Results from ACTIV-6: A Decentralized, Double-Blind, Randomized, Placebo-Controlled Platform Trial of Repurposed Drugs for the Treatment of Mild-to-Moderate COVID-19

Matthew McCarthy, MD
on Behalf of the ACTIV-6 Study team

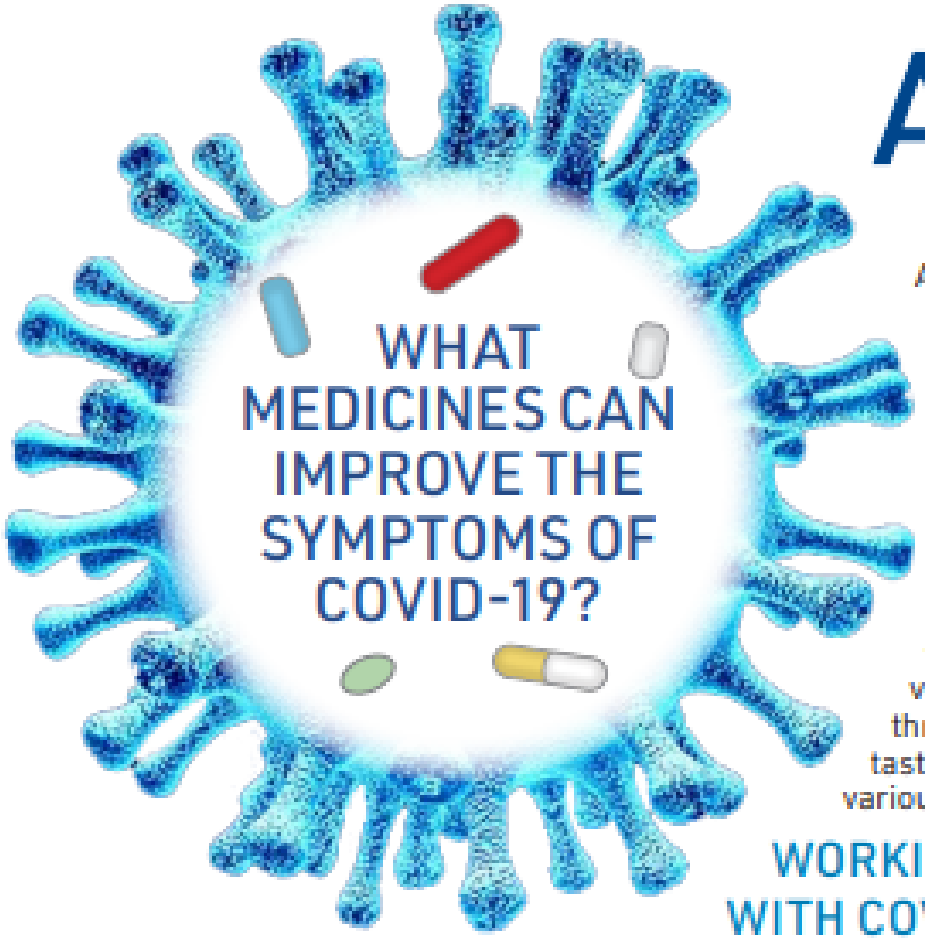
ACTIV-6

Primary Objectives

How to help someone *feel better faster* with newly diagnosed mild-moderate COVID-19?

How to *prevent hospitalizations or death* in someone with newly diagnosed mild-moderate COVID-19?

