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Global Health

Supplementary appendix 2

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Reis G, dos Santos Moreira-Silva EA, Medeiros Silva DC, et al. Effect of early treatment with fluvoxamine on risk of emergency care and hospitalisation among patients with COVID-19: the TOGETHER randomised, platform clinical trial. *Lancet Glob Health* 2021; published online Oct 27. [http://dx.doi.org/10.1016/S2214-109X\(21\)00448-4](http://dx.doi.org/10.1016/S2214-109X(21)00448-4).

Supplementary web-Appendix

This appendix forms part of the original submission to:

Reis G, Silva EASM, Silva DCM et al: Effect of Early Treatment with Fluvoxamine on Risk of Emergency Care and Hospitalization Among Patients with COVID-19: The TOGETHER Randomized Platform Clinical Trial

Trial Infrastructure and the Extended TOGETHER investigators

The COVID-19 TOGETHER Trial initiative was designed to evaluate repurposed treatments for COVID-19 disease through an adaptive trial design in two arms being conducted in Brazil. The trial is supported by a network of primary care research centers located in the state of Minas Gerais, Brazil, devoted to a comprehensive evaluation and treatment of patients with COVID-19. The trial was fully integrated with local public health authorities (Brazilian Unified Health System – SUS) as part of coping strategy for COVID-19 pandemic. Namely, the main institutions involved were: Cardresearch – Cardiologia Assistencial e de Pesquisa. This initiative is funded by FastGrants and The Rainwater Foundation.

Brazilian Executive Committee

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Participating Enrolling Centres

Included below are representatives from the enrolling centres at participating cities that enrolled at least 1 patient. Centres are listed in order of enrolment contribution. All study sites were located in the State of Minas Gerais, Brazil.

Cardresearch – Cardiologia Assistencial e de Pesquisa

Aline Lúcia de Jesus Martins, Anna Clara de Jesus Oliveira, Bárbara Nogueira Roberti, Carina Daniela Lira Moreira Figueiredo, Carolina Couto de Azevedo Cysne, Clara Bensemman Gontijo Pereira, Daniela Carla Medeiros, Túlio Fonseca e Silva Quadros, Emanuelle Cristina Soares Gonçalves, Heloisa Alves Costa, João Victor Barbosa Silveira, Joselaine Gomes de Souza, Kênia Sthéfane Guimarães Gonçalves, Laura Campos Oliveira, Letícia Campos Siqueira, Letícia de Fatimas Costa, Lorena Mesquita Alves, Luana Rosa Rodrigues, Lucas Júnio da Silva, Mariana Campos Siqueira, Marina Guimarães Bragatto, Rosemary Muniz de Oliveira, Stephanny Kelvyn Bessa, Tainara Silva Vieira, Tatiana Aparecida Gomes da Silva, Túlio Fonseca e Silva Quadros, Thais Campos Siqueira, Vânia Regina Carmo, Vitor Augusto Lima do Vale, Vitor Vilaça Oliveira.

City of Ibirité

Aline Cruz Milagres, Ana Carolina Aguiar Estevam, Ana Martins de Oliveira, André Henrique de Sousa Oliveira, Carla Stefany Oliveira França, Laylla Michelle Pereira, Luciléia Alcântara Gomes e Silva, Patrícia Santana Assis, Regiane Aparecida de Andrade, Thaís de Paula Ferreira da Silva, Thiago de Alcântara César

City of Sete Lagoas

Amanda Luiza do Espírito Santo Pinheiro, Ana Carolina Matos Ferreira, Ana Caroline Santos Silva, Ana Luiza Silva Taveira, Bruno Victor de Souza Lima, Débora Siqueira Diana, Emanuela Pontes Pereira Silveira, Francisca Lina Campos Gonçalves, Gabriel Corrêa Costa, Geraldo César Barroso de Souza, Guilherme Aurelio D'Oliveira Alves, Isadora Luiza Teixeira Neto, Jordanna Porto Inácio, Lara Silveira Marques, Larissa Martins do Nascimento, Larissa Oliveira Moreira, Lorena Luiza Soares de Oliveira, Lucas Eduardo Lessa Mussi, Lucas Medeiros Ruas, Luiza Nogueira Assis Barbosa, Marcelo Rodrigues da Costa Fernandes, Maria Eduarda Guimarães de Souza, Maria Thereza Figueiredo Bélem Calazans, Mariana Rodrigues Marinho de Bastos, Pedro Henrique Arcanjo Alvarenga, Quimberli Vassinave Cujú, Vinicius Alves Correa, Vitória Aparecida Cunha, Viviane Costa Santos

