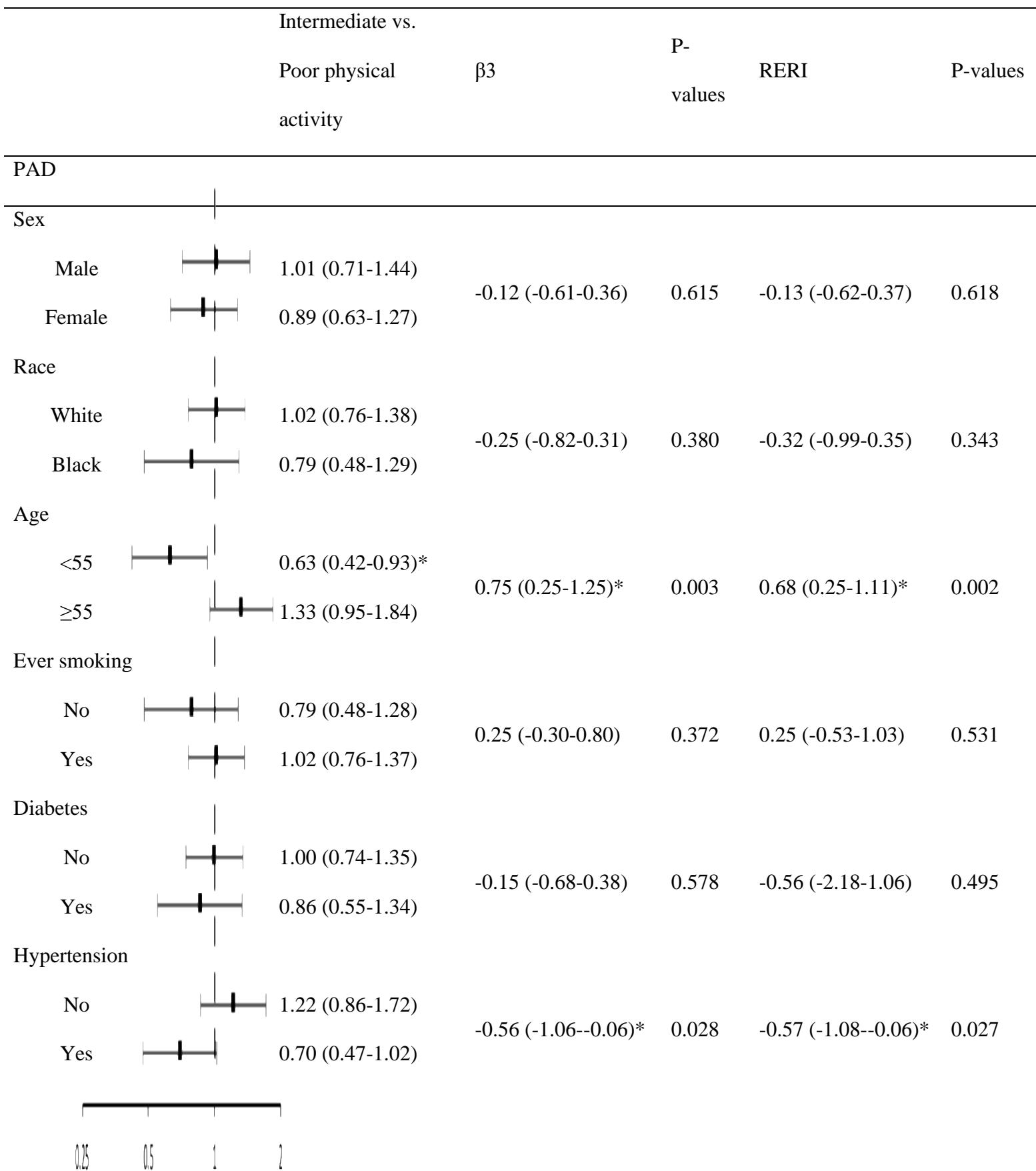


## **SUPPLEMENTAL MATERIAL**

**Table S1. Hazard ratios of incident PAD and CLI, multiplicative and additive interaction (95% confidence intervals) of American Heart Association-defined intermediate physical activity level with demographic and clinical conditions.**



(Continue Table S1)