Study Population



ACTIV-6

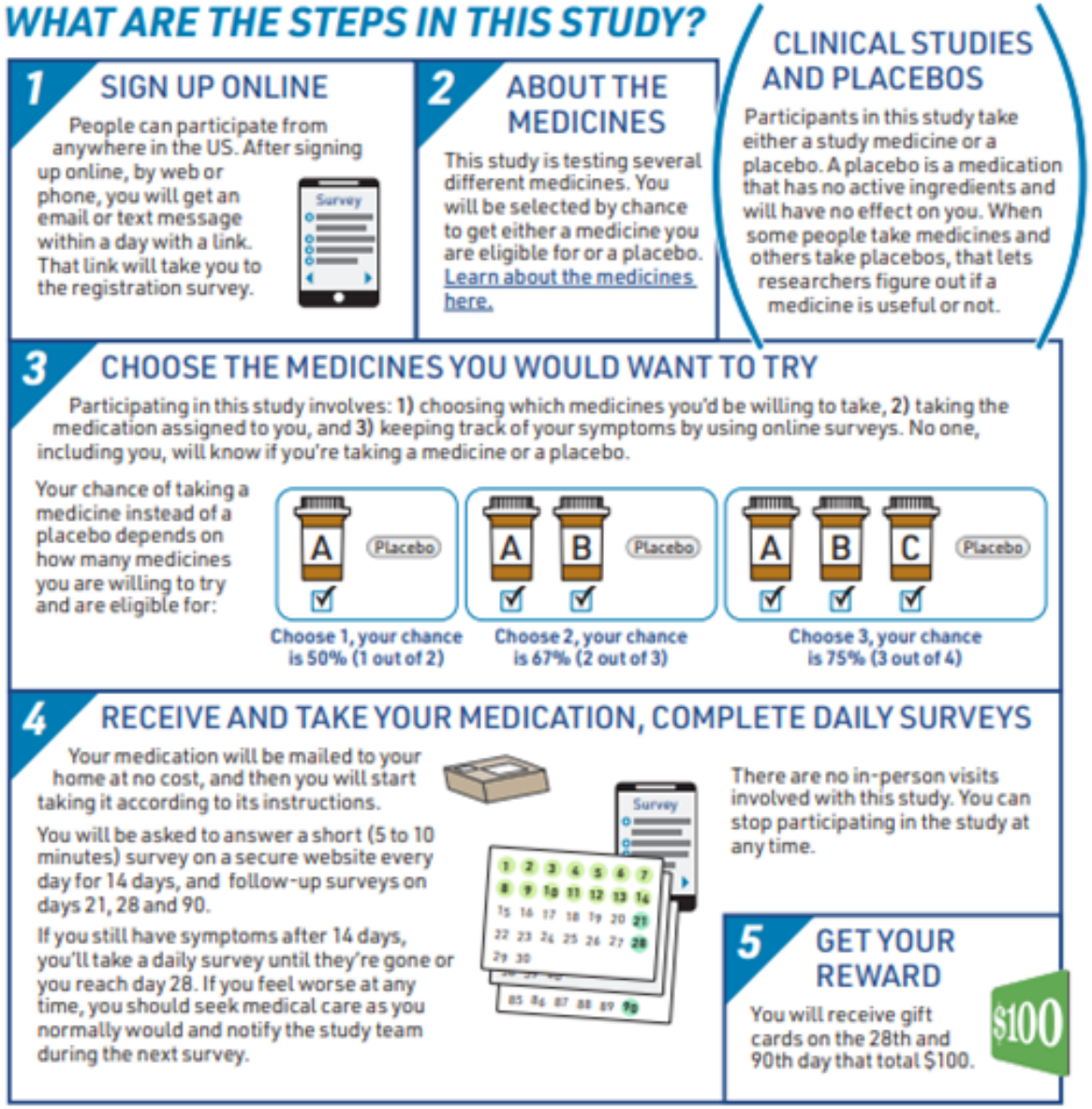
ACTIV-6 is a nationwide study to test medicines that are already approved for other diseases to see if they can help people with mild to moderate COVID-19 feel better faster and stay out of the hospital. ACTIV-6 is part of the Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) program.

WHO CAN PARTICIPATE? Adults age 30 or older with COVID-19 symptoms, a positive test within the last 10 days, and at least two symptoms of the illness for seven days or less. Symptoms include fatigue, difficulty breathing, fever, cough, nausea, vomiting, diarrhea, body aches, chills, headache, sore throat, nasal symptoms, and/or new loss of sense of taste or smell. You may be excluded from the study for various reasons.

WORKING TOGETHER TO HELP PEOPLE WITH COVID-19 FEEL BETTER FASTER.

Study Design

- Direct-to-participant
- All participants assigned to a site
- Symptom reporting daily
- COVID-19 outcome reporting
- Remote visits
- Continuous safety assessments
- 5 active arms to date



