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# American Journal of Preventive Medicine

## **RESEARCH ARTICLE**

# Associations of Physical Inactivity and COVID-19 Outcomes Among Subgroups

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**Introduction:** Physical activity before COVID-19 infection is associated with less severe outcomes. The study determined whether a dose–response association was observed and whether the associations were consistent across demographic subgroups and chronic conditions.

**Methods:** A retrospective cohort study of Kaiser Permanente Southern California adult patients who had a positive COVID-19 diagnosis between January 1, 2020 and May 31, 2021 was created. The exposure was the median of at least 3 physical activity self-reports before diagnosis. Patients were categorized as follows: always inactive, all assessments at 10 minutes/week or less; mostly inactive, median of 0–60 minutes per week; some activity, median of 60–150 minutes per week; consistently active, median>150 minutes per week; and always active, all assessments>150 minutes per week. Outcomes were hospitalization, deterioration event, or death 90 days after a COVID-19 diagnosis. Data were analyzed in 2022.

**Results:** Of 194,191 adults with COVID-19 infection, 6.3% were hospitalized, 3.1% experienced a deterioration event, and 2.8% died within 90 days. Dose–response effects were strong; for example, patients in the some activity category had higher odds of hospitalization (OR=1.43; 95% CI=1.26, 1.63), deterioration (OR=1.83; 95% CI=1.49, 2.25), and death (OR=1.92; 95% CI=1.48, 2.49) than those in the always active category. Results were generally consistent across sex, race and ethnicity, age, and BMI categories and for patients with cardiovascular disease or hypertension.

**Conclusions:** There were protective associations of physical activity for adverse COVID-19 outcomes across demographic and clinical characteristics. Public health leaders should add physical activity to pandemic control strategies.

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# INTRODUCTION

he coronavirus disease 2019 (COVID-19) pandemic represents one of the largest threats to population health in more than a century. As of September 2022, >6.4 million deaths globally were attributed to COVID-19.<sup>1</sup> As new mutations evolve, it is apparent that the virus will not be eliminated in the near future and that strategies for managing life with COVID-19 are needed.<sup>2</sup>

By winter 2022, it became clear that recommendations for vaccinations, boosters, frequent handwashing, wearing protective face coverings, and social distancing were not sufficient to avoid infection.<sup>3</sup> Although most fully vaccinated people (i.e., those who received the full dose [2 injections for 2 of the 3 vaccines available at the time] but not necessarily booster vaccinations) who become

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infected with COVID-19 had mild symptoms, there remains a proportion who experienced adverse outcomes, including hospitalization and death.<sup>4</sup> Additional behaviors should be considered to reduce the odds of severe outcomes among those infected.

There are now >25 studies<sup>5</sup> and a meta-analysis<sup>6</sup> reporting on the association of physical activity or fitness with adverse outcomes for those infected with COVID-19. For instance, a previous report from Kaiser Permanente Southern California (KPSC) categorized patients as consistently meeting physical activity guidelines<sup>7</sup> ( $\geq$ 3 assessments of at least 150 minutes per week of physical activity), consistently inactive ( $\geq$ 3assessments <10 minutes per week of physical activity), or some activity (3 or more assessments in between these requirements). Patients who were consistently inactive had greater odds of hospitalization, admission to intensive care, and death than patients who were consistently active or engaged in some activity.<sup>8</sup> Regular physical activity can reduce the risk of cardiometabolic diseases and premature mortality,<sup>9</sup> improve immune function, $^{10-12}$  and reduce inflammatory responses,<sup>13</sup> all of which may explain the consistent associations of physical activity with less severe COVID-19 outcomes.<sup>5</sup>

Although evidence is building on the benefits of physical activity and less severe COVID-19 outcomes, knowledge gaps remain. The amount of physical activity associated with less severe COVID-19 outcomes is not clear. Those who were more physically active before infection may have a lower prevalence of underlying chronic conditions that predispose to adverse outcomes. However, studies have yet to identify whether physical activity is associated with less severe outcomes for those who do have chronic conditions. Furthermore, sociodemographic inequities in COVID-19 case rates and outcomes are central concerns in pandemic control. Older age may be the strongest risk factor,<sup>14</sup> and males are more likely to have severe outcomes than females.<sup>15</sup> Racial and ethnic disparities in infection rates and severe COVID-19 outcomes have been apparent since the beginning of the pandemic in the U.S., and disparities persist.<sup>14,16,17</sup> It is important to determine whether the obvious benefits of physical activity for COVID-19 outcomes apply similarly across age, sex, race, and ethnic population subgroups.<sup>18</sup> Knowledge about subgroup effects could help to inform the development of targeted physical activity recommendations as a component of COVID-19 guidelines.

The goal of this study was to assess the association of physical activity with severe COVID-19 outcomes in a dose/response fashion. The study also assessed the strength of associations across major demographic subgroups and for those with and without chronic conditions. Results provide initial information regarding the minimal amount of physical activity that may be associated with less severe COVID-19 outcomes and determine whether potential benefits may be experienced across demographics and chronic conditions.

### METHODS

The study was conducted in KPSC, an integrated health system that serves over 4.7 million members. The region is diverse in racial and ethnic makeup, education, and rurality/urbanicity. KPSC patients comprise about 20% of the Southern California population and reflect the area population, with marginal under-representation of those with extremely low income and with high education.<sup>19</sup> Study data were taken from electronic health records (EHRs), a data system that captures all aspects of patient care, including diagnoses, inpatient and outpatient encounters, pharmacy encounters, and laboratory tests. The study was approved by the KPSC IRB.

#### **Study Participants**

Cohort participants were those who tested positive or were diagnosed with COVID-19 infection between January 1, 2020 and May 31, 2021. Additional eligibility criteria included age  $\geq$ 18 years at the time of infection, continuous enrollment in KPSC for at least 6 months before diagnosis, and 3 or more assessments of physical activity in the 2 years before infection. Pregnant patients with COVID-19 who were hospitalized to give birth during the study period were excluded.

#### Measures

Physical activity was assessed using the Exercise Vital Sign (EVS).<sup>20</sup> This brief self-report has been administered at KPSC outpatient visits since 2009. Trained medical assistants asked patients 2 questions: *On average, how many days per week do you engage in moderate to strenuous exercise (like a brisk walk)?* and *On average, how many minutes do you engage in exercise at this level?* Response choices for days were 0–7, and choices for minutes were recorded as 0, 10, 20, 30, 40, 50, 60, 90, 120, and  $\geq 150$  minutes. Responses were recorded in each patient's EHR, and minutes per week of moderate–vigorous physical activity were calculated. The EVS has a good face, discriminant validity<sup>20,21</sup> and validity with accelerometry-based physical activity.<sup>22,23</sup>

The median EVS for all measures completed on patients in the 2 years before their COVID-19 test or diagnosis was calculated, and patients were categorized as always inactive, 3+ EVS assessments at 10 minutes/week or less; mostly inactive, at least 1 EVS >10 minutes/week (median EVS of 0–60 minutes/week); some activity, median EVS of 60–150 minutes/week; consistently active, at least 1 EVS <150 minutes/week (median EVS greater 150 minutes/week) (meeting national guidelines)<sup>7</sup>; and always active, 3+ EVS assessments >150 minutes/week.

