

Supplemental Materials

Association of the time of day of peak physical activity with cardiovascular mortality:

Findings from the UK Biobank Study

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Figure S1. An example of kmeans clustering for a two-dimensional dataset.

Figure S2. Distribution of individual physical activity volume stratified by sex (Upper Panel) and age (Lower Panel).

Figure S3. The association between the volume of physical activity and CVD mortality.

Figure S4. Diurnal patterns of physical activity by machine learning-based clustering **using a higher number of clusters (5-10 clusters).**

Figure S5. Group labels in sensitivity analysis (based on eight clusters with the two stable clusters merged into one. Therefore, a total of seven groups are presented in this Figure).

Table S1. Cox proportional hazards regression for the association between time of day and CVD mortality **excluding individuals who reported nightshift work.**

	Midday Group (Reference)	Early Morning Group	Late Morning Group	Night Group
Full Sample (n=90,792)				
No. of Deaths	173	113	206	124
No. of Participants	26,751	17,755	25,033	21,253
Hazard Ratio	1 (Reference)	1.53 (1.21 – 1.95)	1.20 (0.98 – 1.47)	1.47 (1.16 – 1.86)
With Pre-Existing CVD (n=6,491)				
No. of Deaths	46	34	68	38
No. of Participants	2,206	1,010	2,158	1,117
Hazard Ratio	1 (Reference)	1.89 (1.21 – 2.95)	1.48 (1.01 – 2.15)	1.77 (1.14 – 2.75)
Without CVD (n=84,301)				
No. of Deaths	127	79	138	86
No. of Participants	24,545	16,745	22,875	20,136
Hazard Ratio	1 (Reference)	1.40 (1.05 – 1.86)	1.11 (0.87 – 1.41)	1.34 (1.02 – 1.77)

Table S2. Cox proportional hazards regression for the association between time of day and CVD mortality **excluding participants who died within two years of follow-up.**

	Midday Group	Early Morning	Late Morning	Night Group
	(Reference)	Group	Group	
Full Sample (n=93,958)				
No. of Deaths	142	96	173	99
No. of Participants	27,642	18,391	25,542	22,383
Hazard Ratio	1 (Reference)	1.58 (1.22 – 2.05)	1.22 (0.97 – 1.52)	1.43 (1.10 – 1.86)
With CVD (n=6,552)				
No. of Deaths	36	28	56	31
No. of Participants	2,237	1,013	2,164	1,138
Hazard Ratio	1 (Reference)	1.96 (1.19 – 3.22)	1.54 (1.01 – 2.35)	1.86 (1.14 – 3.03)
Without CVD (n=87,406)				
No. of Deaths	106	68	117	68
No. of Participants	25,405	17,378	23,378	21,245
Hazard Ratio	1 (Reference)	1.45 (1.06 – 1.97)	1.12 (0.86 – 1.46)	1.28 (0.94 – 1.74)

Table S3. Cox proportional hazards regression for the association between time of day and CVD mortality **with further adjustment for employment and total sleep duration.**

	Midday Group (Reference)	Early Morning Group	Late Morning Group	Night Group
Full Sample (n=94,489)				
No. of Deaths	175	117	208	129
No. of Participants	27,803	18,477	25,700	22,509
Hazard Ratio	1 (Reference)	1.60 (1.26 – 2.02)	1.19 (0.97 – 1.46)	1.52 (1.20 – 1.91)
With Pre-Existing CVD (n=6,672)				
No. of Deaths	46	34	69	41
No. of Participants	2,267	1,035	2,204	1,166
Hazard Ratio	1 (Reference)	1.90 (1.21 – 2.98)	1.50 (1.03 – 2.19)	1.92 (1.25 – 2.95)
Without CVD (n=87,817)				
No. of Deaths	129	83	139	88
No. of Participants	25,536	17,442	23,496	21,343
Hazard Ratio	1 (Reference)	1.48 (1.12 – 1.96)	1.09 (0.86 – 1.39)	1.36 (1.03 – 1.79)

Table S4. Cox proportional hazards regression for the association of time of day with **non-CVD** and **all-cause** mortality.