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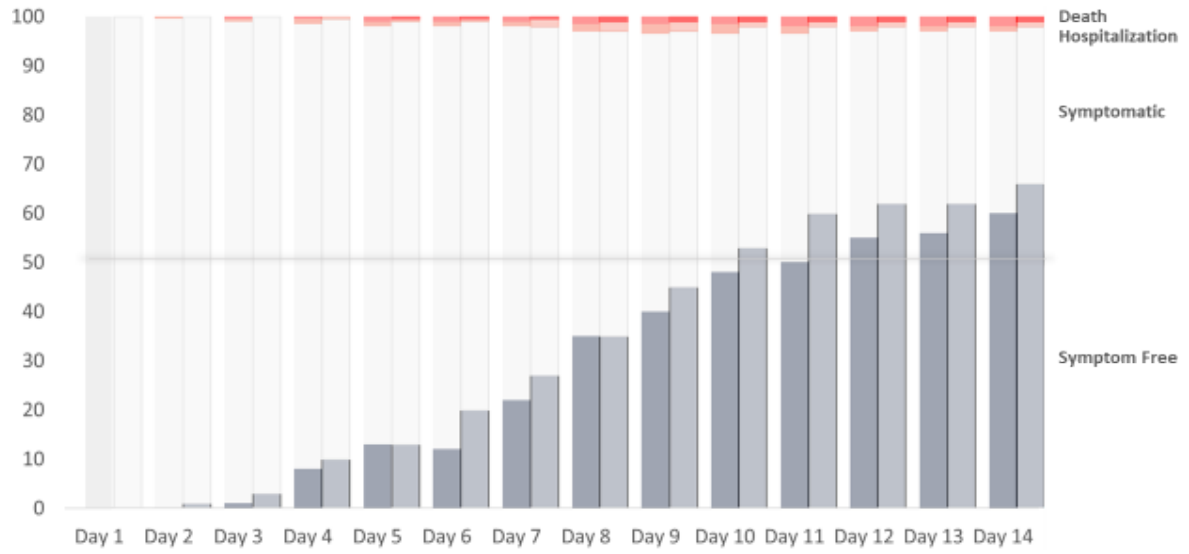
Active Interventions

- Repurposed drugs chosen by independent committee based on existing evidence including human studies
- Ivermectin dosed to achieve ~400 µg/kg (7 mg tablets) daily for 3 days
  - Opened June 23, 2021, Closed February 4, 2022
- Fluticasone furoate 200 µg/day inhaled daily for 14 days
  - Opened August 10, 2021, Closed February 12, 2022
- Fluvoxamine maleate 50 mg tablet twice daily for 10 days
  - Opened August 6, 2021, Closed May 27, 2022

Measurements

No symptoms
Mild symptoms
Moderate symptoms
Severe symptoms
Hospitalization
Death

Primary Outcomes



Time to recovery, clinical events
Days of benefit (Day 28)

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Participant Characteristics

	Ivermectin 400 µg/kg		Fluticasone		Fluvoxamine 50 mg	
	Active (n=817)	Placebo (n=774)	Active (n=656)	Placebo (n=621)	Active (n=674)	Placebo (n=614)
Age, median (IQR), y	47 (39-56)	48 (39-56)	45 (37-55)	46 (38-56)	47 (37-57)	48 (39-58)
Age <50, no. (%)	476 (58.3)	435 (56.2)	405 (61.7)	370 (59.6)	395 (58.6)	350 (57.0)
Female, no. (%)	508 (62.2)	424 (54.8)	431 (65.7)	376 (60.5)	387 (57.4)	347 (56.5)
Race, not mutually exclusive, no. (%):						
Black or African American	57 (7.0)	56 (7.2)	47 (7.2)	44 (7.1)	47 (7.0)	49 (8.0)
White	659 (80.7)	627 (81.0)	523 (79.7)	500 (80.5)	542 (80.4)	496 (80.8)
Ethnicity: Latino	93 (11.4)	70 (9.0)	78 (11.9)	83 (13.4)	119 (17.7)	102 (16.6)

Participant Characteristics

	Ivermectin 400 µg/kg		Fluticasone		Fluvoxamine 50 mg	
	Active (n=817)	Placebo (n=774)	Active (n=656)	Placebo (n=621)	Active (n=674)	Placebo (n=614)
BMI, median (IQR), kg/m^2	28.3 (24.9-33.2)	28.3 (24.9-33.3)	28.1 (24.4-33.6)	28.1 (24.6-32.9)	27.8 (24.5-32.1)	28.1 (24.4-32.4)
BMI >30 kg/m^2, no./No. (%)	334/816 (40.9)	314 (40.6)	260 (39.6)	239/620 (38.5)	246 (36.5)	223/613 (36.4)
Heart disease, no./No. (%)	34/804 (4.2)	36/756 (4.8)	25/640 (3.9)	33/606 (5.4)	23/658 (3.5)	30/587 (5.1)
Diabetes, no./No. (%)	96/804 (11.9)	88/756 (11.6)	56/640 (8.8)	65/606 (10.7)	59/658 (9.0)	56/588 (9.5)
High blood pressure, no./No. (%)	212/804 (26.4)	203/756 (26.9)	156/640 (24.4)	169/606 (27.9)	153/658 (23.3)	151/588 (25.7)
Asthma, no./No. (%)	121/804 (15.05)	120/756 (15.9)	76/640 (11.9)	86/606 (14.2)	89/658 (13.5)	75/587 (12.8)
Smoker (past year), no./No. (%)	134/804 (16.27)	103/756 (13.6)	83/640 (13.0)	72/606 (11.9)	88/658 (13.4)	76/588 (12.9)

