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Appraisals in Meta-journal Hour 3

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The paper:
Physical activity and the risk of SARS-CoV-2 infection, severe COVID-19 illness and COVID-19 related mortality in South Korea: a nationwide cohort study. doi: [10.1136/bjsports-2021-104203](https://doi.org/10.1136/bjsports-2021-104203)

Why was this study conducted?
Previous studies have showed protective health benefits of sufficient physical activity in reducing the risk for all-cause and disease-specific mortality, non-communicable chronic diseases such as metabolic syndrome, type 2 diabetes and cardiovascular disease as well as improved physical functioning, cognition and quality of life. However, the impact of physical activity on infectious disease particularly COVID-19 infectivity and its clinical outcomes remained unclear. This study aimed to investigate the hypothesis that sufficient physical activity may reduce the risk of COVID-19 infectivity, severity and its related mortality among patients who underwent SARS-CoV-2 testing and its association with length of hospital stay.

How was it done?

Study Population and Data Source
The study included all Korean individuals aged ≥20 years who underwent SARS-CoV-2 testing between 1st January 2020 to 30th May 2020 (n=212 768) in which their data were subsequently linked to Korean national general health examination data between 1 January 2018 and 31 December 2019 to obtain the assessment on their level of physical activity and other relevant data such as socioeconomic background, lifestyle habit, comorbidities and medication history and health assessment.

Exposures and Outcomes
For the classification of exposures and outcomes, please refer figure below.

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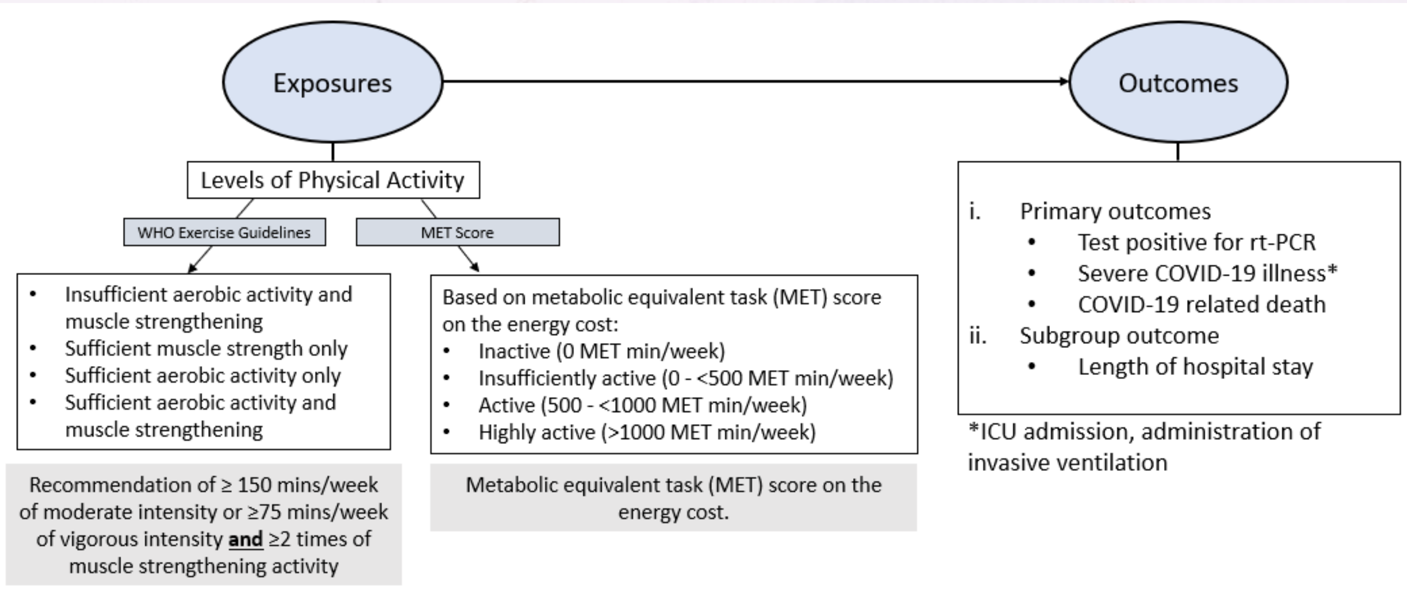