COVID-19 diagnosis was determined by a positive test or a diagnosis in a patient's EHR. COVID-19 severity was assessed by (1) requiring hospitalization, (2) experiencing deterioration while hospitalized, and (3) death. COVID-19 hospitalizations were those occurring within 21 days of a diagnosis. A deterioration event was requiring intensive respiratory care, intensive-level care, or intensive-care-unit admission. Only cases of hospitalizations

occurring at KPSC hospitals were included because data derived from non-Kaiser Permanente facilities do not include the same level of detail.

Age was categorized into <40 years, 40–49 years, 50–59 years, 60–69 years, and  $\geq$ 70 years. Sex, race, and ethnicity were obtained from the EHR on the basis of self-report and categorized as male, female, other and Asian or Pacific Islander, Black or African American, Hispanic, non-Hispanic White, or other (e.g., American Indian, >1 race or ethnicity). Medicaid status (enrolled versus not) was determined from enrollment files. Smoking status (never versus ever) was queried during outpatient visits and recorded in the EHR. Height was typically measured once in adults. Weight was assessed at all outpatient visits, and the most recent value before diagnosis was used to calculate BMI (kg/m<sup>2</sup>). BMI was categorized as normal or underweight (<25 kg/m<sup>2</sup>), overweight (25–29 kg/m<sup>2</sup>), Class 1 obesity (30–34 kg/m<sup>2</sup>), or Class 2 obesity ( $\geq$ 35 kg/m<sup>2</sup>).

Clinical conditions included underlying medical conditions identified by the Centers for Disease Control and Prevention (CDC) as associated with adverse COVID-19 outcomes,<sup>24</sup> present before COVID-19 infection. Previous organ transplantation was documented in the EHR. The ICD-10 codes of I10.XX, I11.XX, I12.XX, I13.XX, and I15.XX identified hypertension. The Charlson Comorbidity Index<sup>25</sup> disease categories were used to identify cardiovascular disease (i.e., myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease), chronic obstructive pulmonary disease, and cancer and metastatic cancer. The most recent value of HbA1c in the EHR was categorized as <7%, 7% to <8%,  $\geq8\%$ , or missing (HbA1c is routinely measured for patients at risk for or diagnosed with prediabetes or diabetes). Given that patients with other underlying conditions may have increased susceptibility to adverse COVID-19 outcomes, the authors controlled for the number of emergency department visits and hospitalizations in the 6 months before diagnosis.

#### **Statistical Analysis**

Patient demographics, utilization, clinical characteristics, and comorbidities across physical activity groups were compared using chi-square tests. Logistic regression was used to estimate the odds of hospitalization or death after a COVID-19 diagnosis. Covariates included age category, sex, race, ethnicity, BMI, ever smoker, hospital utilization, HbA1c, comorbidities, Medicaid status, and vaccination status before COVID-19 diagnosis. Patients with a missing BMI were excluded from the analysis. To account for multiple comparisons, a conservative Bonferroni correction  $\alpha$ =0.05/21=0.00238 was used for the *p*-values for interaction, and the 95% CIs were Bonferroni adjusted. All analyses and figures were produced using SAS 9.4 (Cary, NC). Analyses were completed in 2022.

### RESULTS

Between January 1, 2020 and May 31, 2021, 481,061 KPSC patients with a COVID-19–positive test or diagnosis were identified. After applying inclusion and exclusion criteria, the analytic cohort included 194,191 adults (Appendix Figure 1, available online) with a mean of 6.4±4.6 EVS assessments. Those excluded were more likely to be aged <40 years (51.6% vs 32.4%) or over 60 years (11.2% vs 29.2%), more likely to be male (55.1% vs 37.5%), more likely to be categorized as other race/ ethnicity (9.0% vs 3.0%), and less likely to have any comorbidities than patients in the cohort. As displayed in Table 1, most were of Hispanic ethnicity (61.3%), with 21.4% identified as White patients, 7.3% identified as Black patients, and 6.8% identified as Asian or Pacific Islander patients. Over half had BMI ≥30 kg/m<sup>2</sup>. There were 21.8% with a diagnosis of hypertension and 9.2% with a cardiovascular disease diagnosis.

Table 1 shows the categorization of physical activity by median EVS. There were 15.0% categorized as always inactive, 43.0% categorized as mostly inactive, 21.9% categorized as some activity, 14.3% categorized as consistently active, and 5.8% categorized as always active. At higher physical activity categories (i.e., consistently active, always active), patients were more likely to be younger, male, never smokers, and in the lower BMI categories. Patients classified in the lower physical activity categories (e.g., always inactive, mostly inactive) were more likely to be of Hispanic ethnicity or Black race, have a diagnosis of cardiovascular disease or hypertension, or have a BMI  $\geq$  30 kg/m<sup>2</sup>. About 2% of patients were vaccinated before a COVID-19 infection, which did not differ by physical activity category (during the study period, vaccinations were not readily available).

Over the study period, 12,530 (6.3%) patients were hospitalized, 5,943 (3.1%) experienced a deterioration event, and 5,427 (2.8%) patients died within 90 days of a COVID-19 diagnosis. There was a higher prevalence of adverse COVID-19 outcomes across lower physical activity categories; patients classified as always inactive had the highest prevalence of hospitalization, deterioration event, or death (Figure 1).