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Participant Characteristics

	Ivermectin 400 µg/kg		Fluticasone		Fluvoxamine 50 mg	
	Active (n=817)	Placebo (n=774)	Active (n=656)	Placebo (n=621)	Active (n=674)	Placebo (n=614)
Vaccine status, no. (%)						
Not vaccinated	420 (51.4)	394 (50.9)	220 (33.5)	211 (34.0)	210 (31.3)	195 (32.1)
Vaccinated (1 dose)	12 (1.5)	12 (1.6)	8 (1.2)	11 (1.8)	8 (1.2)	7 (1.2)
Vaccinated (2+ doses)	385 (47.1)	368 (47.6)	428 (65.2)	399 (64.3)	452 (67.5)	405 (66.7)
Days between symptom onset and receipt of study drug, median (IQR)	6 (5-8)	6 (4-7)	6 (4-7)	5 (4-7)	5 (4-7)	5 (4-7)
Symptom burden on study day 1, no. (%)						
None	55 (6.73)	54 (6.98)	35 (5.3)	39 (6.3)	36 (5.8)	37 (6.5)
Mild	490 (60.0)	434 (56.1)	402 (61.3)	371 (59.7)	396 (63.7)	353 (62.0)
Moderate	221 (27.1)	247 (31.9)	186 (28.4)	174 (28.0)	176 (28.3)	166 (29.2)
Severe	51 (6.2)	39 (5.0)	11 (1.7)	25 (4.0)	14 (2.3)	13 (2.3)

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Safety Events

	Ivermectin 400 µg/kg		Fluticasone		Fluvoxamine 50 mg	
	Active (n=817)	Placebo (n=774)	Active (n=656)	Placebo (n=621)	Active (n=674)	Placebo (n=614)
Experienced an adverse events, No. (%)	25 (3.1)	27 (3.7)	13 (1.98)	16 (2.58)	29 (4.30)	31 (5.05)
Experienced a serious adverse events, No. (%)	10 (1.2)	9 (1.2)	3 (0.46)	6 (0.97)	3 (0.48)	4 (0.65)
Serious adverse events, No. (not mutually exclusive)						
COVID-19 pneumonia or NOS	5	7	3	1	0	1
Venous thromboembolism (including PE)	1	5	0	0	0	0
Bacteremia	0	1	0	0	0	0
Diplopia	0	1	0	1	0	0
Pneumonia due to bacteria	2	0	0	0	0	0
Acute kidney injury	1	0	0	0	0	0
Hospitalization (shortness of breath)	1	0	0	0	0	0
Viral bronchopneumonia	1	0	0	0	0	0
COPD exacerbation	0	0	0	0	2	0
Coronary vasospasm	0	0	0	1	0	1
Nausea and vomiting	0	0	0	1	0	0
Other Infection (UTI, finger)	0	0	0	1	1	0
Adverse drug reaction	0	0	0	1	0	0

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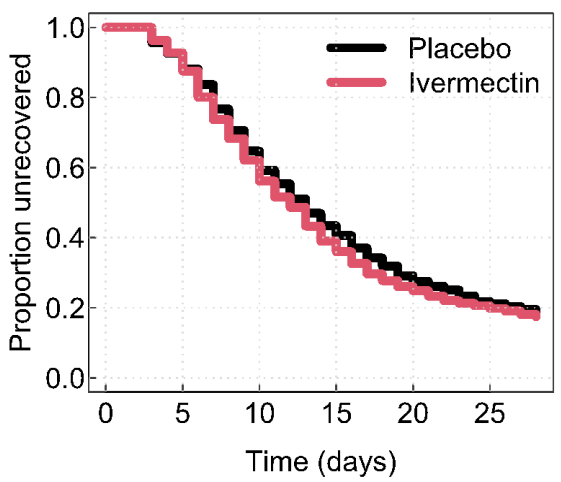
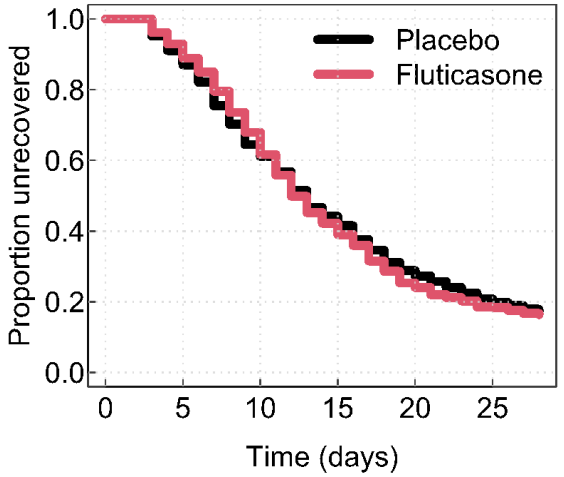
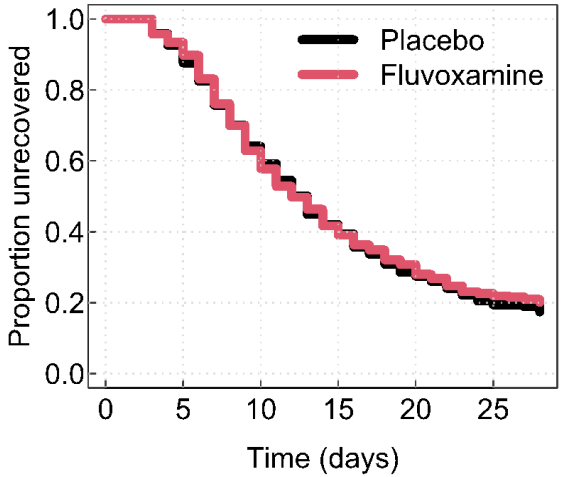
Other SAE: both in fluvoxamine placebo arm: broken ankle, ophthalmic migraine