CLI						
Sex						
Male		1.02 (0.55-1.90)				
Female		0.71 (0.40-1.28)	-0.36 (-1.19-0.46)	0.392	-0.35 (-1.16-0.46)	0.394
Race						
White		1.06 (0.62-1.82)	-0.68 (-1.63-0.27)	0.163	-1.02 (-2.15-0.11)	0.076
Black		0.54 (0.24-1.20)				
Age						
<55		0.72 (0.37-1.37)	0.29 (-0.54-1.12)	0.495	0.23 (-0.55-1.01)	0.563
≥55		0.95 (0.55-1.67)				
Ever smoking						
No		0.69 (0.34-1.38)	0.32 (-0.53-1.17)	0.460	0.23 (-0.68-1.14)	0.620
Yes		0.95 (0.56-1.61)				
Diabetes						
No		0.76 (0.42-1.40)	0.19 (-0.63-1.01)	0.650	-0.34 (-4.50-3.83)	0.874
Yes		0.92 (0.51-1.66)				
Hypertension						
No		1.22 (0.65-2.30)	-0.71 (-1.56-0.14)	0.102	-0.85 (-1.84-0.13)	0.088
Yes		0.60 (0.33-1.10)				
						
						

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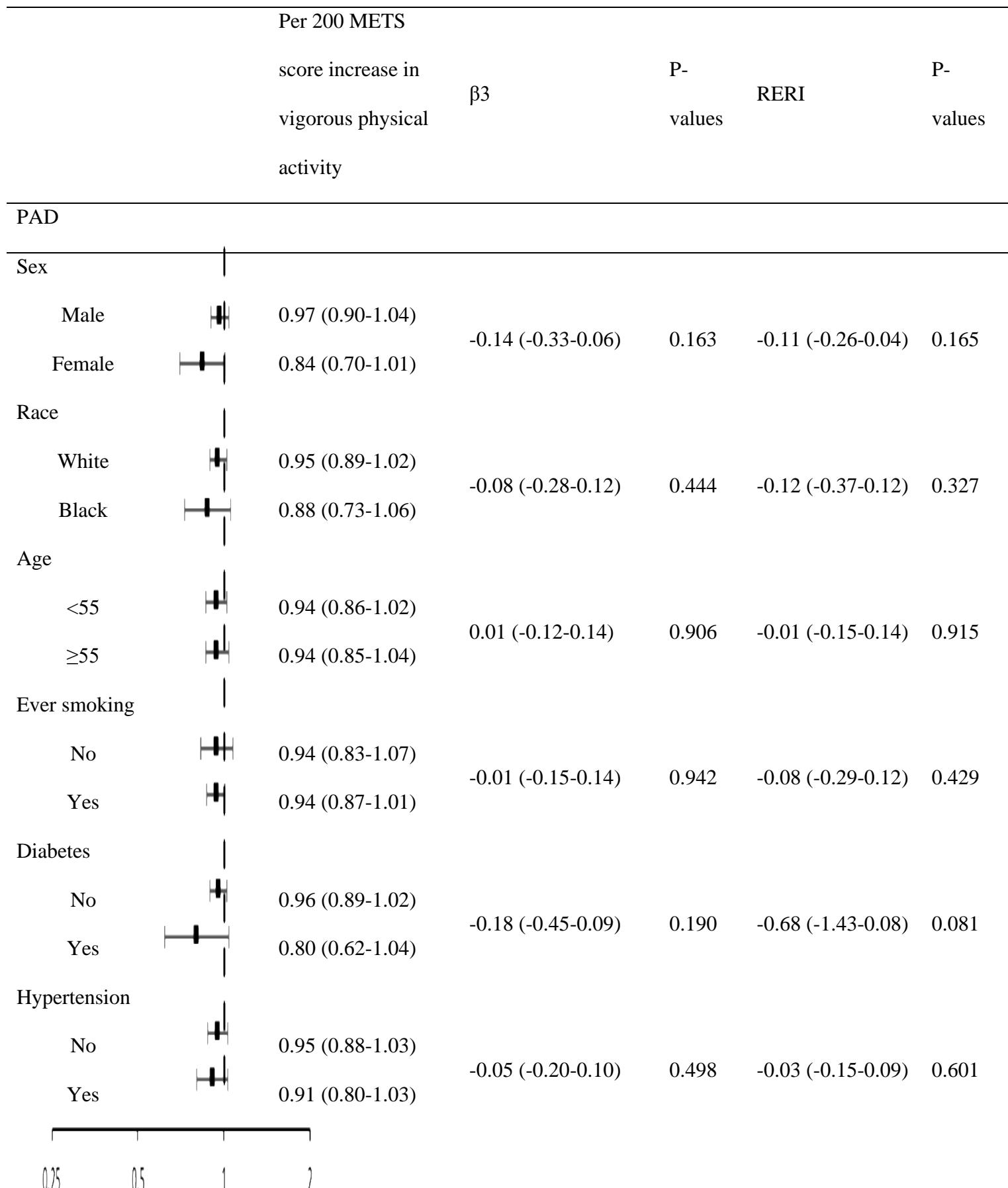
\* Statistically significant at 5%