Appendix Figure 1 (available online) displays the odds of hospitalization and death across physical activity categories, controlling for demographics and comorbidities. Results for deterioration events are provided in Appendix Figure 2 (available online). Patients in the some activity category (median EVS of 60–150 minutes/week) had 43% greater odds of hospitalization (OR=1.43; 95%) CI=1.26, 1.63), 83% higher odds of a deterioration event (Appendix Figure 2, available online) (OR=1.83; 95% CI=1.49, 2.25), and 92% greater odds of death (OR=1.92; 95% CI=1.48, 2.49) than patients in the always active category (median EVS of 300 minutes/ week). There was a consistent dose-response association across lower physical activity categories, with the strongest association comparing the always active with the always inactive category. Patients in the always inactive category (median EVS≤10 minutes/week) had 91%

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### (A) hospitalization

hospitalization		Odds Ratio
		(95% CI)
Median Exercise Vital Sign Category		
Always inactive vs Always active	M	1.91 (1.68-2.17)
Mostly inactive vs Always active		1.72 (1.52-1.95)
Some activity vs Always active	iei .	1.43 (1.26-1.63)
Consistently active vs Always active	H	1.25 (1.10-1.43)
Age Category		
40-49 years vs <40 years		1.98 (1.81-2.16)
50-59 years vs <40 years		3.34 (3.08-3.62)
60-69 years vs <40 years	M	5.73 (5.29-6.21)
70+ years vs <40 years	M	11.13 (10.25-12.0)
Male (yes vs no)	•	1.80 (1.73-1.88)
Race/Ethnicity		
Asian/PI vs White	H	2.16 (2.00-2.32)
Black vs White		1.28 (1.19-1.38)
Hispanic vs White		1.37 (1.31-1.44)
Other vs White	Hel "	0.53 (0.44-0.65)
Body Mass Index (BMI)	•	
25-29 vs <25		0.97 (0.92-1.03)
30-34 vs <25	1	1.13 (1.06-1.20)
35+ vs <25		1.63 (1.53-1.73)
Ever Smoker (yes vs no)		1.06 (1.01-1.10)
Emergency Visit (yes vs no)	Ē.	1.40 (1.34-1.48)
Inpatient Visit (yes vs no) Hemoglabin Alc Category		1.21 (1.14-1.28)
The moglobin A1c Category		1.31 (1.21-1.41)
7-<8% vs < 7%	H L	
>=8% vs $< 7%$		1.90 (1.78-2.03)
Not Tested vs < 7%		1.07 (1.02-1.12)
Organ Transplant (yes vs no)	. ++	2.92 (2.43-3.51)
Cardiovascular Disease (yes vs no)		1.20 (1.14-1.27)
Chronic Obstructive Pulmonary Disease (yes vs no	D) M	1.31 (1.24-1.39)
Renal Disease (yes vs no)	H	1.62 (1.53-1.72)
Cancer (yes vs no)	H	1.32 (1.22-1.43)
Hypertenison (yes vs no)		1.06 (1.01-1.12)
Medicaid (yes vs no)		1.21 (1.14-1.28)
Vaccination Status (yes vs no)	1 10	0.80 (0.70-0.91) 100
	1 10	100
0.1	1 10	100 Odds Ratio
0.1 death Median Exercise Vital Sign Category	1 10 Adjusted Odds Ratios	100 Odds Ratio (95% Cl)
0.1	1 10	100 Odds Ratio
0.1 death Median Exercise Vital Sign Category	1 10 Adjusted Odds Ratios	100 Odds Ratio (95% Cl)
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0.1 death Median Exercise Vital Sign Category Always inactive vs Always active Mostly inactive vs Always active Some activity vs Always active Consistently active vs Always active <b>Age Category</b> 40-49 years vs <40 years 50-59 years vs <40 years 60-69 years vs <40 years 60-69 years vs <40 years 70+ years vs <40 years 70+ years vs <40 years 70+ years vs <40 years Male (yes vs no) <b>Race/Ethnicity</b> Asian/PI vs White Black vs White Hispanic vs White Black vs White Black vs White Black vs White Black vs White Black vs White 30-34 vs <25 30-34 vs <25	Adjusted Odds Ratios	Odds Ratio (95% Cl)           3.91 (3.01-5.07)           2.88 (2.23-3.71)           1.92 (1.48-2.49)           1.55 (1.18-2.03)           3.96 (2.97-5.27)           9.02 (6.96-11.70)           24.62 (19.13-31.6           +→           74.92 (58.30-96.2           2.19 (2.06-2.33)           1.45 (1.29-1.62)           1.03 (0.92-1.15)           1.21 (1.12-1.29)           0.86 (0.66-1.13)           0.65 (0.60-0.70)           0.67 (0.61-0.73)           0.94 (0.86-1.03)
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0.1 death Median Exercise Vital Sign Category Always inactive vs Always active Mostly inactive vs Always active Some activity vs Always active Consistently active vs Always active <b>Age Category</b> 40-49 years vs <40 years 50-59 years vs <40 years 60-69 years vs <40 years 70+ years vs <40 years Male (yes vs no) Race/Ethnicity Asian/Pl vs White Black vs White Hispanic vs White Hispanic vs White Body Mass Index (BMI) 25-29 vs <25 30-4 vs <25 35+ vs <25 Ever Smoker (yes vs no) Emergency Visit (yes vs no) Inpatient Visit (yes vs no) Inpatient Visit (yes vs no) Hemoglobin A1c Category	Adjusted Odds Ratios	IOO           Odds Ratio (95% Cl)           3.91 (3.01-5.07)           2.88 (2.23-3 71)           1.92 (1 48-2 49)           1.55 (1.18-2.03)           3.96 (2.97-5.27)           9.02 (6.96-11.70)           24.62 (19.13-31.6           74.92 (58 30-96.2           2.19 (2.06-2.33)           1.45 (1 29-1 62)           1.03 (0.92-1.15)           1.21 (1.12-1.29)           0.86 (0.66-1.13)           0.65 (0.60-0.70)           0.67 (0.61-0.73)           0.94 (0 86-1.03)           1.15 (1.08-1.22)           1.51 (1.41-1.63)           1.44 (1.33-1.55)           1.32 (1.18-1.47)
0.1 death Median Exercise Vital Sign Category Always inactive vs Always active Mostly inactive vs Always active Some activity vs Always active Consistently active vs Always active Age Category 40-49 years vs <40 years 50-59 years vs <40 years 50-59 years vs <40 years 50-69 years vs <40 years 50-69 years vs <40 years 70+ years vs <40 years 70+ years vs <40 years 70+ years vs <40 years Male (yes vs no) Race/Ethnicity Asian/PI vs White Black vs White Hispanic vs White Body Mass Index (BMI) 25-29 vs <25 30-34 vs <25 35+ vs <25 Ever Smoker (yes vs no) Emergency Visit (yes vs no) Inpatient Visit (yes vs no) Inpatient Visit (yes vs no) Hemoglobin A1c Category 7-<8% vs < 7%	Adjusted Odds Ratios	100 Odds Ratio (95% Cl) 3.91 (3.01-5.07) 2.88 (2.23-3.71) 1.92 (1.48-2.49) 1.55 (1.18-2.03) 3.96 (2.97-5.27) 9.02 (6.96-11.70) 24.62 (19.13-31.6 → 24.62 (19.13-31.6 74.92 (58.30-96.2 2.19 (2.06-2.33) 1.45 (1.29-1.62) 1.03 (0.92-1.15) 1.21 (1.12-1.29) 0.86 (0.66-1.13) 0.65 (0.60-0.70) 0.65 (0.60-0.70) 0.67 (0.61-0.73) 0.94 (0.86-1.03) 1.15 (1.08-1.22) 1.51 (1.41-1.63) 1.44 (1.33-1.55) 1.32 (1.18-1.47) 1.83 (1.66-2.03)