Primary Endpoint: Time to Sustained Recovery

Among participants that did not die during follow-up, recovery was defined as **three consecutive days without COVID-19** symptoms, as affirmatively reported by the study participant. Time to recovery was administratively censored at 28 days.

	IVERMECTIN 400 µg/kg	FLUTICASONE	FLUVOXAMINE 50 mg
Kaplan-Meier			
HR (95% CrI) P(HR>1)	1.07 (0.96, 1.17) 0.91	1.01 (0.91, 1.12) 0.56	0.96 (0.87, 1.07) 0.22
Median time (IQR), active vs placebo	12 (11-13) vs 13 (12-14)	11 (10.9-11.2) vs 11.5 (11.3-11.6)	12 (11-14) vs 13 (12-13)

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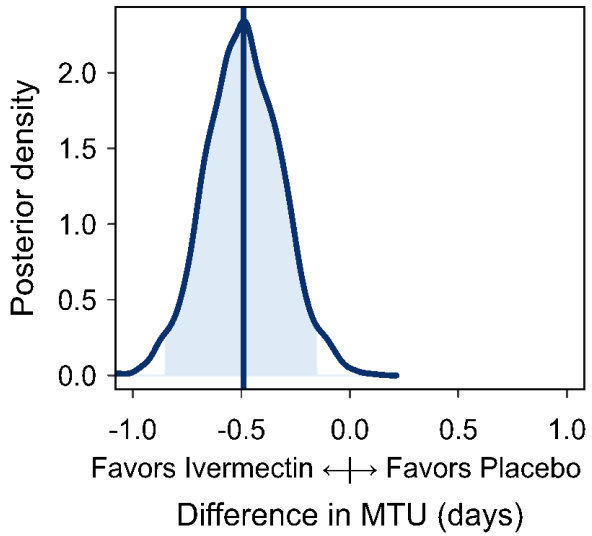
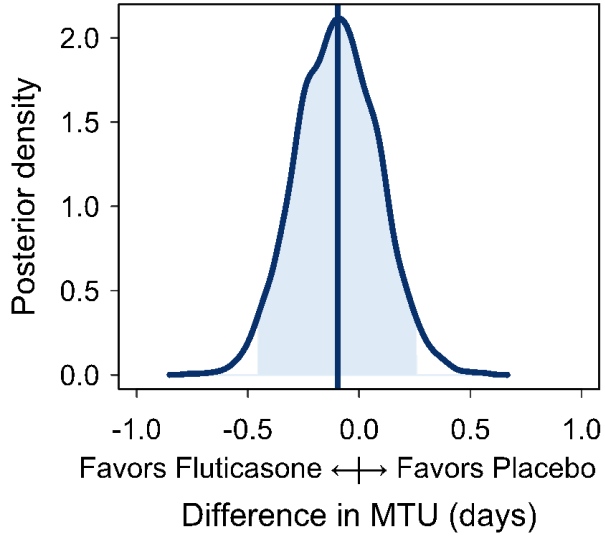
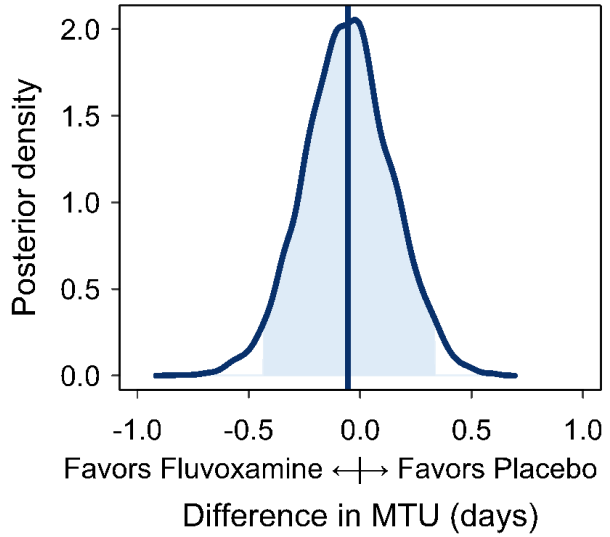
Secondary Endpoint: Time Spent Unwell