City of Governador Valadares

Adriana Marcos Mendes Rabelo, Aline do Carmo Rosa, Ana Paula Vilas Boas Wherberth, Arthur Henrique Nunes Leite Oliveira, Damiana Rogai Siqueira, Felipe Coelho Soares de Oliveira, Felipe Fraga Damaceno, Guilherme Rhis, Iandra Silva Almeida, Igor Barros de Araújo Borges, Igor Brandão Rocha, Jorge Carlos do Amaral Júnior, José Pio Marques II, Laura Lima Vargas, Luiz Eduardo Coelho Fava, Marina Lacerda Marques, Maura Alina Morais Veríssimo, Neila Rodrigues

Vargas de Paula, Pâmela de Sousa Dias Demuner, Rafaella Rosa de Oliveira Fernandes, Ramail Santos Pouzas, Roberta Coelho de Marco, Ronan Figueiredo Mourão, Sabrina Stefany da Silva Souza, Sara Silva Ferraz

City of Brumadinho

Ana Beatriz Amorim, Carolina Francisca Martins, Huisnei Ferreira Lourenço, Jussara Carolina Assis Ribeiro Nascimento, Solange Santos Moreira Sales

City of Nova Lima

Leticia de Fatima Costa, Maria do Carmo, Fernanda Freitas Pinheiro, Felipe Viana Santos

Public health authorities and mayors

We are in debt with the following local public health authorities and mayors (listed by enrollment):

City of Sete Lagoas

Duílio de Castro (Mayor), Flávio Pimenta Silveira (public health authority), Alber Alípio Ribeiro (public health authority)

City of Montes Claros

Humberto Guimarães Souto (Mayor), Dulce Pimenta Gonçalves (public health authority)

City of Governador Valadares

André Luiz Coelho Merlo (Mayor), Edna Gomes Leite (public health authority)

City of Ibitaré

William Parreira Duarte (Mayor), Carina Bitarães (public health authority)

City of Brumadinho

Avimar de Melo Barcelos (Mayor), Eduardo Diniz Callegari (public health authority)