0.1 death Median Exercise Vital Sign Category Always inactive vs Always active Mostly inactive vs Always active Some activity vs Always active Consistently active vs Always active Age Category 40-49 years vs <40 years 50-59 years vs <40 years 50-59 years vs <40 years 70+ years vs <40 years 70+ years vs <40 years Male (yes vs no) Race/Ethnicity Asian/P vs White Black vs White Hispanic vs White Hispanic vs White Body Mass Index (BMI) 25-29 vs <25 30-34 vs <25 35+ vs <25 Ever Smoker (yes vs no) Emergency Visit (yes vs no) Inpatient Visit (yes vs no) Inpatient Visit (yes vs no) Hemoglobin A1c Category 7-<8% vs < 7% >=8% vs < 7%	Adjusted Odds Ratios	IOO           Odds Ratio (95% Cl)           3.91 (3.01-5.07)           2.88 (2.23-3.71)           1.92 (1.48-2.49)           1.55 (1.18-2.03)           3.96 (2.97-5.27)           9.02 (6.96-11.70)           24.62 (19.13-31.6)           74.92 (58.30-96.2)           2.19 (2.06-2.33)           1.45 (1.29-1.62)           1.03 (0.92-1.15)           1.21 (1.12-1.29)           0.86 (0.66-1.13)           0.67 (0.61-0.73)           0.94 (0.86-1.03)           1.15 (1.08-1.22)           1.51 (1.41-1.63)           1.44 (1.33-1.55)           1.32 (1.18-1.47)           1.83 (1.66-2.03)           1.40 (1.31-1.51)
0.1 death Median Exercise Vital Sign Category Always inactive vs Always active Mostly inactive vs Always active Some activity vs Always active Consistently active vs Always active Age Category 40-49 years vs <40 years 50-59 years vs <40 years 50-59 years vs <40 years 70+ years vs <40 years 70+ years vs <40 years Male (yes vs no) Race/Ethnicity Asian/PI vs White Black vs White Hispanic vs White Black vs White Black vs White Black vs White Body Mass Index (BMI) 25-29 vs <25 30-34 vs <25 35+ vs <25 Ever Smoker (yes vs no) Emergency Visit (yes vs no) Inpatient Visit (yes vs no) Impatient Visit (yes vs no) Hemoglobin A1c Category 7-<8% vs < 7% Not Tested vs < 7% Organ Transplant (yes vs no)	Adjusted Odds Ratios	IOO           Odds Ratio (95% Cl)           3.91 (3.01-5.07)           2.88 (2.23-3.71)           1.92 (1.48-2.49)           1.55 (1.18-2.03)           3.96 (2.97-5.27)           9.02 (6.96-11.70)           24.62 (19.13-31.6           4.45 (1.29-1.62)           1.03 (0.92-1.15)           1.21 (1.12-1.29)           0.86 (0.66-1.13)           0.65 (0.60-0.70)           0.67 (0.61-0.73)           0.94 (0.86-1.03)           1.15 (1.08-1.22)           1.51 (1.41-1.63)           1.44 (1.33-1.55)           1.32 (1.18-1.47)           1.83 (1.66-2.03)           1.40 (1.31-1.51)           2.44 (1.90-3.14)
0.1 death Median Exercise Vital Sign Category Always inactive vs Always active Mostly inactive vs Always active Some activity vs Always active Consistently active vs Always active Age Category 40-49 years vs <40 years 50-59 years vs <40 years 50-59 years vs <40 years 50-59 years vs <40 years 70+ years vs <40 years 70+ years vs <40 years Male (yes vs no) Race/Ethnicity Asian/PI vs White Black vs White Hispanic vs White Other vs White Body Mass Index (BMI) 25-29 vs <25 30-34 vs <25 35+ vs <25 Ever Smoker (yes vs no) Emergency Visit (yes vs no) Inpatient Visit (yes vs no) Inpatient Visit (yes vs no) Hemoglobin A1c Category 7-<8% vs < 7% Not Tested vs < 7% Organ Transplant (yes vs no)	Adjusted Odds Ratios	IOO           Odds Ratio (95% Cl)           3.91 (3.01-5.07)           2.88 (2.23-3.71)           1.92 (1.48-2.49)           1.55 (1.18-2.03)           3.96 (2.97-5.27)           9.02 (6.96-11.70)           24.62 (19.13-31.6           74.92 (58.30-96.2           2.19 (2.06-2.33)           1.45 (1.29-1.62)           1.03 (0.92-1.15)           1.21 (1.12-1.29)           0.65 (0.60-0.70)           0.65 (0.60-0.70)           0.65 (0.60-0.70)           0.65 (0.60-1.13)           0.94 (0.86-1.13)           1.15 (1.08-1.22)           1.51 (1.41-1.63)           1.44 (1.33-1.55)           1.32 (1.18-1.47)           1.83 (1.66-2.03)           1.40 (1.31-151)           2.44 (1.90-3.14)           1.43 (1.32-1.54)
0.1 death Median Exercise Vital Sign Category Always inactive vs Always active Mostly inactive vs Always active Some activity vs Always active Consistently active vs Always active Age Category 40-49 years vs <40 years 50-59 years vs <40 years 60-69 years vs <40 years 60-69 years vs <40 years 70+ years vs <40 years 70+ years vs <40 years Male (yes vs no) Race/Ethnicity Asian/PI vs White Black vs	Adjusted Odds Ratios	IOO           Odds Ratio (95% Cl)           3.91 (3.01-5.07)           2.88 (2.23-3.71)           1.92 (1.48-2.49)           1.55 (1.18-2.03)           3.96 (2.97-5.27)           9.02 (6.96-11.70)           24.62 (19.13-31.6           74.92 (58.30-96.2           2.19 (2.06-2.33)           1.45 (1.29-1.62)           1.03 (0.92-1.15)           1.21 (1.12-1.29)           0.86 (0.66-1.13)           0.65 (0.60-0.70)           0.67 (0.61-0.73)           0.94 (0.86-1 0.3)           1.15 (1.08-1.22)           1.51 (1.41-1.63)           1.44 (1.33-1.55)           1.32 (1.18-1.47)           1.83 (1.66-2.03)           1.40 (1.31-1.51)           2.44 (1.90-3.14)           1.43 (1.32-1.54)           1.43 (1.32-1.54)           1.43 (1.32-1.54)           1.43 (1.32-1.54)