Eight Cohorts Studied

The researchers generated eight cohorts for robustness and generalization of the results. Cohort A was the main study whereby physical activity level of the participants was classified according to WHO exercise guidelines. The characteristics of participants in each cohort as shown in table below:

Cohort	Characteristics	No. of participants
Cohort A	Participants who received general health examination between 2018 and 2019 whom the physical activity was classified according to WHO exercise guidelines.	76 395
Matched cohort A	Propensity score matching of two groups (insufficient aerobic and muscle strengthening vs aerobic and muscle strengthening)	5298
Cohort B	COVID-19 confirmed patients in cohort A	1293
Cohort C	Physical activity was categorised based on MET Score	76 395
Matched cohort C	Propensity score matching of two groups (insufficient physical activity group (0–500 MET min/week) vs sufficient physical activity group (more than 500 MET min/week)	59 986
Cohort D	Participants who received general health examination between 2015 and 2019	118 768
Matched cohort D	Propensity score matching of two groups (insufficient physical activity group (0–500 MET min/week) vs sufficient physical activity group (more than 500 MET min/week)	23 860
Cohort E	COVID-19 confirmed patients in cohort C	3882

Refer to supplemental paper for detailed explanation for each cohort entries.

Sample Size Calculation

There was no study on association between SARS-CoV-2 infectivity and physical activities. Therefore, the sample size was calculated using previous study on the relationship between COVID-19 severity and physical activity [1]. They had calculated for each group to have 80% power to show a 2.8-fold improvement of severity among COVID-19 patient at 5% significant level which they need 900 patients at each group. They able to include 1293 patients with COVID-19 who had insufficient physical activity 1002 patients with COVID-19 who had sufficient muscle strengthening, aerobic or both physical activities.

Statistical Analysis

To assess the different confounding effects, researcher used three sequential inclusion adjusting model by modified Poisson regression presented by adjusted relative risk (aRR) with 95% CI or multivariate analysis of covariance presented by adjusted mean difference with 95% CI. The covariate adjustment was done using three model as below:

Model	Adjustments
Model 1	Adjusted for age (20–39, 40–59 and ≥60 years) and sex.
Model 2	Adjusted for age; sex; region of residence (Seoul Capital Area, Daegu/Gyeongbuk area and other area); Charlson comorbidity index (0, 1 and ≥2); history of diabetes mellitus, tuberculosis, stroke and cardiovascular disease; body mass index (continuous, using the cubic spline function); systolic blood pressure (continuous); diastolic blood pressure (continuous); fasting blood glucose (continuous); serum total cholesterol (continuous); glomerular filtration rate (≥90, 60–89 and ≤59 mL/min); household income (low, middle and high); smoking (never, ex and current); alcoholic drinks (<1, 1–2, 3–4 and ≥5 days per week); and medication for hypertension, diabetes mellitus and cardiovascular disease.
Model 3	Adjusted for minimal selected potential confounders by directed acyclic graph approach.

The stability and reliability of the result researcher performed several analyses with multiple condition.

1. Analysed two differential conditions of exposure such as using the physical activity guidelines (cohorts A and B) and MET score (cohorts C-E).
2. Performed propensity score matching to reduce confounding effects and to balance the baseline characteristic.
3. Sensitivity analysis was conducted by generating cohorts B and E, including only patients with COVID-19 only.
4. Directed acyclic graph approach was used to confirm adequate potential mediator in order to avoid overfitting issues.
5. Subgroup analysis was done by stratification according to age, gender, smoking status and Charlson comorbidity index.
6. Sidak's correction for multiple comparisons was done to reduce probability type 1 error.

Statistical analysis was performed using SPSS V.25.

What was the finding?