The difference in the mean time spent unwell reflects the **difference in symptomatic days** during the first 14 days of follow-up when taking active drug compared with placebo. A negative number favors active drug.

	IVERMECTIN 400 µg/kg	FLUTICASONE	FLUVOXAMINE 50 mg
Δ: Difference in time unwell			
Δ (95% CrI) P(Δ<0)	-0.49 (-0.82, -0.15) 0.99	-0.10 (-0.45, 0.26) 0.70	-0.06 (-0.43, 0.33) 0.61

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Secondary Outcomes – 28 Day Events

	Ivermectin 400 μg/kg				Fluticasone				Fluvoxamine 50 mg			
	Active (n=817)	Placebo (n=774)	HR (CrI)	P*	Active (n=817)	Placebo (n=774)	HR (CrI)	P*	Active (n=674)	Placebo (n=614)	HR (CrI)	P*
Mortality	1 (0.1)	0 (0.0)	-	-	0 (0.0)	0 (0.0)	-	-	0 (0.0)	0 (0.0)	-	-
Death or hospitalization	10 (1.2)	9 (1.16)	1.1 (0.4-2.6)	-	3 (0.5)	3 (0.5)	0.94 (0.2-4.7)	-	1 (0.2)	2 (0.2)	0.45 (0.04-4.99)	-
Hospitalization, urgent or emergency care visit, or death	32 (3.9)	28 (3.6)	1.2 (0.6-1.8)	0.32	24 (3.7)	13 (2.1)	1.9 (0.8-3.5)	0.035	26 (3.9)	23 (3.8)	1.1 (0.6, 1.8)	0.34
WHO Clinical Progression Scale		OR (CrI)		P*	OR (CrI)		P*			OR (CrI)		P*
Day 7		0.81 (0.50-1.13)		0.88	1.10 (0.62-1.63)		0.41			1.32 (0.72-1.98)		0.15
Day 14		0.76 (0.39-1.13)		0.89	0.91 (0.42-1.50)		0.67			1.17 (0.49-2.01)		0.39
Day 28		1.11 (0.52-1.91)		0.45	2.74 (0.50-5.94)		0.07			1.46 (0.79-2.28)		0.10

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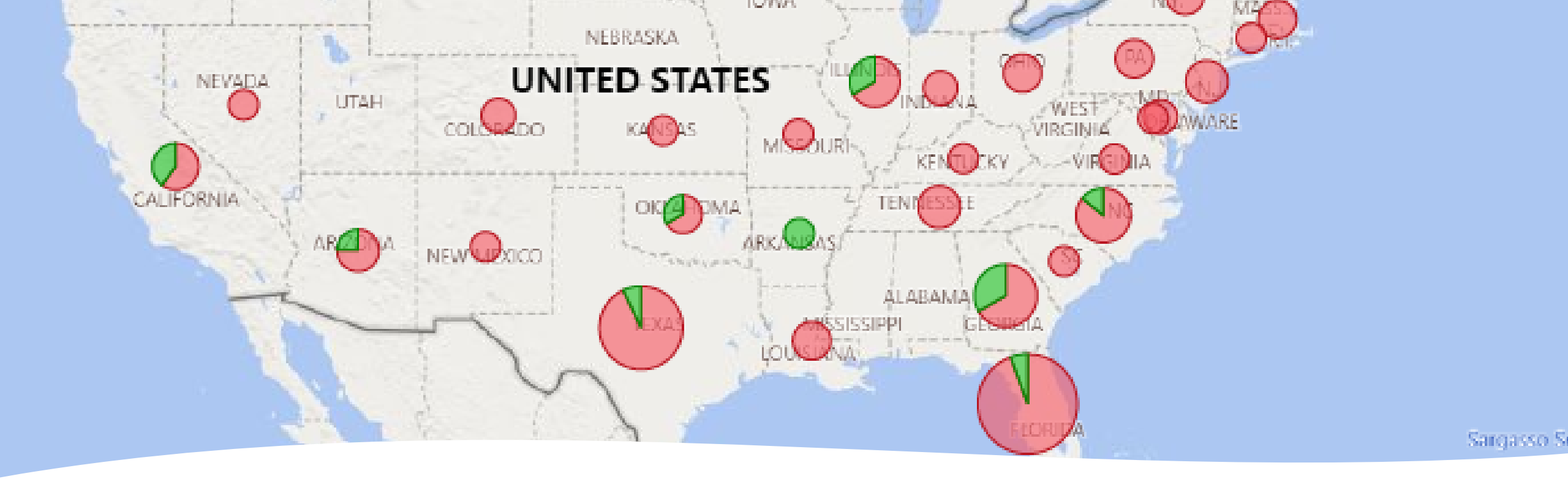
*Posterior P(efficacy)
HR & OR>1 favors placebo