0.1 death Median Exercise Vital Sign Category Always inactive vs Always active Mostly inactive vs Always active Some activity vs Always active Consistently active vs Always active Age Category 40-49 years vs <40 years 50-59 years vs <40 years 50-59 years vs <40 years 70- years vs <40 years Male (yes vs no) Race/Ethnicity Asian/P vs White Black vs White Hispanic vs White Black vs White Black vs White Black vs White Body Mass Index (BMI) 25-29 vs <25 30-34 vs <25 35+ vs <25 Ever Smoker (yes vs no) Emergency Visit (yes vs no) Inpatient Visit (yes vs no) Hemoglobin A1c Category 7-<8% vs < 7% >=8% vs < 7% Organ Transplant (yes vs no) Chronic Obstructive Pulmonary Disease (yes vs no)	Adjusted Odds Ratios	IOO           Odds Ratio (95% Cl)           3.91 (3.01-5.07)           2.88 (2.23-3.71)           1.92 (1 48-2 49)           1.55 (1.18-2.03)           3.96 (2.97-5.27)           9.02 (6.96-11.70)           24.62 (19.13-31.6           4           24.62 (19.13-31.6           1.92 (1.92-162)           1.03 (0.92-1.15)           1.21 (1.12-1.29)           0.86 (0.66-1.13)           0.65 (0.60-0.70)           0.67 (0.61-0.73)           0.94 (0.86-1.03)           1.15 (1.08-1.22)           1.51 (1.41-1.63)           1.44 (1.33-1.55)           1.32 (1.18-1.47)           1.83 (1.66-2.03)           1.40 (1.31-151)           2.41 (1.90-3.14)           1.43 (1.32-1.54)           1.20 (1.10-1.29)           1.91 (1.77-2.06)
0.1 death Median Exercise Vital Sign Category Always inactive vs Always active Mostly inactive vs Always active Some activity vs Always active Consistently active vs Always active Age Category 40-49 years vs <40 years 50-59 years vs <40 years 50-59 years vs <40 years 50-59 years vs <40 years 70+ years vs <40 years Male (yes vs no) Race/Ethnicity Asian/Pl vs White Black vs White Black vs White Black vs White Black vs White Body Mass Index (BMI) 25-29 vs <25 30-34 vs <25 35+ vs <25 Ever Smoker (yes vs no) Emergency Visit (yes vs no) Emergency Visit (yes vs no) Emergency Visit (yes vs no) Cardiovascular Disease (yes vs no) Chronic Obstructive Pulmonary Disease (yes vs no) Caraci (yes vs no)	Adjusted Odds Ratios	IOO           Odds Ratio (95% Cl)           3.91 (3.01-5.07)           2.88 (2.23-3.71)           1.92 (1 48-2 49)           1.55 (1.18-2.03)           3.96 (2.97-5.27)           9.02 (6.96-11.70)           24.62 (19.13-31.6           74.92 (58 30-96.2           2.19 (2.06-2.33)           1.45 (1 29-1 62)           1.03 (0.92-1.15)           1.21 (1.12-1.29)           0.86 (0.66-1.13)           0.65 (0.60-0.70)           0.67 (0.61-0.73)           0.94 (0 86-1.03)           1.15 (1.08-1.22)           1.51 (1.41-1.63)           1.44 (1.33-1.55)           1.32 (1.18-1.47)           1.83 (1.66-2.03)           1.40 (1 31-1.51)           1.21 (1.12-1.29)           0.94 (0.98-1.02)           1.51 (1.41-1.63)           1.43 (1.30-1.22)           1.51 (1.41-1.63)           1.40 (1 31-1.51)           1.43 (1.32-1.54)           1.20 (1.10-1.29)           1.91 (1.77-2.06)           1.91 (1.77-2.06)           1.58 (1.43-1.74)
0.1 death Median Exercise Vital Sign Category Always inactive vs Always active Mostly inactive vs Always active Some activity vs Always active Consistently active vs Always active Age Category 40-49 years vs <40 years 50-59 years vs <40 years 50-59 years vs <40 years 50-69 years vs <40 years 60-69 years vs <40 years 70+ years vs <40 years 70+ years vs <40 years 70+ years vs <40 years Male (yes vs no) Race/Ethnicity Asian/PI vs White Black vs White Black vs White Other vs White Body Mass Index (BMI) 25-29 vs <25 30-34 vs <25 35+ vs <25 Ever Smoker (yes vs no) Emergency Visit (yes vs no) Inpatient Visit (yes vs no) Inpatient Visit (yes vs no) Hemoglobin A1c Category 7-<8% vs < 7% Not Tested vs < 7% Not Tested vs < 7% Organ Transplant (yes vs no) Cardiovascular Disease (yes vs no) Cancer (yes vs no) Cancer (yes vs no)	Adjusted Odds Ratios	IOO           Odds Ratio (95% Cl)           3.91 (3 01-5 07) 2.88 (2.23-3.71)           1.92 (1 48-2 49)           1.55 (1.18-2.03)           3.96 (2.97-5.27)           9.02 (6.96-11.70)           24.62 (19.13-31.6           74.92 (58 30-96.2)           2.19 (2.06-2.33)           1.45 (1.29-1.62)           1.03 (0.92-1.15)           1.21 (1.12-1.29)           0.86 (0.66-1.13)           0.65 (0.60-0.70)           0.67 (0.61-0.73)           0.94 (0 86-1 03)           1.15 (1.08-1.22)           1.51 (1.41-1.63)           1.44 (1.33-1.55)           1.32 (1.18-1.47)           1.83 (1.66-2.03)           1.43 (1.32-1.54)           1.22 (1.18-1.47)           1.83 (1.66-2.03)           1.44 (1.33-1.55)           1.32 (1.18-1.47)           1.83 (1.66-2.03)           1.40 (1.31-1.51)           2.44 (1.90-3.14)           1.43 (1.32-1.54)           1.91 (1.77-2.06)           1.58 (1.43-1.74)           1.13 (1.05-1.22)
0.1 death Median Exercise Vital Sign Category Always inactive vs Always active Mostly inactive vs Always active Some activity vs Always active Consistently active vs Always active Age Category 40-49 years vs <40 years 50-59 years vs <40 years 50-59 years vs <40 years 50-59 years vs <40 years 70+ years vs <40 years Male (yes vs no) Race/Ethnicity Asian/Pl vs White Black vs White Black vs White Black vs White Black vs White Body Mass Index (BMI) 25-29 vs <25 30-34 vs <25 35+ vs <25 Ever Smoker (yes vs no) Emergency Visit (yes vs no) Emergency Visit (yes vs no) Emergency Visit (yes vs no) Cardiovascular Disease (yes vs no) Chronic Obstructive Pulmonary Disease (yes vs no) Caraci (yes vs no)	Adjusted Odds Ratios	IOO           Odds Ratio (95% Cl)           3.91 (3.01-5.07)           2.88 (2.23-3.71)           1.92 (1 48-2 49)           1.55 (1.18-2.03)           3.96 (2.97-5.27)           9.02 (6.96-11.70)           24.62 (19.13-31.6           74.92 (58 30-96.2           2.19 (2.06-2.33)           1.45 (1 29-1 62)           1.03 (0.92-1.15)           1.21 (1.12-1.29)           0.86 (0.66-1.13)           0.65 (0.60-0.70)           0.67 (0.61-0.73)           0.94 (0 86-1.03)           1.15 (1.08-1.22)           1.51 (1.41-1.63)           1.44 (1.33-1.55)           1.32 (1.18-1.47)           1.83 (1.66-2.03)           1.40 (1 31-1.51)           1.21 (1.12-1.29)           0.94 (0.98-1.02)           1.51 (1.41-1.63)           1.43 (1.30-1.22)           1.51 (1.41-1.63)           1.40 (1 31-1.51)           1.43 (1.32-1.54)           1.20 (1.10-1.29)           1.91 (1.77-2.06)           1.91 (1.77-2.06)           1.58 (1.43-1.74)

