with 1 indicating the highest probability of having MetS), controlled for age, sex, race/ethnicity, and smoking status. End-users can adjust the value of the respective MIMS metric, as well as levels of the aforementioned covariates, and visualize how the probability of MetS changes. The black vertical line represents the end-user's MIMS metric value, and their risk probability is located at the intersection of the two black lines. Second, end users can examine how various combinations of volume and intensity (Tab 4: Peak 1_{MIMS} vs. $Daily_{MIMS}$; and Tab 5: Peak 30_{MIMS} vs. $Daily_{MIMS}$), with the aforementioned covariates controlled for, impacts the probability of having MetS. We used a color gradient from red (high probability) to green (lowest probability) to aid visual

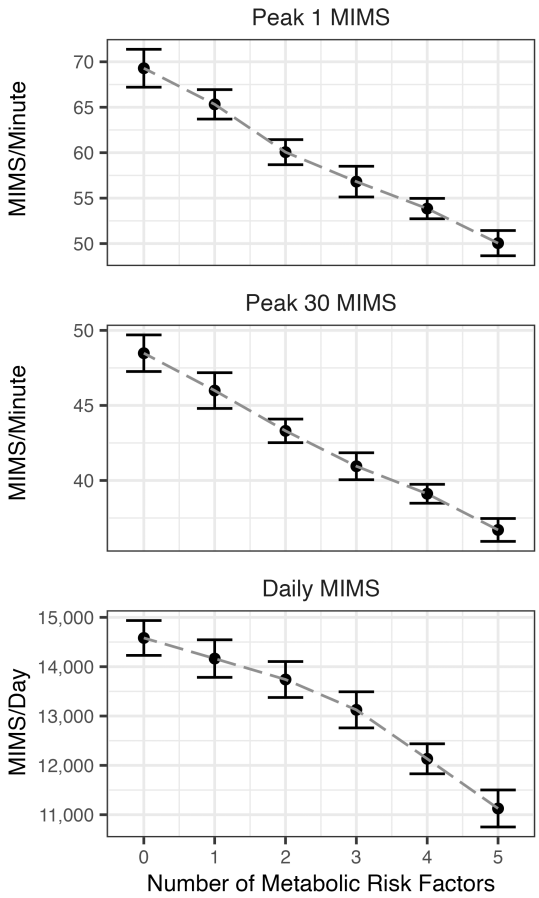

FIGURE 1 | Association between the number of metabolic risk factors and physical activity ($Daily_{MIMS}$ or $Peak_{MIMS}$ metrics). Values displayed are means with 95% confidence intervals.

interpretation of risk level, with the individual's probability of MetS indicated by a dot on the graph. Model fit was evaluated using Akaike Information Criteria (AIC). Adding $Daily_{MIMS}$ to the Peak 1_{MIMS} model improved fit (AIC: 191 to 164). However, adding $Daily_{MIMS}$ to the Peak 30_{MIMS} model did not improve fit (AIC: 346 to 462). For consistency and visualization purposes, the final models underlying tabs 4 and 5 included $Daily_{MIMS}$ and either Peak 1_{MIMS} or Peak 30_{MIMS}, respectively.

4 | Discussion

To the best of our knowledge, this is the first study to examine the relationships between volume and intensity-based expressions of MIMS as PA metrics with cardiometabolic risk factors. Herein, we reported strong inverse associations between MIMS variables and MetS risk factors/classification. In the Decision Tree analysis, we further observed that a combination of higher $Peak_{MIMS}$ and higher $Daily_{MIMS}$ was generally associated with fewer MetS risk factors or absence of MetS classification. Considering each of the analyses presented here (Table 2 and Figures 1 and 2), Peak 1_{MIMS} values of ~60–65 MIMS/min, Peak 30_{MIMS} ~43–45 MIMS/min, and $Daily_{MIMS}$ ~12 250–14 000 MIMS/day were associated with the absence of MetS classification. Although future prospective studies are warranted, especially those examining the relationships between $Daily_{MIMS}$ and $Peak_{MIMS}$ and incident cardiovascular disease and/or mortality, these findings may serve as preliminary benchmark values for MIMS values associated with cardiometabolic risk.

