The COVID-19 pandemic produced life disturbances and loss of routine which affected diet and sleep quality as well as physical exercise frequency. Interestingly, mental distress was higher even in those who exercised. The purpose of this study was to assess exercise frequency in relation to different levels of mental distress severity in men and women while accounting for working days and weekends. A de-identified secondary data set was analyzed. Regression analyses produced models of the different stages of COVID-19 in relation to physical exercise frequency and mental distress levels. Margin analysis generated predictive models that could be used prophylactically to customize physical exercise frequencies in men and women to reduce their risk of mental distress during future pandemics. Mental distress during the lockdown and after ease of restrictions was associated with different physical exercise frequencies, with a noticeable difference between men and women. During a pandemic, sedentary men are more likely to be mentally distressed during working days. Nevertheless, moderately active, but not very active women, may be less distressed during pandemic weekends. These findings may provide a framework to optimize mental health during different stages of a pandemic by customizing physical exercise frequencies based on gender and time of the week.

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