Figure 1. ORs of the association between physical activity categories and (A) hospitalization and (B) death, adjusted for age category, sex, race, ethnicity, BMI, ever smoker, hospital utilization, HbA1c, comorbidities, Medicaid status, and vaccination status before COVID-19 diagnosis.

10

Adjusted Odds Ratios

0.1

100

2022

 Table 1. Characteristics of Patients Diagnosed or Tested Positive by Physical Activity Category and Total

		Ph	ysical activity categor	y			
	Always inactive (All EVS ≤10 min/week; median=0) ( <i>n</i> =29,099; 15.0%)	Mostly inactive(EVS median 0–60 min/ week; median=0) (n=83,452; 43.0%)	Some activity (EVS median 61–150 min/week; median=90) (n=42,490; 21.9%)	Consistently active (EVS median >150 min/week; median=210) (n=27,871; 14.3%)	Always active (All EVS >150 min/ week; median=300) (n=11,279; 5.8%)		<i>p</i> -Value <sup>a</sup>
Age category, n (%)							<0.01
<40 years	8,109 (27.9)	24,798 (29.7)	13,941 (32.8)	10,868 (39.0)	5,193 (46.0)	62,909 (32.4)	
40–49 years	5,698 (19.6)	14,629 (17.5)	7,805 (18.4)	4,839 (17.4)	1,953 (17.3)	34,924 (18.0)	
50–59 years	6,357 (21.8)	17,142 (20.5)	8,875 (20.9)	5,130 (18.4)	1,992 (17.7)	39,496 (20.3)	
60–69 years	4,546 (15.6)	13,948 (16.7)	6,975 (16.4)	4,109 (14.7)	1,381 (12.2)	30,959 (15.9)	
≥70 years	4,389 (15.1)	12,935 (15.5)	4,894 (11.5)	2,925 (10.5)	760 (6.7)	25,903 (13.3)	
Sex, n (%)							<0.01
Female	18,218 (62.6)	54,383 (65.2)	27,499 (64.7)	15,667 (56.2)	5,660 (50.2)	121,427 (62.5)	
Male	10,881 (37.4)	29,067 (34.8)	14,991 (35.3)	12,202 (43.8)	5,619 (49.8)	72,760 (37.5)	
Other	0 (0.0)	2 (0.0)	0 (0.0)	2 (0.0)	0 (0.0)	4 (0.0)	
Race and ethnicity, n (%)							<0.01
Asian or Pacific Islander	1,617 (5.6)	5,437 (6.5)	3,420 (8.0)	1,957 (7.0)	857 (7.6)	13,288 (6.8)	
Black	2,097 (7.2)	6,791 (8.1)	3,009 (7.1)	1,961 (7.0)	586 (5.2)	14,444 (7.4)	
Hispanic	18,707 (64.3)	52,178 (62.5)	25,939 (61.0)	16,142 (57.9)	6,000 (53.2)	118,966 (61.3)	
Other	842 (2.9)	2,220 (2.7)	1,255 (3.0)	988 (3.5)	553 (4.9)	5,858 (3.0)	
White	5,836 (20.1)	16,826 (20.2)	8,867 (20.9)	6,823 (24.5)	3,283 (29.1)	41,635 (21.4)	
Smoking status							<0.01
Ever smoker, n (%)	8,315 (28.6)	22,649 (27.1)	9,945 (23.4)	6,522 (23.4)	2,232 (19.8)	49,663 (25.6)	
BMI category, n (%)							<0.001
<25	4,153 (14.3)	12,758 (15.3)	7,682 (18.1)	6,295 (22.6)	3,345 (29.7)	34,233 (17.6)	
25–29	7,903 (27.2)	24,519 (29.4)	14,171 (33.4)	9,938 (35.7)	4,322 (38.3)	60,853 (31.3)	
30–34	7,980 (27.4)	22,472 (26.9)	11,014 (25.9)	6,823 (24.5)	2,368 (21.0)	50,657 (26.1)	
≥35	9,054 (31.1)	23,678 (28.4)	9,607 (22.6)	4,811 (17.3)	1,238 (11.0)	48,388 (24.9)	
Missing	9 (0.0)	25 (0.0)	16 (0.0)	4 (0.0)	6 (0.1)	60 (0.0)	
Emergency encounters before infection							<0.01
Yes, n (%)	4,279 (14.7)	13,210 (15.8)	4,976 (11.7)	3,193 (11.5)	886 (7.9)	26,544 (13.7)	
Inpatient encounters before infection							<0.01
Yes, n (%)	2,715 (9.3)	9,376 (11.2)	3,807 (9.0)	2,179 (7.8)	519 (4.6)	18,596 (9.6)	
						(continued o	n next page`