	Midday Group (Reference)	Early Morning Group	Late Morning Group	Night Group
Hazard Ratios of Non-CVD Mortality (n=94,489)				
No. of Deaths	870	395	814	478
No. of Participants	27,803	18,477	25,700	22,509
Hazard Ratio	1 (Reference)	1.02 (0.91 – 1.15)	0.98 (0.89 – 1.07)	1.02 (0.91 – 1.15)
Hazard Ratios of All-Cause Mortality (n=94,489)				
No. of Deaths	1045	512	1022	607
No. of Participants	27,803	18,477	25,700	22,509
Hazard Ratio	1 (Reference)	1.11 (1.0 – 1.24)	1.02 (0.93 – 1.11)	1.10 (0.99 – 1.22)

Table S5. Competing risk regression analysis of time-of-day groups and CVD mortality in the presence of a competing event (non-CVD mortality).

	Midday Group (Reference)	Early Morning Group	Late Morning Group	Night Group
Full Sample (n=94,489)				
No. of CVD Deaths	175	117	208	129
No. of Competing Events	870	395	814	478
No. of Participants	27,803	18,477	25,700	22,509
Hazard Ratio of CVD Mortality	1 (Reference)	1.61 (1.27 – 2.05)	1.22 (0.99 – 1.49)	1.50 (1.19 – 1.89)
With Pre-Existing CVD (n=6,672)				
No. of CVD Deaths	46	34	69	41
No. of Competing Events	142	57	136	78
No. of Participants	2,267	1,035	2,204	1,166
Hazard Ratio of CVD Mortality	1 (Reference)	1.84 (1.18 – 2.89)	1.50 (1.03 – 2.19)	1.87 (1.23 – 2.85)
Without CVD (n=87,817)				
No. of CVD Deaths	129	83	139	88
No. of Competing Events	728	338	678	400
No. of Participants	25,536	17,442	23,496	21,343
Hazard Ratio of CVD Mortality	1 (Reference)	1.50 (1.14 – 1.99)	1.13 (0.89 – 1.43)	1.35 (1.02 – 1.78)

Table S6. Cox proportional hazards regression for the association between time of day and CVD mortality **based on eight clusters** (the two stable clusters were merged into one in the analysis, see **Figure S5** for illustrations of group labels).

	Midday	Early	Mid-	Late	Afternoon	Night	Stable
	Group	Morning	Morning	Morning	Group	Group	Group
	(Reference)	Group	Group	Group			
Full Sample (n=94,489)							
No. of Deaths	76	48	84	85	64	30	242
No. of Participants	11,654	8,631	11,382	9,347	13,288	9,755	30432
Hazard Ratio	1	1.56 (1.08	1.35 (0.99	1.36 (0.99	0.94 (0.68	1.61 (1.04	1.46 (1.12
	(Reference)	- 2.25)	- 1.84)	- 1.86)	-1.32)	- 2.49)	- 1.89)

Figure S1. An example of kmeans clustering for a two-dimensional dataset.