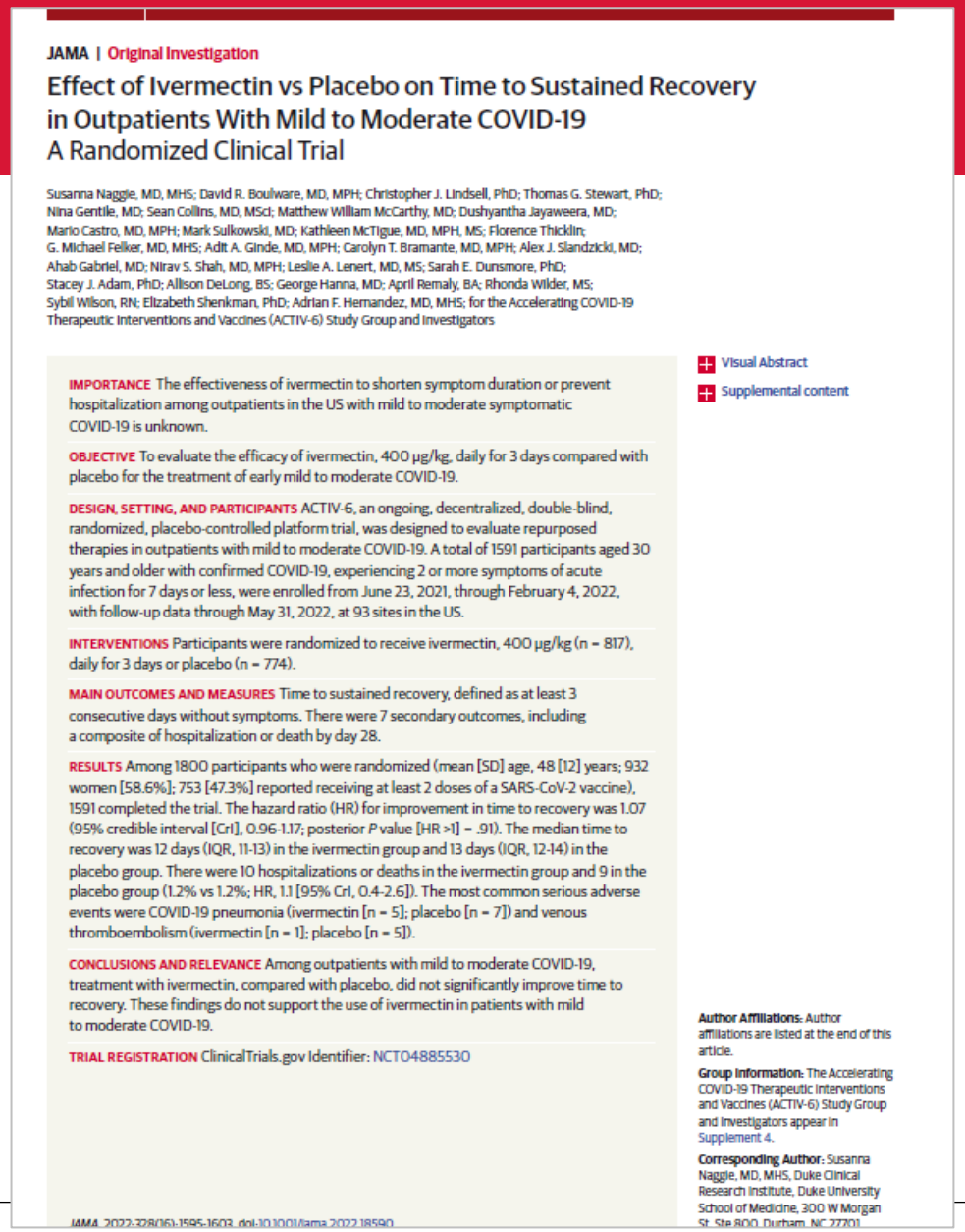
Conclusion

- ACTIV-6 is a large, randomized trial platform designed to evaluate multiple repurposed medications for benefits of symptomatic improvement or prevention of major clinical events in non-hospitalized adults with mild-to-moderate COVID-19 illness.
- We observed no significant differences in relief of mild-to-moderate symptoms between participants taking ivermectin 400 µg/kg, fluticasone, or fluvoxamine 50 mg twice daily and participants taking placebo.
- There was no difference observed in the number of hospitalizations or deaths between participants taking ivermectin 400 µg/kg, fluticasone, or fluvoxamine and participants taking placebo.
- There were no safety concerns identified in any active arm.