	Physical activity category						
Characteristics	Always inactive (All EVS ≤10 min/week; median=0) ( <i>n</i> =29,099; 15.0%)	Mostly inactive(EVS median 0–60 min/ week; median=0) (n=83,452; 43.0%)	Some activity (EVS median 61–150 min/week; median=90) (n=42,490; 21.9%)	Consistently active (EVS median >150 min/week; median=210) (n=27,871; 14.3%)	Always active (All EVS >150 min/ week; median=300) (n=11,279; 5.8%)	) Total (N=194,191)	<i>p</i> -Value <sup>®</sup>
HbA1c, n (%)							<0.01
<7%	7,255 (24.9)	23,556 (28.2)	12,071 (28.4)	7,427 (26.6)	2,632 (23.3)	52,941 (27.3)	
7-<8%	1,310 (4.5)	4,220 (5.1)	1,844 (4.3)	923 (3.3)	209 (1.9)	8,506 (4.4)	
≥8%	1,880 (6.5)	5,544 (6.6)	2,167 (5.1)	1,072 (3.8)	218 (1.9)	10,881 (5.6)	
Missing	18,654 (64.1)	50,132 (60.1)	26,408 (62.2)	18,449 (66.2)	8,220 (72.9)	121,863 (62.8)	
Ever had organ transplantation							<0.01
Yes, n (%)	66 (0.2)	338 (0.4)	171 (0.4)	91 (0.3)	13 (0.1)	679 (0.3)	<0.01
Hypertension diagnosis							<0.01
Yes, n (%)	6,772 (23.3)	21,556 (25.8)	8,362 (19.7)	4,604 (16.5)	1,082 (9.6)	42,376 (21.8)	
Cardiovascular disease diagnosis							<0.01
Yes, n (%)	3,066 (10.5)	9,593 (11.5)	3,101 (7.3)	1,817 (6.5)	380 (3.4)	17,957 (9.2)	
Chronic pulmonary disease diagnosis							<0.01
Yes, n (%)	2,591 (8.9)	8,234 (9.9)	3,189 (7.5)	2,072 (7.4)	550 (4.9)	16,636 (8.6)	
Renal disease diagnosis							<0.01
Yes, n (%)	2,080 (7.1)	6,320 (7.6)	1,846 (4.3)	977 (3.5)	185 (1.6)	11,408 (5.9)	<0.01
Cancer or metastatic cancer diagnosis							
Yes, n (%)	794 (2.7)	3,119 (3.7)	1,200 (2.8)	614 (2.2)	136 (1.2)	5,863 (3.0)	<0.01
COVID-19 vaccination status							<0.01
Yes, n (%)	584 (2.0)	1,754 (2.1)	1,014 (2.4)	600 (2.2)	252 (2.2)	4,204 (2.2)	<0.01

Table 1. Characteristics of Patients Diagnosed or Tested Positive by Physical Activity Category and Total (continued)

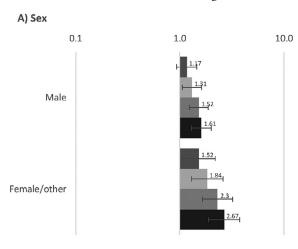
Note: Boldface indicates statistical significance (p<0.01). EVS, Exercise Vital Sign; min, minute.

<sup>a</sup>Chi-square *p*-value.

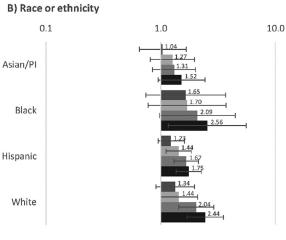
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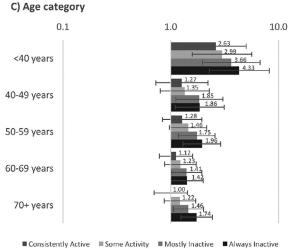
Asian/PI



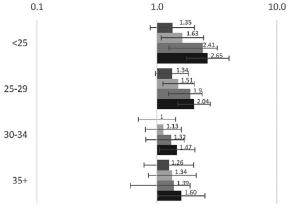
■ Consistently Active ■ Some Activity ■ Mostly Inactive ■ Always Inactive



■ Consistently Active ■ Some Activity ■ Mostly Inactive ■ Always Inactive



### D) Body mass index category 0.1



■ Consistently Active ■ Some Activity ■ Mostly Inactive ■ Always Inactive



### F) History of hypertension

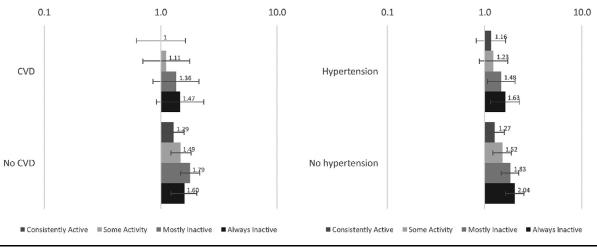


Figure 2. AORs of the association between physical activity categories and hospitalization by (A) sex, (B) race and ethnicity, (C) age group, (D) BMI category, (E) with and without a diagnosis of cardiovascular disease, and (F) with and without a diagnosis of hypertension. ORs were adjusted for age, sex, race, ethnicity, BMI, ever smoker, emergency department visits, inpatient visits, comorbidities, cardiovascular disease, hypertension, Medicaid status, and vaccination before COVID-19 diagnosis. CVD, cardiovascular disease; PI, Pacific Islander.

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higher odds of hospitalization (OR=1.91; 95% CI=1.68, 2.17), 139% higher odds of a deterioration event (Appendix Figure 2, available online) (OR=2.39; 95% CI=1.94, 2.94), and 291% higher odds of death (OR=3.91; 95% CI=3.01, 5.07) than patients in the always active category.

Figure 2 displays the adjusted odds of hospitalization across physical activity categories by demographic and chronic condition categories. Deterioration events are presented in Appendix Figure 3 (available online). The odds of hospitalization for patients in the some activity category were 31% greater for males (OR=1.31; 95% CI=1.05, 1.62) and 84% greater for females (OR=1.84: 95% CI=1.30, 260) than for those in the always active category, with an interaction indicating greater odds for females than for males across physical activity categories (p < 0.001). Results were consistent across racial and ethnic and age categories, although not always reaching statistical significance. Patients in the higher BMI categories had higher odds of hospitalization than patients in lower BMI categories (p < 0.001), but dose-response associations with physical activity were apparent for all BMI categories. Dose-response effects were strong for patients with cardiovascular disease or hypertension diagnosis for odds of hospitalization. Appendix Table 1 (available online) presents the ORs and corresponding 95% CIs for all comparisons.

Figure 3 displays the adjusted odds of death across physical activity categories by demographic and chronic conditions categories. Dose–response effects were strong across all categories except for patients aged <40 years. For patients with hypertension, even the some activity category had higher odds of death than the always active category (OR=1.89, 95% CI=1.05, 3.40). Significant ORs were noted for patients with cardiovascular disease comparing the mostly inactive with the always active category (OR=2.39, 95% CI=1.21, 4.75). Odds were similar in magnitude for patients with or without a diagnosis of either condition (Figure 3 and Appendix Table 1, available online).

### DISCUSSION

The results of this study document substantially higher odds of hospitalization, deterioration events, and death, with lower amounts of self-reported physical activity in a stepwise fashion for adults infected with COVID-19. The ORs are striking. In the full sample, those who were consistently inactive were 191% more likely to be hospitalized and 391% more likely to die than those who were consistently active. Dose–response effects were mostly present across sex, race/ethnicity, age category, BMI category, and history of cardiovascular disease and hypertension, although the CIs sometimes included one. Although the odds were highest for patients in the always inactive category, every lower category of physical inactivity increased the odds of adverse COVID-19 outcomes.