The authors presented the findings by each cohort in the paper. In the main study (cohort A), it was identified that 41 293 (54.1%), 5036 (6.6%), 18 994 (24.9%) and 11 072 (14.5%) adults with insufficient aerobic and muscle strengthening, muscle strengthening only, aerobic only and aerobic and muscle strengthening, respectively. Table 1 in the paper shows the baseline characteristics of patients who performed the SARS-CoV-2 testing in the Korean nationwide cohort (cohort A). In general, the results of the study indicated that those who engaged in both aerobic and muscle strengthening activity according to the exercise recommendations had a lower risk of SARS-CoV-2 infection (adjusted relative risk [aRR], 0.85; 95% CI 0.72 to 0.96), severe COVID-19 illness (aRR 0.42; 95% CI 0.19 to 0.91) and COVID-19 related death (aRR, 0.24; 95% CI 0.05 to 0.99) than those who did not. It was also found that the recommended key target range of metabolic equivalent task (MET; 500–1000 MET min/week) was associated with reduced risk of SARS-CoV-2 infection (aRR 0.78; 95% CI 0.66 to 0.92), severe COVID-19 illness (aRR 0.62; 95% CI 0.43 to 0.90) and COVID-19 related death (aRR 0.17; 95% CI 0.07 to 0.98). The length of stay in hospital was shortened about approximately 2 days in patients with both aerobic and muscle strengthening or with 500–1000 MET min/week.

How much can we take out from this research/paper?

The protective effect of physical activity on SARS-CoV-2 infection, severe COVID-19 and deaths were around 15%, 50% and 80% (less consistent due to low event rates), respectively. Overall, it is a good research and report that used credible data sources and measurements, and multiple statistical analyses to verify the results. Physical activity as classified according to the level of intensity in minutes (150 mins moderate or 75 mins vigorous) per week and frequency of muscle strengthening per week are practically useful for most users. However, this may not be the case with MET classification although it is a more accurate and informative measurement to some professionals. The observed protective effects of physical activities on the outcomes were quite huge and large on some COVID deaths and severe diseases. It was well discussed of residual confounding from inaccurate measurement of some the included factors, and missed factors (dietary habits, etc) [2]. The MET classification of the physical activity suggested that active instead highly active physical activity category conferred best benefits from suffering from the adverse outcomes. Unfortunately, MET is not a useful measurement that is practical to many people, and it was also not properly defined in the paper.

The researchers noted some possible interaction between some sociodemographic and the physical activity categories. Further subgroup analyses revealed interesting results of differential effects of different physical activity groups in different age groups, gender, smoking and comorbidity status on the outcomes (refer to Table 3 in the paper) [3]. For example, compared to those doing less than 150 mins moderate or 75 mins vigorous physical activity per week, physical activity when done at that level or higher prevented infection only in those aged 40-56 year-old and lowered the severe COVD-19 in those ≥ 60 year-old; combined aerobic and muscle strengthening done at or higher than that defined benefited only men from infection but female require only the aerobic exercises to lower risk of severe COVID-19 significantly. Lastly, physical activity has no observed effects among smokers (ex- and current) and those who scored other than zero on the Charlson comorbidity index.

The external validity of the findings from this study may become less due to the vaccination against COVID-19 assuming that the vaccines provided a relative large protective effects on the studied outcomes in the paper. Nonetheless, the actual benefits from physical activity in the presence of the vaccination is unknown and this require a repeat of the study by the researchers. However, the indirect effects of physical activity on health and from COVID-19 are believed to be presence.

References

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2. Chin YS, Chew BH and Widyahening IS. Dietary Practices and Nutrition for the Prevention of COVID-19. RECRUS Res. Newsl. 2021;1 (3): 1-5. Access on 19 November 2021, https://hpupm.upm.edu.my/upload/dokumen/20210722171045Dietary_Practices_and_Nutrition_for_the_Prevention_of_COVID-19_The_Brief_&_Summary.pdf
3. Lee SW, Lee J, Moon SY, et al. Physical activity and the risk of SARS-CoV-2 infection, severe COVID-19 illness and COVID-19 related mortality in South Korea: a nationwide cohort study. Br J Sports Med. 2021 Jul 22:bjsports-2021-104203. doi: 10.1136/bjsports-2021-104203.