In our design-based regression models, $Daily_{MIMS}$ and Peak 1- and 30_{MIMS} were all strongly inversely associated with MetS risk factors and classification. Notably, in models where daily volume, peak intensity (Peak 1_{MIMS} and Peak 30_{MIMS}) and covariates were included, the peak intensity variables remained significant. This finding was also observed in the Decision Tree analysis, whereby high Peak 1_{MIMS} was the only pathway to 0 risk factors, and where high $Daily_{MIMS}$ combined with high Peak 30_{MIMS} corresponded with absence of MetS classification. For example, individuals ≥46.5 years achieving ≥12 245 MIMS/day were also required to perform high intensity (Peak 30_{MIMS} of ≥45.1 MIMS/min) PA to avoid MetS classification. These results are also supported by our logistic regression models, which underly the interactive figures in the R Shiny app. Specifically, Tabs 4 and 5 (Peak 1_{MIMS} vs. $Daily_{MIMS}$ and Peak 30_{MIMS} vs. $Daily_{MIMS}$, respectively) demonstrate that lower levels of $Daily_{MIMS}$ could be offset by increasing the value of Peak 1_{MIMS} or Peak 30_{MIMS} (transition from red [higher risk] to yellow/green [lower risk]). We also generated a panel figure (Figure S1) displaying the dose–response association for each MIMS variable and risk factor (continuous). In these one-on-one looks, the dose–response associations generally followed the expected pattern, whereby higher MIMS values were associated with more favorable outcomes, and moreover, higher MIMS values resulted in a decrease in the risk factor value below the MetS threshold (or vice-versa for HDL-C). However, there were some responses that displayed an uptick at one or both ends (extreme low or high) of the MIMS variable. These are difficult to interpret, however, as they may be influenced by the distribution/density of observations at the extreme ends of the dataset. Thus, some caution is advised when interpreting these figures.

Given the lack of similar studies examining the association between MIMS variables and cardiometabolic risk factors, we instead drew comparison to studies that have reported on the associations between daily stepping, peak cadence and cardiometabolic risk. The results in the present study agree with our previous analysis of NHANES step-based metrics and cardiometabolic risk factors [13, 14], whereby individuals with lower daily volume (steps/day) or peak-cadence metrics (steps/min) generally displayed less favorable cardiometabolic outcomes, and vice-a-versa. Additionally, our results align with findings from Cruz and colleagues [15], who reported that both higher daily volume and peak intensity (peak 30 min cadence) of PA were associated with a lower risk of all-cause and cardiovascular disease mortality. Notably, Cruz and colleagues [15] reported that the relationships for peak cadence metrics were stronger in magnitude and offered additional risk reduction beyond the benefits observed for steps per day. Similar results were also reported by Paluch et al. [16], whereby models characterizing the relationship between peak cadence metrics and all-cause mortality were somewhat attenuated, but remained significant, when controlled for volume (steps/day). However, it is important to acknowledge that not all studies support stronger or independent relationships for peak versus volume-based measures of PA and all-cause mortality [17–19]. Nevertheless, the concordance of our findings with similarly constructed daily and peak step-based metrics is a