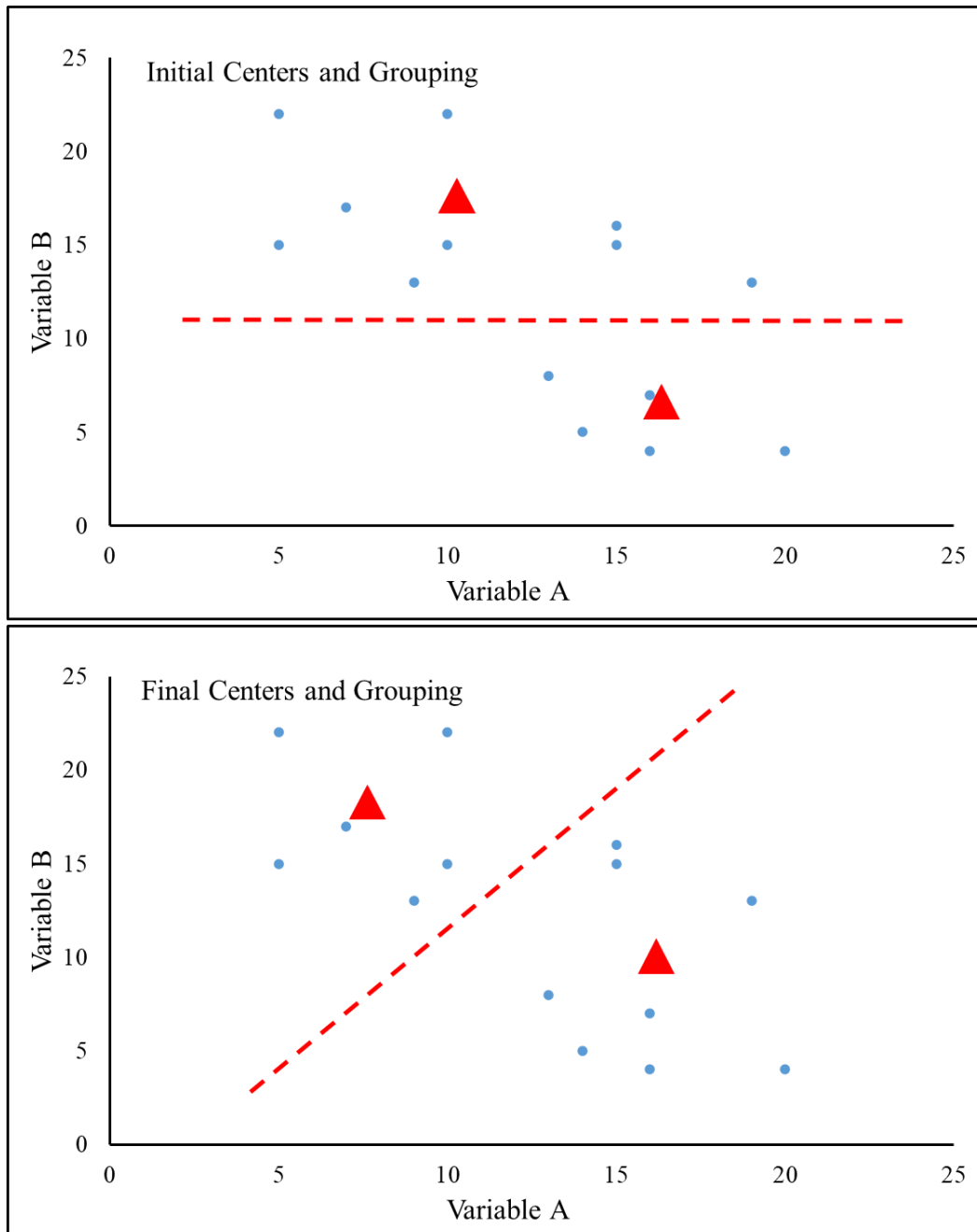
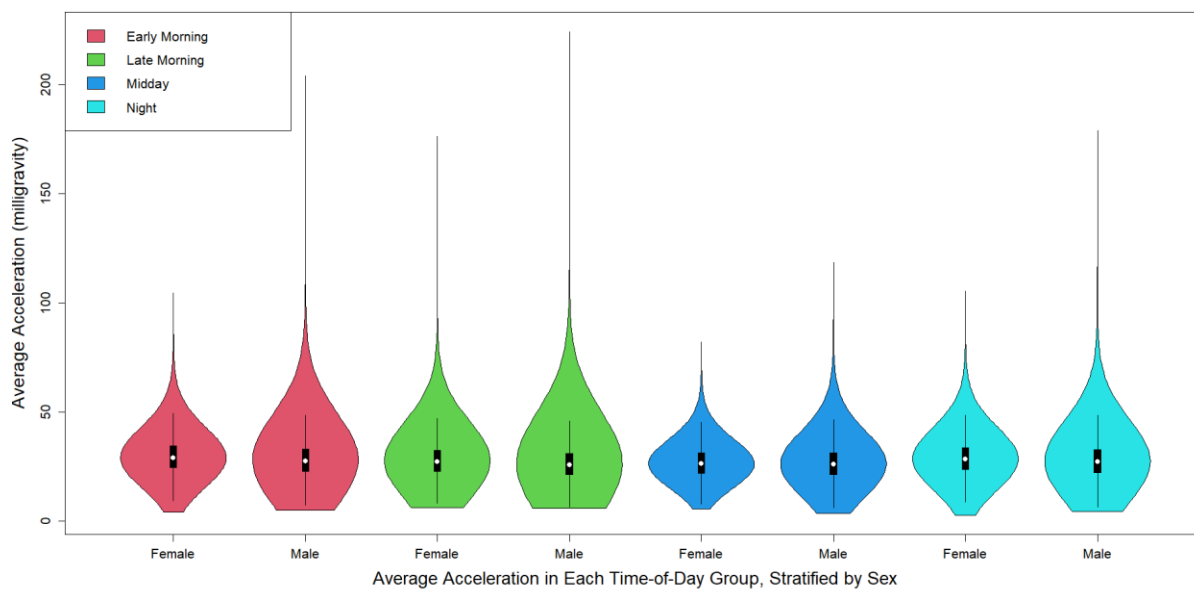