Higher odds of adverse COVID-19 outcomes among physically inactive patients were documented in all racial and ethnic categories, in most age categories, in all BMI categories, and for patients with and without diagnoses of cardiovascular disease or hypertension. However, there were some variations across categories, with trends for lesser effect sizes in the older ages and higher BMI categories. Regardless of demographic factors and common chronic health conditions, results suggest that reducing physical inactivity may be one pathway to lowering the odds of adverse COVID-19 outcomes. The benefits of reducing physical inactivity should lead to its recommendation as an additional pandemic control strategy for all, regardless of demographics or chronic disease status.

Black, Hispanic, and Asian patients who contracted COVID-19 have a greater risk of adverse outcomes than their White counterparts.<sup>16,17</sup> Reasons for these disparities are complex and likely stem from social inequities rooted in historical disenfranchisement and discrimination. Although physical activity has similar benefits for all racial and ethnic groups,<sup>7</sup> it is more difficult to be physically active for people of low SES (who are disproportionately non-White), who have fewer financial resources, who are more likely to live in unsafe neighborhoods, and who may have limited time for physical activity owing to multiple jobs.<sup>26</sup> Public health leaders should take the results as further impetus to develop and implement equitable promotional strategies and opportunities for physical activity for all people.

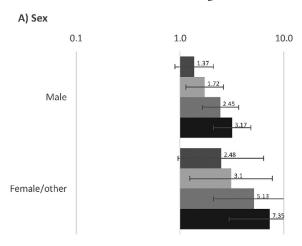
Pre-existing chronic conditions, such as obesity, CVD, diabetes, and hypertension, are strongly associated with COVID-19–related deaths.<sup>27</sup> People with these conditions are cautioned to take all safeguards to avoid contracting COVID-19. These data indicate that if a person with chronic disease was infected, the odds of hospitalization, inpatient deterioration event, and death were lowered among those who were engaged in some physical activity before COVID-19 diagnosis, compared with those in the always inactive category.

### Limitations

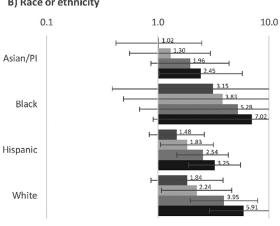
One important limitation was that physical activity was determined from a brief self-report instrument. None-theless, the instrument has been validated,<sup>20–22</sup> and at least 3 assessments improved measurement quality. A study from South Africa assessed physical activity from smart devices on over 60,000 adults who tested positive

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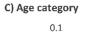
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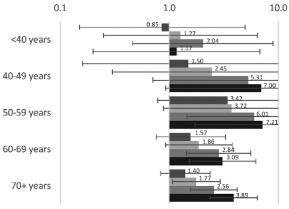


Consistently Active Some Activity Mostly Inactive Always Inactive



■ Consistently Active ■ Some Activity ■ Mostly Inactive ■ Always Inactive

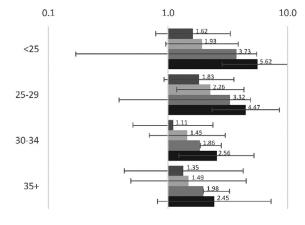




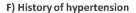
Consistently Active Some Activity Mostly Inactive Always Inactive



D) Body mass index category



Consistently Active Some Activity Mostly Inactive Always Inactive



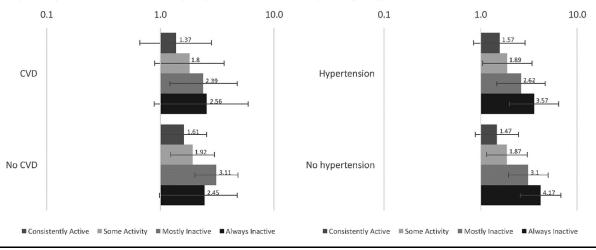


Figure 3. AORs of the association between physical activity categories and death by (A) sex, (B) race and ethnicity, (C) age group, (D) BMI category, (E) with and without a diagnosis of cardiovascular disease, and (F) with and without a diagnosis of hypertension. ORs were adjusted for age, sex, race, ethnicity, BMI, ever smoker, emergency department visits, inpatient visits, comorbidities, cardiovascular disease, hypertension, Medicaid status, and vaccination before COVID-19 diagnosis. CVD, cardiovascular disease; PI, Pacific Islander.

B) Race or ethnicity

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for COVID-19, with results similar to those of this study.<sup>28</sup> Evidence from both these large studies is consistent with those from other studies included in CDC's systematic review<sup>5</sup> and a meta-analysis,<sup>6</sup> providing strong and consistent evidence of the benefits of physical activity and fitness for adverse COVID-19 outcomes.

The actual cause of hospitalization or death was not able to be ascertained. The study used previously used protocols to identify COVID-19-related hospitalizations and death.<sup>29-31</sup> The cohort consisted of adults living in Southern California, and results may not be generalizable to other regions. Some of the CIs were large in the subgroup analyses; nonetheless, the trends were consistent. The cohort consisted of patients with a COVID-19 diagnosis or positive test available in their EHR, which may have resulted in selection bias. Vaccines were just becoming available, so the study could not detect whether physical activity improved outcomes among the vaccinated. Patients were not randomized to physical activity category, so there may be underlying unaccounted confounders. Thus, causality cannot be established. The definitions used for categorizing physical activity undoubtedly led to some misclassification. All patients were insured, and whereas Medicaid patients were included, uninsured patients were excluded.

### CONCLUSIONS

In CDC review of the protective effects of physical activity or fitness on severe COVID-19 outcomes, consistent and conclusive evidence of benefits was found.<sup>5</sup> This study showed stepwise higher odds of adverse COVID-19 outcomes with each increment in physical inactivity. It examined the critical question of the amount of physical inactivity among patients with COVID-19 with the highest risk for severe outcomes; those with common chronic diseases; older individuals; and Asian or Pacific Islander, Black, and Hispanic persons. Across virtually all subgroups, substantial deleterious effects of higher amounts of physical inactivity were found. The cumulative evidence of less physical inactivity's benefits for people with COVID-19, even those in the highest risk categories, has public health significance. Adults, regardless of demographic category or chronic disease status, should be encouraged to reduce their physical inactivity as another COVID-19 mitigation strategy.

### ACKNOWLEDGMENTS

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### SUPPLEMENTAL MATERIAL

Supplemental materials associated with this article can be found in the online version at <a href="https://doi.org/10.1016/j.amepre.2022.10.007">https://doi.org/10.1016/j.amepre.2022.10.007</a>.

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