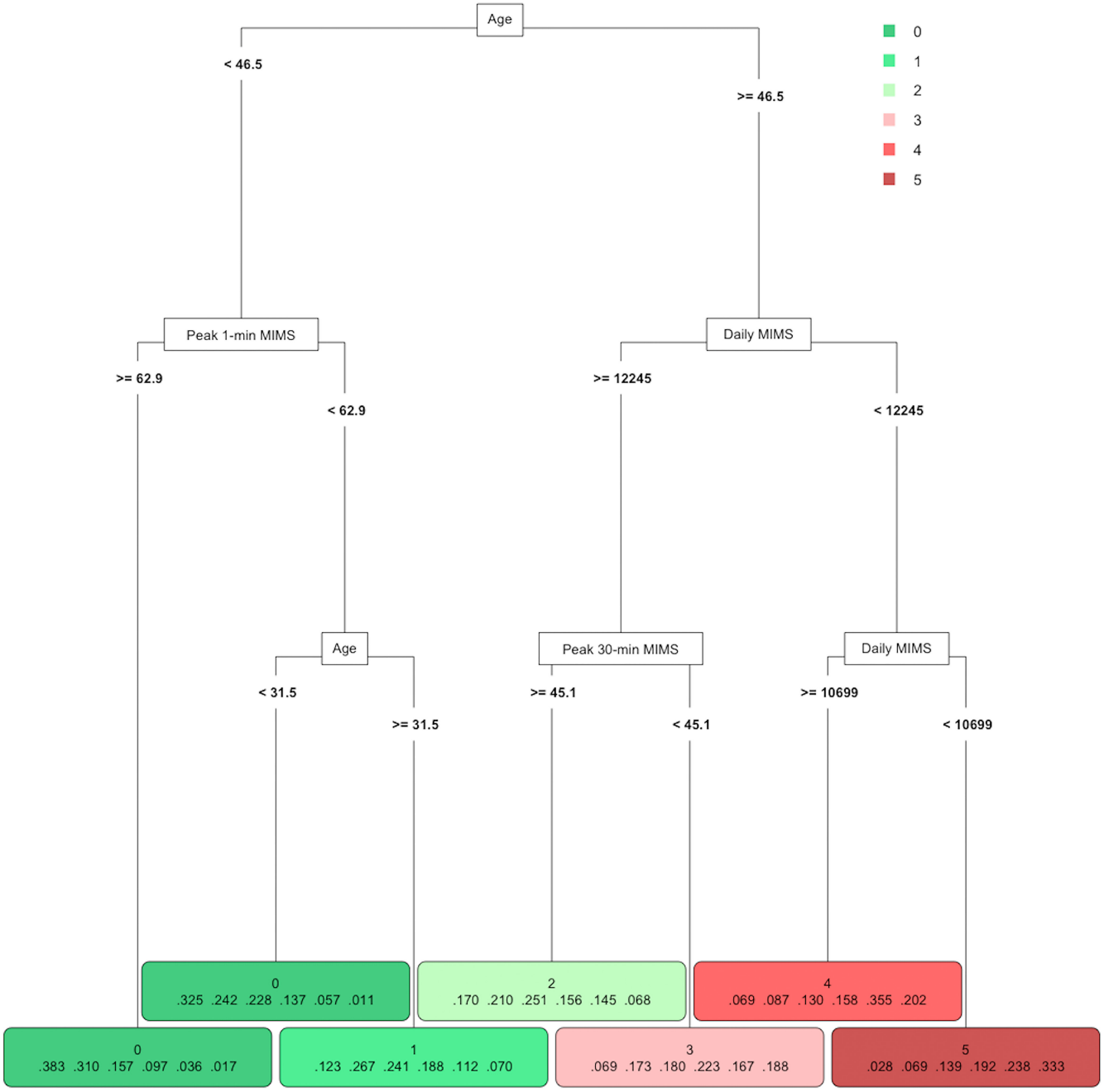

FIGURE 2 | Decision Tree describing classification of the number of Metabolic Syndrome risk factors (0–5) based on $Daily_{MIMS}$, $Peak_{MIMS}$ values, and covariates. Age, sex, race/ethnicity, and smoking status were added to the model, though only age appeared to have discriminatory power as a risk classifier. The values within each terminal node box (from top to bottom) indicates the number of risk factors classified for the sample at that node, the proportion of individuals within that terminal node who actually had 0, 1, 2, 3, 4 or 5 risk factors.

promising finding for establishing the construct validity of Daily and $Peak_{MIMS}$ metrics.

