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# Regular Use of Ivermectin as Prophylaxis for COVID-19 Led Up to a 92% Reduction in COVID-19 Mortality Rate in a Dose-Response Manner: Results of a Prospective Observational Study of a Strictly Controlled Population of 88,012 Subjects

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## Abstract

**Background** We have previously demonstrated that ivermectin used as prophylaxis for coronavirus disease 2019 (COVID-19), irrespective of the regularity, in a strictly controlled citywide program in Southern Brazil (Itajaí, Brazil), was associated with reductions in COVID-19 infection, hospitalization, and mortality rates. In this study, our objective was to determine if the regular use of ivermectin impacted the level of protection from COVID-19 and related outcomes, reinforcing the efficacy of ivermectin through the demonstration of a dose-response effect. **Methods** This exploratory analysis of a prospective observational study involved a program that used ivermectin at a dose of 0.2 mg/kg/day for two consecutive days, every 15 days, for 150 days. Regularity definitions were as follows: regular users had 180 mg or more of ivermectin and irregular users had up to 60 mg, in total, throughout the program. Comparisons were made between non-users (subjects who did not use ivermectin), and regular and irregular users after multivariate adjustments. The full city database was used to calculate and compare COVID-19 infection and the risk of dying from COVID-19. The COVID-19 database was used and propensity score matching (PSM) was employed for hospitalization and mortality rates. **Results** Among 223,128 subjects from the city of Itajaí, 159,560 were 18 years old or up and were not infected by COVID-19 until July 7, 2020, from which 45,716 (28.7%) did not use and 113,844 (71.3%) used ivermectin. Among ivermectin users, 33,971 (29.8%) used irregularly (up to 60 mg) and 8,325 (7.3%) used regularly (more than 180 mg). The remaining 71,548 participants were not included in the analysis. COVID-19 infection rate was 49% lower for regular users (3.40%) than non-users (6.64%) (risk rate (RR): 0.51; 95% CI: 0.45-0.58;  $p < 0.0001$ ), and 25% lower than irregular users (4.54%) (RR: 0.75; 95% CI: 0.66-0.85;  $p < 0.0001$ ). The infection rate was 32% lower for irregular users than non-users (RR: 0.68; 95% CI: 0.64-0.73;  $p < 0.0001$ ). Among COVID-19 participants, regular users were older and had a higher prevalence of type 2 diabetes and hypertension than irregular and non-users. After PSM, the matched analysis contained 283 subjects in each group of non-users and regular users, between regular users and irregular users, and 1,542 subjects between non-users and irregular users. The hospitalization rate was reduced by 100% in regular users compared to both irregular users and non-users ( $p < 0.0001$ ), and by 29% among irregular users compared to non-users (RR: 0.781; 95% CI: 0.49-1.05;  $p = 0.099$ ). Mortality rate was 92% lower in regular users than non-users (RR: 0.08; 95% CI: 0.02-0.35;  $p = 0.0008$ ) and 84% lower than irregular users (RR: 0.16; 95% CI: 0.04-0.71;  $p = 0.016$ ), while irregular users had a 37% lower mortality rate reduction than non-users (RR: 0.67; 95%

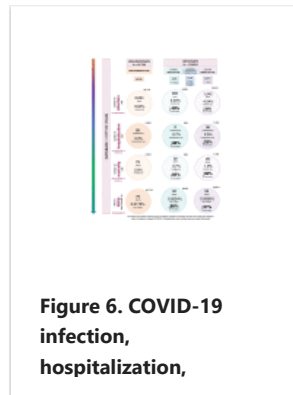
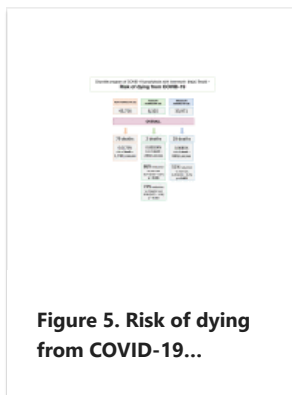
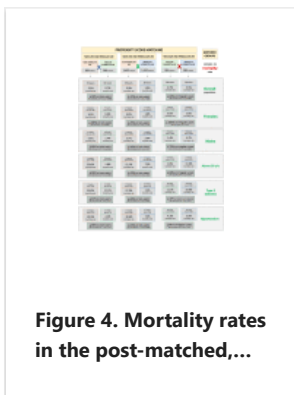
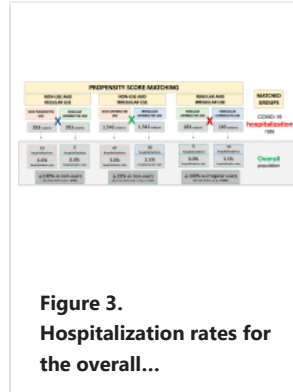
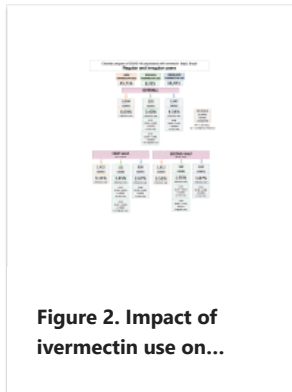
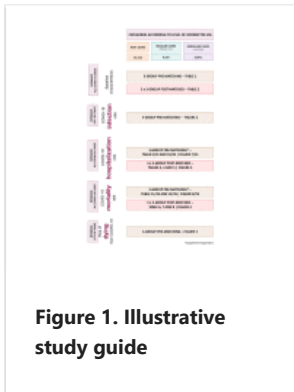
CI: 0.40-0.99;  $p = 0.049$ ). Risk of dying from COVID-19 was 86% lower among regular users than non-users (RR: 0.14; 95% CI: 0.03-0.57;  $p = 0.006$ ), and 72% lower than irregular users (RR: 0.28; 95% CI: 0.07-1.18;  $p = 0.083$ ), while irregular users had a 51% reduction compared to non-users (RR: 0.49; 95% CI: 0.32-0.76;  $p = 0.001$ ). Conclusion Non-use of ivermectin was associated with a 12.5-fold increase in mortality rate and a seven-fold increased risk of dying from COVID-19 compared to the regular use of ivermectin. This dose-response efficacy reinforces the prophylactic effects of ivermectin against COVID-19.

**Keywords:** coronavirus; coronavirus disease 2019; covid-19; ivermectin; ivermectin (ivm); prevention; prophylaxis; rtpcr-sars-cov-2; sars-cov-2.

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