† All models adjusted for age, sex, race, education, smoking status, drinking status, health insurance, leisure score, work score, body mass index, systolic blood pressure, total and HDL cholesterol, creatinine-derived eGFR, white blood cell, diabetes, antihypertensive medication use, cholesterol-lowering medication use, aspirin use, and interaction term

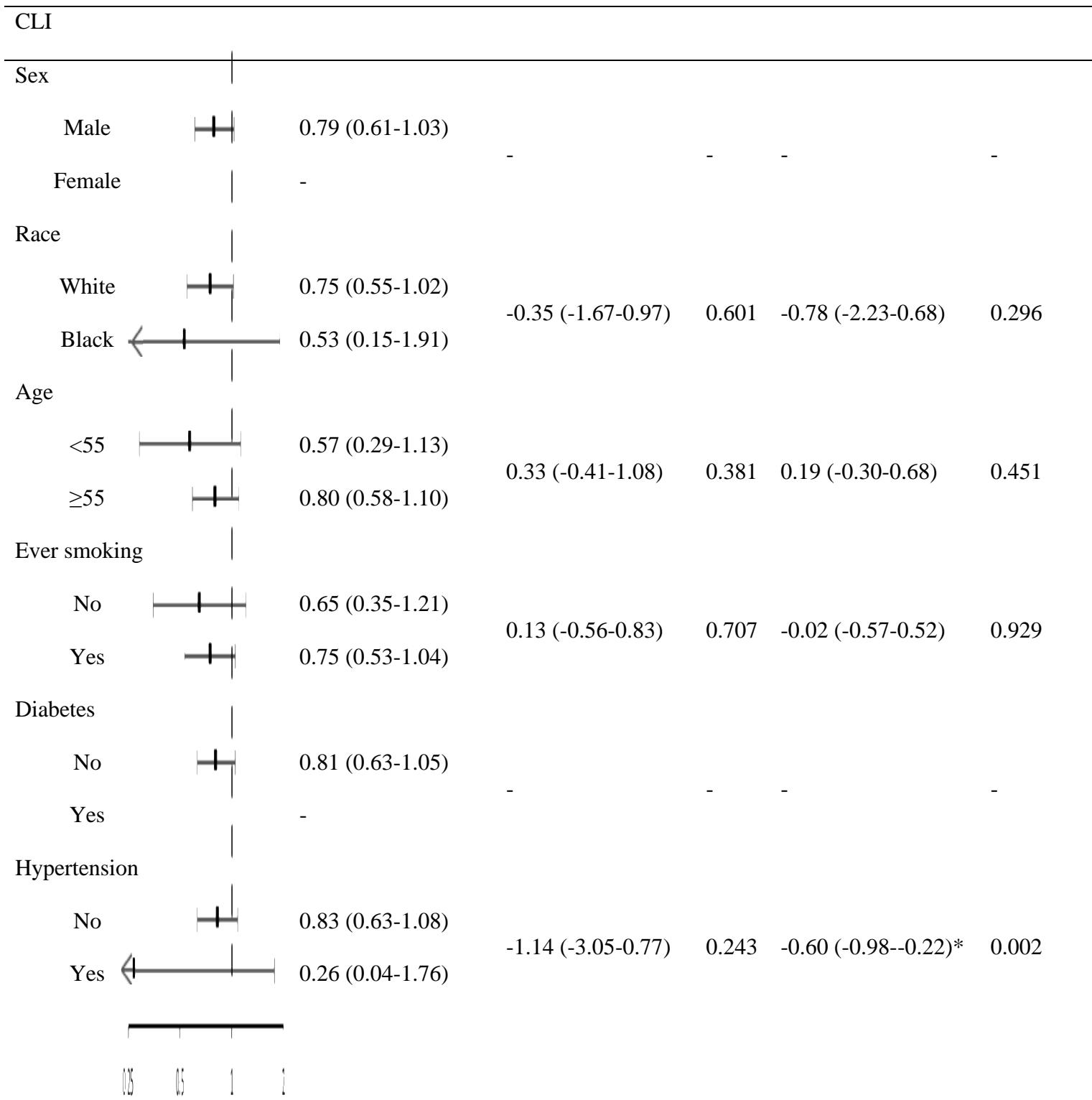
‡  $\beta_3$ , coefficient of interaction term; RERI, relative excess risk for interaction

§ PAD, peripheral artery disease; CLI, critical limb ischemia; Poor physical activity: 0 min/week of moderate or vigorous exercise; Intermediate physical activity: 1-74 min/week of vigorous exercise or 1-149 min/week of moderate plus vigorous exercise