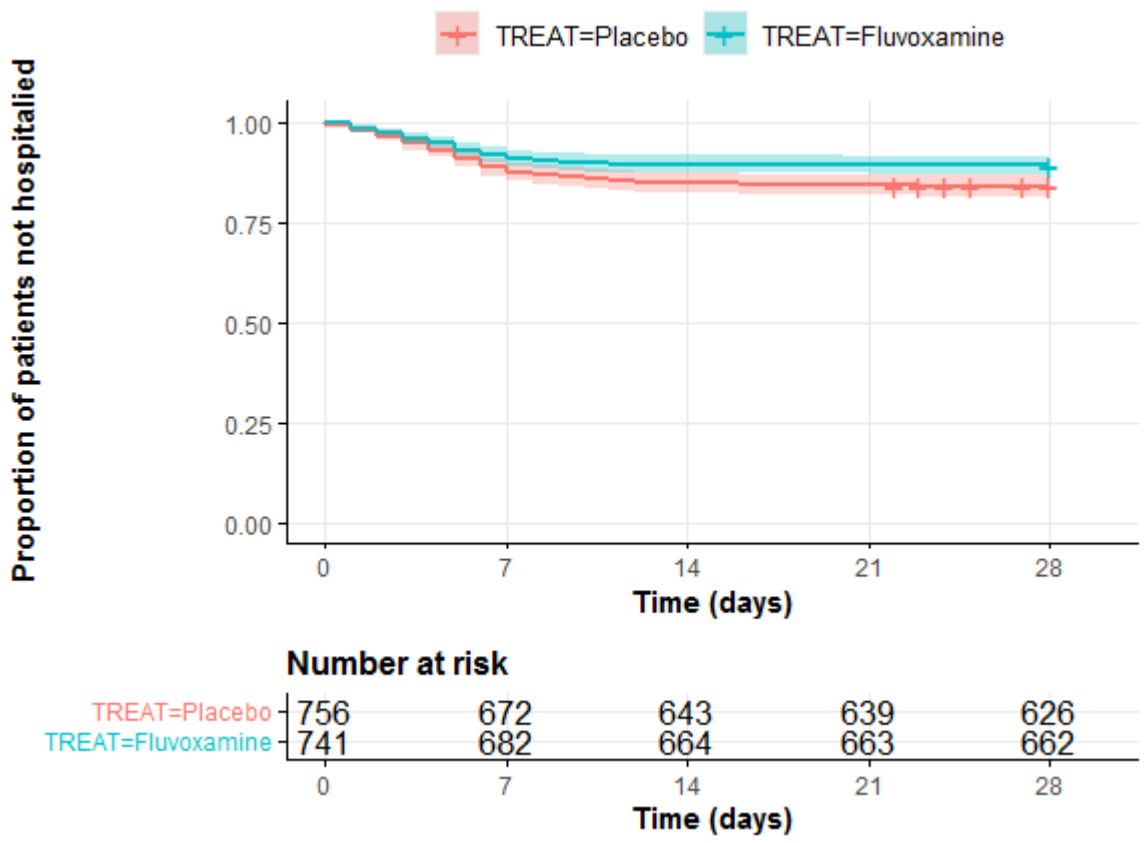
City of Nova Lima

João Marcelo Diegues Pereira (Mayor), Diogo Jonata Ribeiro (public health authority)

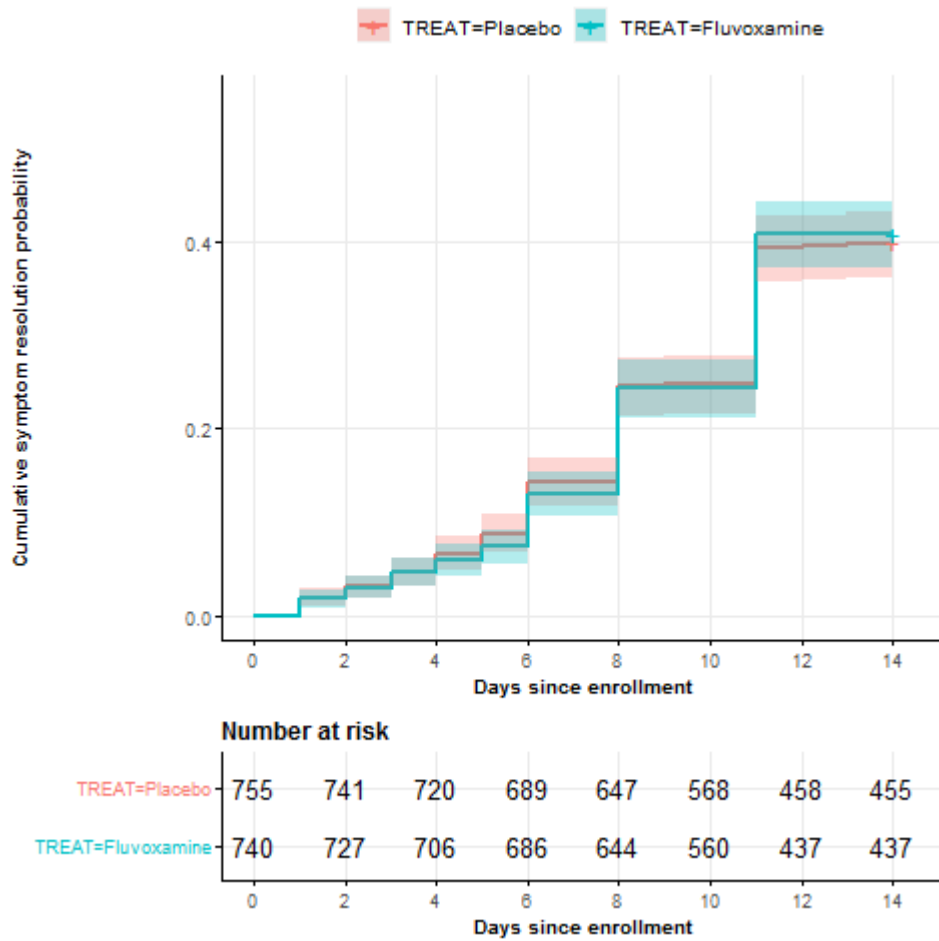
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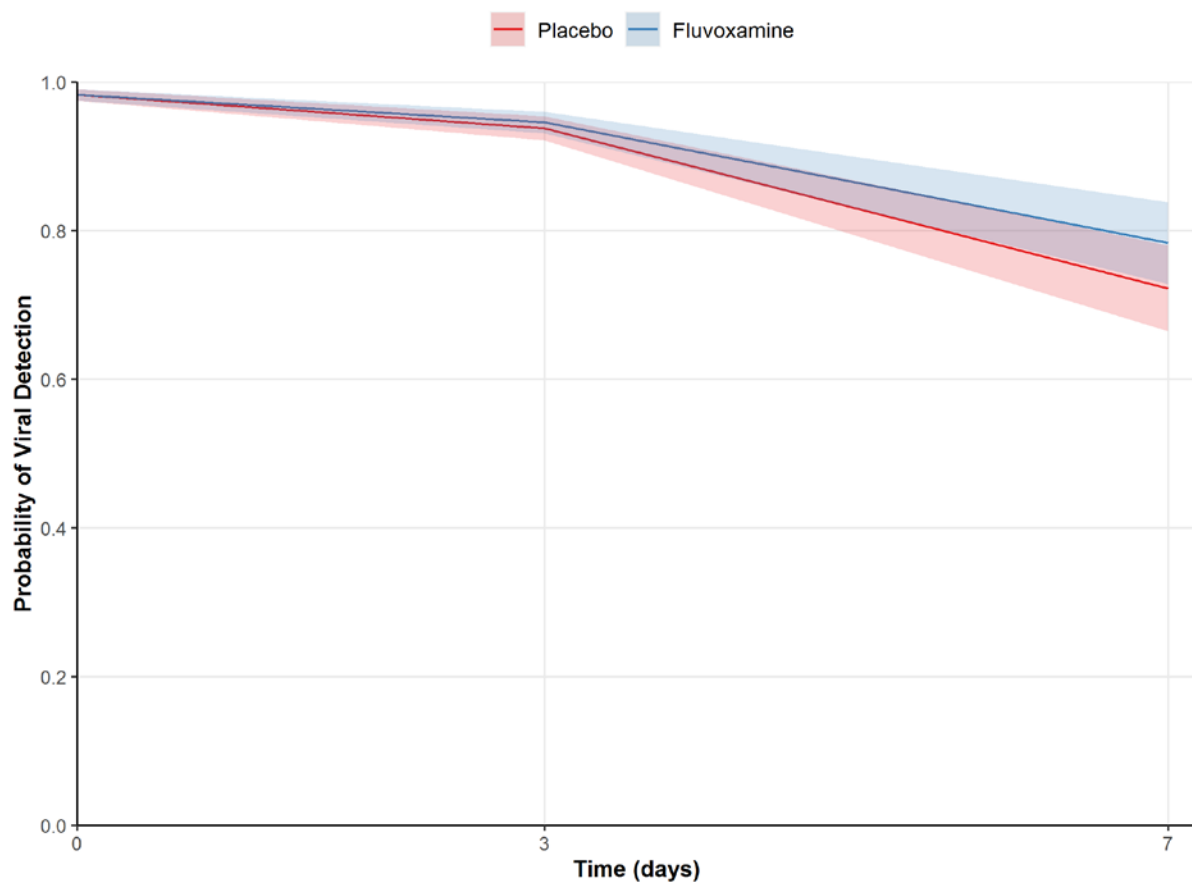
eFigure 1: Time to hospitalization or extended emergency room visit due to COVID-19