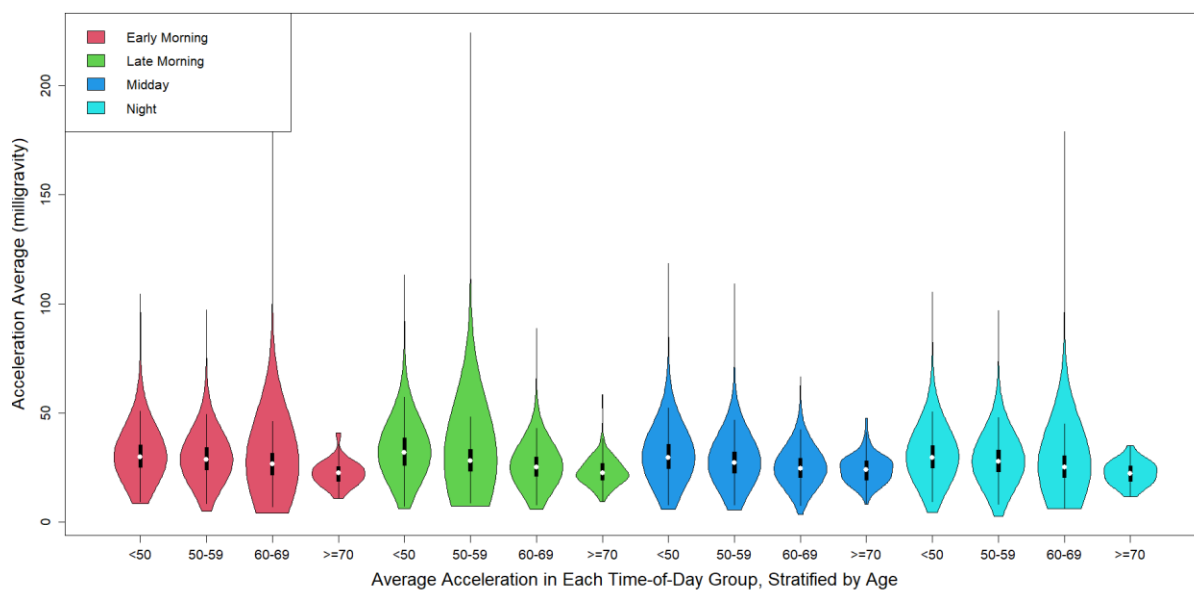