**Table S2. Hazard ratios of incident PAD and CLI, multiplicative and additive interaction (95% confidence intervals) of per 200 METS\*mins/week increase in vigorous physical activity with demographic and clinical conditions.**



(Continue Table S2)



\* Statistically significant at 5%

† All models adjusted for age, sex, race, education, smoking status, drinking status, health insurance, leisure score, work score, body mass index, systolic blood pressure, total and HDL cholesterol, creatinine-derived eGFR, white blood cell, diabetes, antihypertensive medication use, cholesterol-lowering medication use, aspirin use, and

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interaction term

‡  $\beta_3$ , coefficient of interaction term; RERI, relative excess risk for interaction

§ PAD, peripheral artery disease; CLI, critical limb ischemia

**Table S3. Hazard Ratios (95% Confidence Interval) for associations between American Heart Association-defined physical activity category with incident PAD and CLI with adjustment on baseline ABI category.**

AHA-defined Physical Activity categories	Number of participants	Number of events	model 1†	model 2‡	model 3§	model 4	model 5#
<b>PAD</b>							
<b>Poor</b>	4656	193	1(ref.)	1(ref.)	1(ref.)	1(ref.)	1(ref.)
<b>Intermediate</b>	3096	101	0.74 (0.58-0.94) *	0.81 (0.63-1.03)	0.92 (0.72-1.18)	0.91 (0.71-1.17)	0.94 (0.73-1.21)
<b>Recommended</b>	4761	140	0.68 (0.54-0.84) *	0.69 (0.55-0.87) *	0.84 (0.67-1.06)	0.83 (0.65-1.05)	0.84 (0.66-1.07)
<b>CLI</b>							
<b>Poor</b>	4656	88	1(ref.)	1(ref.)	1(ref.)	1(ref.)	1(ref.)
<b>Intermediate</b>	3096	32	0.51 (0.34-0.76) *	0.65 (0.43-0.98) *	0.76 (0.50-1.15)	0.77 (0.50-1.17)	0.83 (0.54-1.26)
<b>Recommended</b>	4761	46	0.49 (0.34-0.70) *	0.62 (0.42-0.89) *	0.77 (0.52-1.12)	0.79 (0.53-1.18)	0.81 (0.54-1.21)

\* Statistically significant at 5%

† Model 1: Baseline ABI category

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‡ Model 2: + Age, sex, race

§ Model 3: + Education, smoking status, drinking status, and health insurance

|| Model 4: + Leisure score and work score

# Model 5: + Body mass index, systolic blood pressure, total and HDL cholesterol, creatinine-derived eGFR, white blood cell, diabetes, antihypertensive medication use, cholesterol-lowering medication use, and aspirin use

\*\* PAD, peripheral artery disease; CLI, critical limb ischemia; AHA, American Heart Association

†† Poor: 0 min/week of moderate or vigorous exercise; Intermediate: 1-74 min/week of vigorous exercise or 1-149 min/week of moderate plus vigorous exercise;

Recommended:  $\geq 75$  min/week of vigorous exercise or  $\geq 150$  min/week of moderate plus vigorous exercise

**Table S4. Hazard Ratios (95% Confidence Interval) of incident PAD and CLI per 200 METS\*mins/week increase in moderate or vigorous physical activity with adjustment on baseline ABI category.**

<b>Physical activity</b>	<b>model 1†</b>	<b>model 2‡</b>	<b>model 3§</b>	<b>model 4  </b>	<b>model 5#</b>
<b>intensity</b>					
<b>PAD</b>					
<b>Moderate</b>	0.99 (0.95-1.02)	0.98 (0.95-1.02)	1.00 (0.96-1.03)	1.00 (0.96-1.03)	1.00 (0.96-1.03)
<b>Vigorous</b>	0.89 (0.83-0.95) *	0.90 (0.84-0.96) *	0.93 (0.87-0.99) *	0.93 (0.87-0.99) *	0.95 (0.89-1.02)
<b>CLI</b>					
<b>Moderate</b>	0.95 (0.90-1.01)	0.97 (0.92-1.03)	0.99 (0.94-1.05)	1.00 (0.94-1.06)	1.00 (0.94-1.06)
<b>Vigorous</b>	0.60 (0.43-0.84) *	0.65 (0.47-0.89) *	0.69 (0.51-0.93) *	0.70 (0.52-0.94) *	0.72 (0.53-0.97) *

\* Statistically significant at 5%

† Model 1: Baseline ABI category

‡ Model 2: + Age, sex, race

§ Model 3: + Education, smoking status, drinking status, and health insurance

|| Model 4: + Leisure score and work score

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# Model 5: + Body mass index, systolic blood pressure, total and HDL cholesterol, creatinine-derived eGFR, white blood cell, diabetes, antihypertensive medication use, cholesterol-lowering medication use, and aspirin use