This study has several strengths. First, NHANES is a large, US representative sample, and thus the results of the present study are generalizable to the wider US population. Second, we used several analytical techniques, which all provided similar findings relating to the combined and independent associations between MIMS variables and risk of MetS. This study also has some limitations. No studies to date have directly defined MIMS/min levels (cut-points) associated with intensity levels (such as moderate or vigorous intensities) using criterion measures of absolute or relative intensity (e.g., oxygen uptake [VO_2], metabolic equivalent of task [METs] or percentage of maximal heart rate or heart rate reserve). Thus, we could not interpret the Peak MIMS values with reference to intensity thresholds or calculate time spent in various intensity categories. Notably, Karas et al. [5] recently reported high correlations (mean $r \geq 0.87$) between MIMS/min values and other prevalent PA measures including Euclidean Norm Minus One (ENMO), Mean Amplitude Deviation (MAD), and activity intensity. Further, John et al. in their original publication of the MIMS algorithm, demonstrated that higher MIMS/min values were observed at incremental treadmill walking/running speeds. Thus, our interpretation of the Peak MIMS variables as a proxy

of ambulatory intensity is plausible based on the finding of Karas et al. [5], and the established relationship between ambulatory speed and intensity [20, 21]. In addition, we chose a 1-day valid wear time criteria in accordance with the original report from Belcher et al. [2], who first reported US population-referenced values for Daily$_{MIMS}$ from the 2011–12 and 2013–14 NHANES survey cycles. It is important to note that, although a minimum of 1 valid day was required, wear time compliance was very good: 24.00 ± 0.03 h/day across 6.0 ± 1.6 days of recording. We subsequently ran a sensitivity analysis (design-based multivariable linear regression models; Table S1) using a wear time criterion of ≥4 days, which is an alternative and commonly used wear time criteria in the physical activity literature. Notably, the sensitivity analysis showed no major differences in the adjusted β (95% CIs) values, and did not meaningfully change the p-values of the MIMS variables in the models. Thus, this sensitivity analysis did not reveal any findings that would change the overall interpretation of the models. We also ran an additional sensitivity analysis (Table S2) replacing the US reference values for waist circumference (males ≥102 cm, females ≥88 cm) for Asian-specific reference values (IDF/WHO values: males ≥90 cm, females ≥80 cm) reported in the harmonized definition of MetS [9]. Notably, there were no major differences, with β (95% CIs) values for Peak 1 and Peak 30$_{MIMS}$ changing at the decimal level, while for Daily$_{MIMS}$, the values differed a negligible amount. Finally, due to the cross-sectional nature of this study, we cannot rule out the potential for bi-directional or reverse causality between the predictor and outcome variables examined herein.

5 | Perspective

Herein, we report that higher Daily$_{MIMS}$ and Peak$_{MIMS}$ values were associated with absence of MetS risk factors, with a progressive decline as the number of MetS risk factors increased. Importantly, peak intensity variables remained significant in models where daily volume was controlled for. Given the current absence of reports on the relationship between MIMS-based expressions of PA and cardiometabolic risk, our findings may be considered as preliminary benchmark values for Daily$_{MIMS}$ and Peak$_{MIMS}$ associated with either absence or presence of clinically meaningful cardiometabolic risk factors. Our findings may aid the understanding of these novel MIMS metrics across a broad audience of researchers, clinicians, and practitioners. For clinicians and practitioners, our implementation of the R Shiny app (https://ua-cv-health-and-physical-activity-lab.shinyapps.io/metabolic_syndrome_risk_viewer/) allows for quick visualization and estimation of MetS risk based on MIMS metric values, and also visually illustrates the importance of PA intensity (vs. volume) for cardiometabolic disease prevention/management. Researchers are encouraged to explore additional cross-sectional and longitudinal relationships (e.g., from PA randomized controlled trials) between Daily$_{MIMS}$ and Peak$_{MIMS}$ and a broad array of health risk factors. Ultimately, studies examining prospective associations with incident disease (e.g., cardiovascular disease and cancer), disease-specific mortality, and all-cause mortality are required. Furthermore, given the universal nature of the MIMS algorithm, which allows users to process raw accelerometry signals from various device manufacturers, there is potential for its implementation in large wrist-worn accelerometry cohort studies, such as the UK Biobank, among others, which would allow for country/region specific comparisons. Such studies are required to firmly establish the construct validity of MIMS as a PA metric related to health outcomes.

Acknowledgments

The authors have nothing to report.

Ethics Statement

NHANES study procedures were approved by the National Center for Health Statistics ethics review board and participants provided written informed consent.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Open access to data and a description of data collection procedures can be found at https://wwwn.cdc.gov/nchs/nhanes/.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.