Figure S2. Distribution of individual physical activity volume stratified by sex (Upper Panel)

and age (Lower Panel).



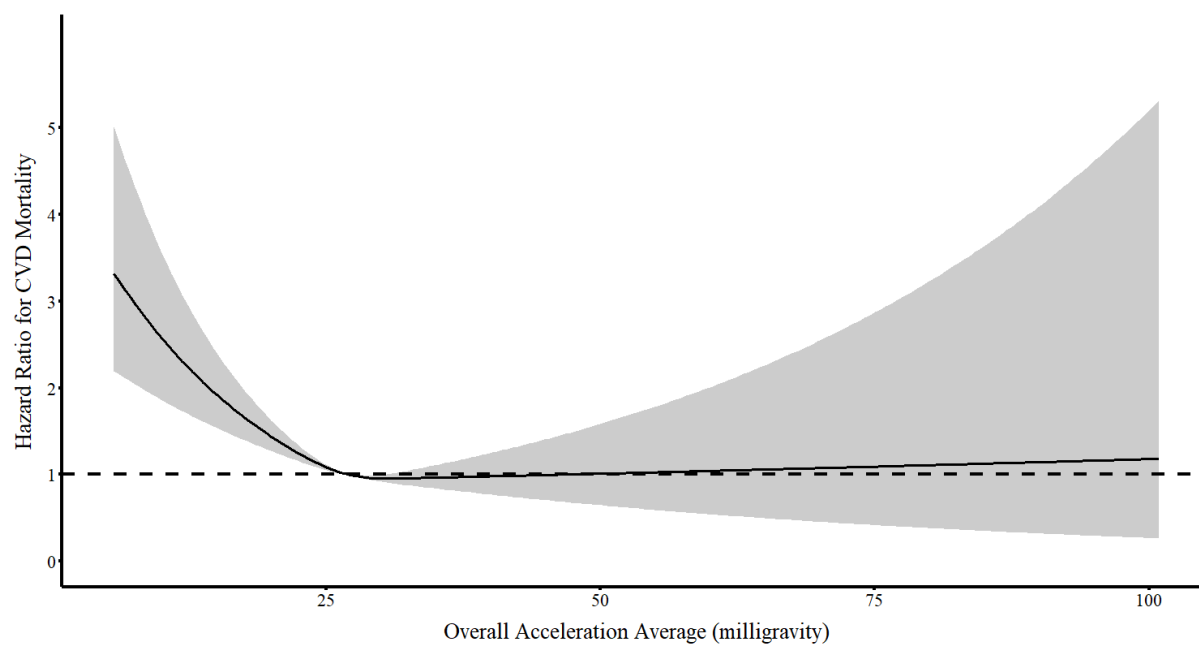
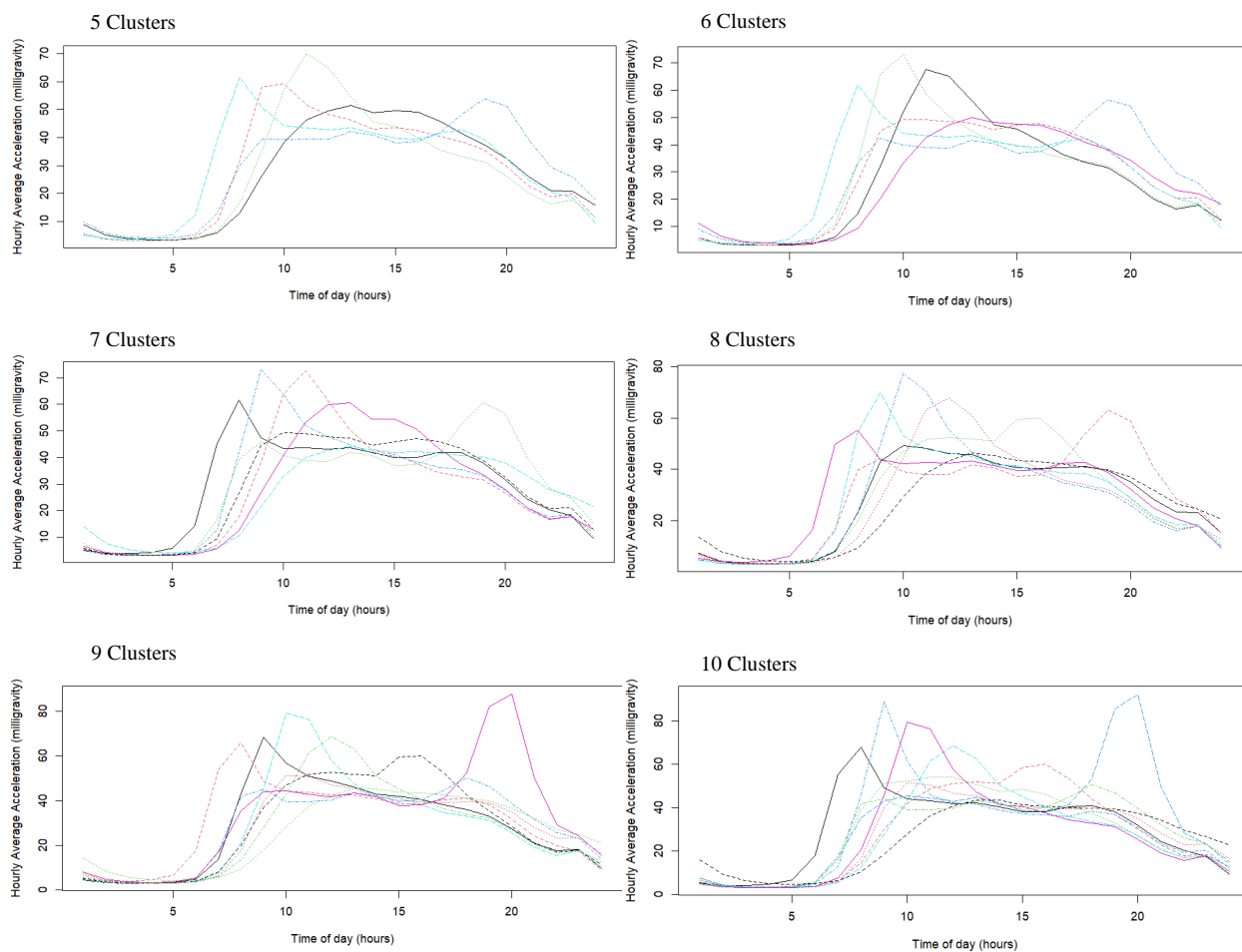
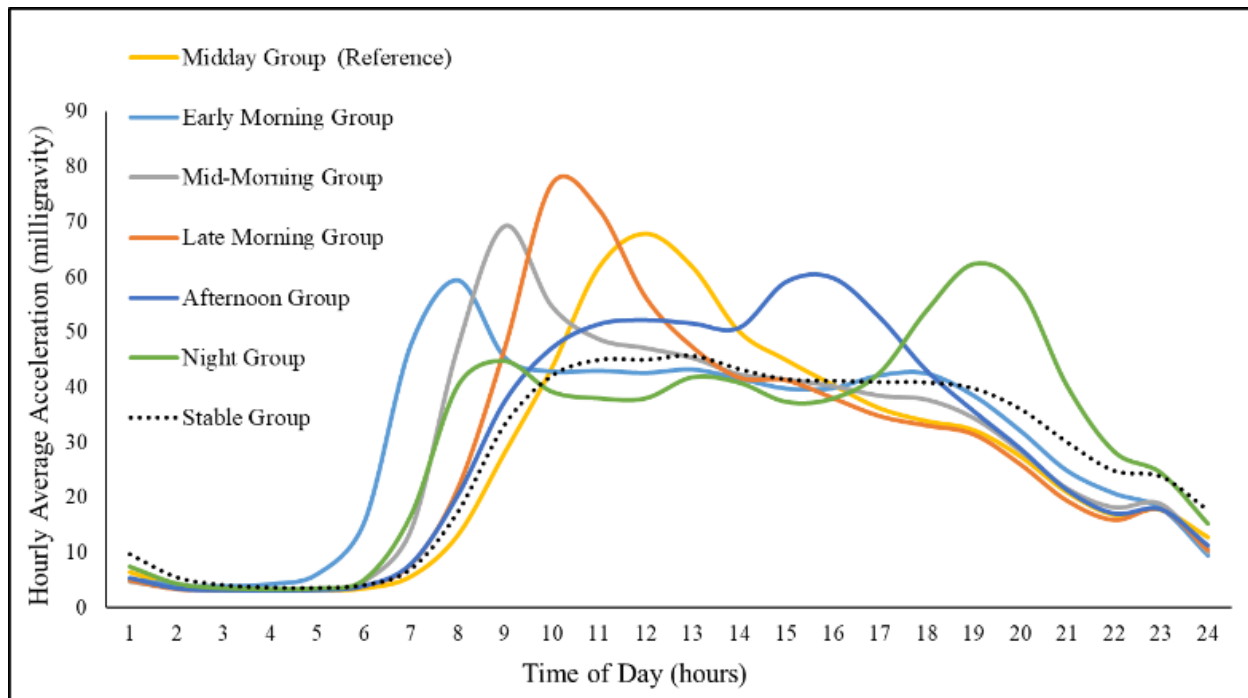


Figure S3. The association between the volume of physical activity and CVD mortality.

Figure S4. Diurnal patterns of physical activity by machine learning-based clustering **using a**

higher number of clusters (5-10 clusters).

Figure S5. Group labels in sensitivity analysis (based on eight clusters with the two stable



clusters merged into one. Therefore, a total of seven groups are presented in the Figure).