\*\* PAD, peripheral artery disease; CLI, critical limb ischemia

**Table S5. Hazard Ratios (95% Confidence Interval) for associations between American Heart Association-defined physical activity category with incident PAD and CLI with additional censoring on incident cardiovascular diseases.**

AHA-defined Physical Activity categories	Number of participants	Number of events	model 1†	model 2‡	model 3§	model 4	model 5#
<b>PAD</b>							
<b>Poor</b>	4656	168	1(ref.)	1(ref.)	1(ref.)	1(ref.)	1(ref.)
<b>Intermediate</b>	3096	93	0.78 (0.60-0.99) *	0.84 (0.65-1.08)	0.96 (0.74-1.24)	0.95 (0.73-1.23)	0.98 (0.75-1.28)
<b>Recommended</b>	4761	130	0.70 (0.56-0.89) *	0.71 (0.56-0.90) *	0.87 (0.68-1.11)	0.85 (0.66-1.09)	0.87 (0.67-1.12)
<b>CLI</b>							
<b>Poor</b>	4656	74	1(ref.)	1(ref.)	1(ref.)	1(ref.)	1(ref.)
<b>Intermediate</b>	3096	27	0.51 (0.33-0.79) *	0.63 (0.41-0.99) *	0.75 (0.47-1.17)	0.76 (0.48-1.21)	0.84 (0.53-1.33)
<b>Recommended</b>	4761	43	0.53 (0.36-0.77) *	0.65 (0.44-0.96) *	0.82 (0.55-1.22)	0.86 (0.57-1.31)	0.90 (0.59-1.38)

\* Statistically significant at 5%

† Model 1: Crude model

‡ Model 2: + Age, sex, race

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§ Model 3: + Education, smoking status, drinking status, and health insurance

|| Model 4: + Leisure score and work score

# Model 5: + Body mass index, systolic blood pressure, total and HDL cholesterol, creatinine-derived eGFR, white blood cell, diabetes, antihypertensive medication use, cholesterol-lowering medication use, and aspirin use

\*\* PAD, peripheral artery disease; CLI, critical limb ischemia; AHA, American Heart Association

†† Poor: 0 min/week of moderate or vigorous exercise; Intermediate: 1-74 min/week of vigorous exercise or 1-149 min/week of moderate plus vigorous exercise;

Recommended:  $\geq 75$  min/week of vigorous exercise or  $\geq 150$  min/week of moderate plus vigorous exercise

**Table S6. Hazard Ratios (95% Confidence Interval) of incident PAD and CLI per 200 METS\*mins/week increase in moderate or vigorous physical activity with additional censoring on incident cardiovascular diseases.**

Physical activity	model 1†	model 2‡	model 3§	model 4	model 5#
<b>intensity</b>					
<b>PAD</b>					
<b>Moderate</b>	0.99 (0.95-1.02)	0.98 (0.94-1.02)	1.00 (0.96-1.03)	0.99 (0.96-1.03)	0.99 (0.96-1.03)
<b>Vigorous</b>	0.90 (0.84-0.96) *	0.90 (0.84-0.97) *	0.94 (0.88-1.01)	0.94 (0.88-1.01)	0.96 (0.90-1.03)
<b>CLI</b>					
<b>Moderate</b>	0.96 (0.90-1.02)	0.97 (0.91-1.04)	1.00 (0.94-1.06)	1.00 (0.94-1.07)	1.01 (0.94-1.08)
<b>Vigorous</b>	0.63 (0.45-0.87) *	0.67 (0.49-0.91) *	0.71 (0.53-0.95) *	0.72 (0.54-0.97) *	0.74 (0.55-0.99) *

\* Statistically significant at 5%

† Model 1: Crude model

‡ Model 2: + Age, sex, race

§ Model 3: + Education, smoking status, drinking status, and health insurance

|| Model 4: + Leisure score and work score

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# Model 5: + Body mass index, systolic blood pressure, total and HDL cholesterol, creatinine-derived eGFR, white blood cell, diabetes, antihypertensive medication use, cholesterol-lowering medication use, and aspirin use

\*\* PAD, peripheral artery disease; CLI, critical limb ischemia

**Table S7. Hazard Ratios (95% Confidence Interval) for associations between American Heart Association-defined physical activity category with incident PAD and CLI with lag years.**