eFigure 2: Time to symptom resolution (WHO symptom index scale)



eFigure3: Probability of viral detection (Days 0, 3, 7)



Factor	Subgroup	N_Placebo	N_Fluvoxamine	n_Placebo	n_Fluvoxamine	HR (95% CI)
Age	<=50	379	368	41	23	0.57 [0.34; 0.95]
Age	>50	328	327	72	50	0.67 [0.47; 0.96]
Sex	Female	453	409	61	28	0.49 [0.31; 0.77]
Sex	Male	303	332	58	51	0.80 [0.55; 1.16]
BMI (Kg/m ²)	<30	373	355	52	34	0.67 [0.44; 1.03]
BMI (Kg/m ²)	>30	375	376	67	44	0.64 [0.44; 0.94]
Time from onset of symptoms	0-3 days	310	328	39	30	0.72 [0.45; 1.15]
Time from onset of symptoms	4-7 days	267	239	44	31	0.77 [0.49; 1.23]
Cardiovascular disease	N	747	733	117	79	0.67 [0.51; 0.90]
Cardiovascular disease	Y	8	4	2	0	
Chronic kidney disease	N	702	704	115	78	0.66 [0.50; 0.88]
Chronic kidney disease	Y	54	35	4	1	0.37 [0.04; 3.35]
Smoking status	Current	64	47	5	3	0.80 [0.19; 3.33]
Smoking status	Former	89	107	17	10	0.46 [0.21; 1.00]

Smoking status	Never	601	586	97	66	0.69 [0.50; 0.94]
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eTable1: Summary of Sub-Group Analysis for Hospitalization or Extended Emergency Room Visit Due to COVID-19