<b>Poor</b>	4654	191	1(ref.)	1(ref.)	1(ref.)	1(ref.)	1(ref.)
<b>Intermediate</b>	3096	101	0.74 (0.58-0.94) *	0.82 (0.64-1.04)	0.94 (0.74-1.21)	0.93 (0.72-1.20)	0.96 (0.75-1.24)
<b>Recommended</b>	4755	134	0.64 (0.51-0.80) *	0.66 (0.53-0.83) *	0.82 (0.65-1.04)	0.80 (0.63-1.03)	0.82 (0.64-1.05)
<b>CLI</b>							
<b>Poor</b>	4654	88	1(ref.)	1(ref.)	1(ref.)	1(ref.)	1(ref.)
<b>Intermediate</b>	3096	32	0.51 (0.34-0.76) *	0.64 (0.43-0.97) *	0.77 (0.51-1.16)	0.77 (0.51-1.18)	0.82 (0.53-1.25)
<b>Recommended</b>	4755	46	0.48 (0.33-0.68) *	0.60 (0.42-0.87) *	0.78 (0.53-1.14)	0.79 (0.53-1.18)	0.81 (0.54-1.21)

### Lag 3 years

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<b>PAD</b>							
<b>Poor</b>	4651	188	1(ref.)	1(ref.)	1(ref.)	1(ref.)	1(ref.)
<b>Intermediate</b>	3096	101	0.75 (0.59-0.96) *	0.83 (0.65-1.06)	0.96 (0.75-1.23)	0.95 (0.74-1.22)	0.98 (0.76-1.26)
<b>Recommended</b>	4754	133	0.65 (0.52-0.81) *	0.67 (0.53-0.84) *	0.83 (0.66-1.05)	0.81 (0.63-1.04)	0.83 (0.65-1.07)
<b>CLI</b>							
<b>Poor</b>	4651	86	1(ref.)	1(ref.)	1(ref.)	1(ref.)	1(ref.)
<b>Intermediate</b>	3096	32	0.52 (0.35-0.78) *	0.66 (0.44-1.00)	0.78 (0.52-1.19)	0.79 (0.52-1.21)	0.84 (0.55-1.30)

<b>Recommended</b>	4754	46	0.49 (0.34-0.70) *	0.62 (0.43-0.90) *	0.80 (0.54-1.17)	0.82 (0.55-1.22)	0.84 (0.56-1.25)
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#### Lag 4 years

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<b>PAD</b>							
<b>Poor</b>	4649	186	1(ref.)	1(ref.)	1(ref.)	1(ref.)	1(ref.)
<b>Intermediate</b>	3093	98	0.74 (0.58-0.94) *	0.81 (0.63-1.04)	0.94 (0.73-1.21)	0.93 (0.72-1.20)	0.97 (0.75-1.25)
<b>Recommended</b>	4753	132	0.65 (0.52-0.81) *	0.67 (0.53-0.85) *	0.83 (0.66-1.06)	0.82 (0.64-1.05)	0.85 (0.66-1.09)
<b>CLI</b>							
<b>Poor</b>	4649	86	1(ref.)	1(ref.)	1(ref.)	1(ref.)	1(ref.)
<b>Intermediate</b>	3093	31	0.50 (0.33-0.76) *	0.64 (0.42-0.97) *	0.76 (0.50-1.16)	0.77 (0.50-1.17)	0.82 (0.53-1.26)
<b>Recommended</b>	4753	46	0.49 (0.34-0.70) *	0.62 (0.43-0.90) *	0.79 (0.54-1.16)	0.81 (0.54-1.21)	0.84 (0.56-1.25)

#### Lag 5 years

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<b>PAD</b>							
<b>Poor</b>	4646	183	1(ref.)	1(ref.)	1(ref.)	1(ref.)	1(ref.)
<b>Intermediate</b>	3092	97	0.74 (0.58-0.95) *	0.82 (0.64-1.05)	0.95 (0.74-1.22)	0.94 (0.73-1.22)	0.98 (0.75-1.26)

<b>Recommended</b>	4751	130	0.65 (0.52-0.81) *	0.67 (0.53-0.85) *	0.83 (0.66-1.06)	0.83 (0.64-1.06)	0.85 (0.66-1.10)
<b>CLI</b>							
<b>Poor</b>	4646	84	1(ref.)	1(ref.)	1(ref.)	1(ref.)	1(ref.)
<b>Intermediate</b>	3092	31	0.52 (0.34-0.78) *	0.66 (0.43-1.00)	0.78 (0.51-1.19)	0.79 (0.51-1.21)	0.85 (0.55-1.31)
<b>Recommended</b>	4751	46	0.50 (0.35-0.72) *	0.64 (0.44-0.93) *	0.82 (0.56-1.20)	0.84 (0.56-1.25)	0.86 (0.57-1.29)

\* Statistically significant at 5%

† Model 1: Crude model

‡ Model 2: + Age, sex, race

§ Model 3: + Education, smoking status, drinking status, and health insurance

|| Model 4: + Leisure score and work score

# Model 5: + Body mass index, systolic blood pressure, total and HDL cholesterol, creatinine-derived eGFR, white blood cell, diabetes, antihypertensive medication use, cholesterol-lowering medication use, and aspirin use

\*\* PAD, peripheral artery disease; CLI, critical limb ischemia; AHA, American Heart Association

†† Poor: 0 min/week of moderate or vigorous exercise; Intermediate: 1-74 min/week of vigorous exercise or 1-149 min/week of moderate plus vigorous exercise;

Recommended: ≥75 min/week of vigorous exercise or ≥150 min/week of moderate plus vigorous exercise

**Table S8. Hazard Ratios (95% Confidence Interval) of incident PAD and CLI per 200 METS\*mins/week increase in moderate or vigorous physical activity with lag years.**

<b>Physical activity</b>	<b>model 1†</b>	<b>model 2‡</b>	<b>model 3§</b>	<b>model 4  </b>	<b>model 5#</b>
<b>intensity</b>					
<b>Lag 1 year</b>					
<b>PAD</b>					
<b>Moderate</b>	0.98 (0.94-1.01)	0.98 (0.94-1.01)	1.00 (0.96-1.03)	0.99 (0.96-1.03)	1.00 (0.96-1.03)
<b>Vigorous</b>	0.89 (0.83-0.95) *	0.90 (0.84-0.96) *	0.93 (0.87-1.00) *	0.93 (0.87-1.00) *	0.95 (0.89-1.02)
<b>CLI</b>					
<b>Moderate</b>	0.93 (0.88-0.99) *	0.96 (0.90-1.02)	0.99 (0.93-1.05)	0.99 (0.93-1.06)	1.00 (0.94-1.06)
<b>Vigorous</b>	0.59 (0.42-0.82) *	0.64 (0.47-0.88) *	0.69 (0.51-0.93) *	0.70 (0.52-0.94) *	0.72 (0.54-0.97) *
<b>Lag 2 years</b>					
<b>PAD</b>					
<b>Moderate</b>	0.97 (0.94-1.01)	0.97 (0.94-1.01)	0.99 (0.96-1.03)	0.99 (0.96-1.03)	0.99 (0.96-1.03)
<b>Vigorous</b>	0.89 (0.83-0.95) *	0.90 (0.84-0.96) *	0.93 (0.88-1.00) *	0.94 (0.88-1.00) *	0.95 (0.89-1.02)

**CLI**

<b>Moderate</b>	0.93 (0.88-0.99) *	0.96 (0.90-1.02)	0.99 (0.93-1.05)	0.99 (0.93-1.06)	1.00 (0.94-1.06)
<b>Vigorous</b>	0.59 (0.42-0.82) *	0.64 (0.47-0.88) *	0.69 (0.51-0.93) *	0.70 (0.52-0.94) *	0.72 (0.54-0.97) *

**Lag 3 years****PAD**

<b>Moderate</b>	0.98 (0.94-1.01)	0.97 (0.94-1.01)	1.00 (0.96-1.03)	1.00 (0.96-1.03)	1.00 (0.96-1.03)
<b>Vigorous</b>	0.89 (0.83-0.95) *	0.90 (0.84-0.96) *	0.94 (0.88-1.00) *	0.94 (0.88-1.00)	0.96 (0.89-1.02)

**CLI**

<b>Moderate</b>	0.94 (0.88-0.99) *	0.96 (0.91-1.02)	0.99 (0.93-1.05)	1.00 (0.94-1.06)	1.00 (0.94-1.07)
<b>Vigorous</b>	0.59 (0.42-0.83) *	0.64 (0.47-0.88) *	0.69 (0.51-0.93) *	0.70 (0.52-0.94) *	0.72 (0.54-0.97) *

**Lag 4 years****PAD**

<b>Moderate</b>	0.98 (0.94-1.01)	0.97 (0.94-1.01)	1.00 (0.96-1.03)	1.00 (0.96-1.03)	1.00 (0.96-1.04)
<b>Vigorous</b>	0.89 (0.83-0.95) *	0.90 (0.84-0.96) *	0.94 (0.88-1.00)	0.94 (0.88-1.00)	0.96 (0.90-1.02)

**CLI**

<b>Moderate</b>	0.93 (0.88-0.99) *	0.96 (0.91-1.02)	0.99 (0.93-1.05)	1.00 (0.94-1.06)	1.00 (0.94-1.07)
<b>Vigorous</b>	0.59 (0.42-0.83) *	0.64 (0.47-0.88) *	0.69 (0.51-0.93) *	0.70 (0.52-0.94) *	0.72 (0.54-0.97) *

**Lag 5 years****PAD**

<b>Moderate</b>	0.98 (0.94-1.01)	0.98 (0.94-1.01)	1.00 (0.96-1.03)	1.00 (0.96-1.03)	1.00 (0.96-1.04)
<b>Vigorous</b>	0.89 (0.83-0.95) *	0.90 (0.84-0.96) *	0.94 (0.88-1.00)	0.94 (0.88-1.00)	0.96 (0.90-1.03)

**CLI**

<b>Moderate</b>	0.94 (0.88-1.00) *	0.97 (0.91-1.03)	0.99 (0.94-1.05)	1.00 (0.94-1.06)	1.00 (0.94-1.07)
<b>Vigorous</b>	0.59 (0.43-0.83) *	0.65 (0.47-0.88) *	0.69 (0.51-0.94) *	0.70 (0.52-0.95) *	0.73 (0.54-0.98) *

\* Statistically significant at 5%

† Model 1: Crude model

‡ Model 2: + Age, sex, race

§ Model 3: + Education, smoking status, drinking status, and health insurance

|| Model 4: + Leisure score and work score

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# Model 5: + Body mass index, systolic blood pressure, total and HDL cholesterol, creatinine-derived eGFR, white blood cell, diabetes, antihypertensive medication use, cholesterol-lowering medication use, and aspirin use

\*\* PAD, peripheral artery disease; CLI, critical limb ischemia

**Table S9. Hazard Ratios (95% Confidence Interval) for associations between 5 physical activity categories regardless of intensity with incident PAD and CLI.**

Physical Activity categories	Number of participants	Number of events	model 1†	model 2‡	model 3§	model 4	model 5#
<b>PAD</b>							
<b>0 min/week</b>	4524	189	1(ref.)	1(ref.)	1(ref.)	1(ref.)	1(ref.)
<b>1-74 min/week</b>	1251	35	0.64 (0.45-0.92) *	0.69 (0.48-0.99) *	0.78 (0.54-1.13)	0.77 (0.54-1.11)	0.80 (0.56-1.16)
<b>75-149 min/week</b>	1803	62	0.76 (0.57-1.01)	0.82 (0.62-1.10)	0.98 (0.73-1.32)	0.97 (0.72-1.30)	0.98 (0.73-1.33)
<b>150-299 min/week</b>	2872	88	0.69 (0.53-0.88) *	0.72 (0.56-0.93) *	0.90 (0.69-1.17)	0.88 (0.67-1.15)	0.87 (0.66-1.14)
<b>≥300 min/week</b>	2063	60	0.65 (0.49-0.87) *	0.65 (0.48-0.88) *	0.81 (0.60-1.09)	0.78 (0.57-1.07)	0.89 (0.65-1.22)
<b>P-value for trend</b>			<0.001	0.002	0.232	0.179	0.383
<b>CLI</b>							
<b>0 min/week</b>	4524	87	1(ref.)	1(ref.)	1(ref.)	1(ref.)	1(ref.)
<b>1-74 min/week</b>	1251	13	0.52 (0.29-0.92) *	0.62 (0.35-1.12)	0.73 (0.41-1.32)	0.73 (0.41-1.32)	0.79 (0.44-1.44)
<b>75-149 min/week</b>	1803	18	0.48 (0.29-0.79) *	0.60 (0.36-1.00)	0.73 (0.43-1.22)	0.74 (0.44-1.25)	0.79 (0.47-1.34)
<b>150-299 min/week</b>	2872	29	0.49 (0.32-0.75) *	0.62 (0.41-0.96) *	0.80 (0.51-1.24)	0.81 (0.52-1.27)	0.78 (0.49-1.22)

<b>&gt;300 min/week</b>	2063	19	0.44 (0.27-0.73) *	0.57 (0.34-0.95) *	0.73 (0.44-1.23)	0.75 (0.44-1.28)	0.93 (0.54-1.61)
<b>P-value for trend</b>			<0.001	0.006	0.157	0.216	0.408

\* Statistically significant at 5%

† Model 1: Crude model

‡ Model 2: + Age, sex, race

§ Model 3: + Education, smoking status, drinking status, and health insurance

|| Model 4: + Leisure score and work score

# Model 5: + Body mass index, systolic blood pressure, total and HDL cholesterol, creatinine-derived eGFR, white blood cell, diabetes, antihypertensive medication use, cholesterol-lowering medication use, and aspirin use

\*\* PAD, peripheral artery disease; CLI, critical limb ischemia