Acknowledgements

- Thank you to participants and their families
- Thank you to sites and their community partner organizations and Call Center staff
- Executive Committee, Protocol Oversight Committee, Data Safety and Monitoring Committee, ACTIV Trial Oversight Committee, ACTIV Cross Stats and Trials Committee
- ACTIV-6 is funded by NCATS (3U24TR001608-06S1)
- Other supporting partners: NIH ACTIV Public-Private Partnership, NCATS Trial Innovation Network, PCORI and PCORnet, FNIH, BARDA, CEAL, CEACR
- Study drug was provided by Ingenus, GSK, and Apotex



JAMA | Original Investigation

Effect of Ivermectin vs Placebo on Time to Sustained Recovery in Outpatients With Mild to Moderate COVID-19
A Randomized Clinical Trial

Susanna Naggie, MD, MHS; David R. Boulware, MD, MPH; Christopher J. Lindsell, PhD; Thomas G. Stewart, PhD; Nina Gentile, MD; Sean Collins, MD, MSci; Matthew William McCarthy, MD; Dushyantha Jayaweera, MD; Mario Castro, MD, MPH; Mark Sulkowski, MD; Kathleen McTigue, MD, MPH, MS; Florence Thicklin; G. Michael Felker, MD, MHS; Adit A. Ginde, MD, MPH; Carolyn T. Bramante, MD, MPH; Alex J. Slandzicki, MD; Ahab Gabriel, MD; Nirav S. Shah, MD, MPH; Leslie A. Lenert, MD, MS; Sarah E. Dunsmore, PhD; Stacey J. Adam, PhD; Allison DeLong, BS; George Hanna, MD; April Remaly, BA; Rhonda Wilder, MS; Sybil Wilson, RN; Elizabeth Shenkman, PhD; Adrian F. Hernandez, MD, MHS; for the Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV-6) Study Group and Investigators

IMPORTANCE The effectiveness of ivermectin to shorten symptom duration or prevent hospitalization among outpatients in the US with mild to moderate symptomatic COVID-19 is unknown.

OBJECTIVE To evaluate the efficacy of ivermectin, 400 µg/kg, daily for 3 days compared with placebo for the treatment of early mild to moderate COVID-19.

DESIGN, SETTING, AND PARTICIPANTS ACTIV-6, an ongoing, decentralized, double-blind, randomized, placebo-controlled platform trial, was designed to evaluate repurposed therapies in outpatients with mild to moderate COVID-19. A total of 1591 participants aged 30 years and older with confirmed COVID-19, experiencing 2 or more symptoms of acute infection for 7 days or less, were enrolled from June 23, 2021, through February 4, 2022, with follow-up data through May 31, 2022, at 93 sites in the US.

INTERVENTIONS Participants were randomized to receive ivermectin, 400 µg/kg (n = 817), daily for 3 days or placebo (n = 774).

MAIN OUTCOMES AND MEASURES Time to sustained recovery, defined as at least 3 consecutive days without symptoms. There were 7 secondary outcomes, including a composite of hospitalization or death by day 28.

RESULTS Among 1800 participants who were randomized (mean [SD] age, 48 [12] years; 932 women [58.6%]; 753 [47.3%] reported receiving at least 2 doses of a SARS-CoV-2 vaccine), 1591 completed the trial. The hazard ratio (HR) for improvement in time to recovery was 1.07 (95% credible interval [CrI], 0.96-1.17; posterior *P* value [HR >1] = .91). The median time to recovery was 12 days (IQR, 11-13) in the ivermectin group and 13 days (IQR, 12-14) in the placebo group. There were 10 hospitalizations or deaths in the ivermectin group and 9 in the placebo group (1.2% vs 1.2%; HR, 1.1 [95% CrI, 0.4-2.6]). The most common serious adverse events were COVID-19 pneumonia (ivermectin [n = 5]; placebo [n = 7]) and venous thromboembolism (ivermectin [n = 1]; placebo [n = 5]).

CONCLUSIONS AND RELEVANCE Among outpatients with mild to moderate COVID-19, treatment with ivermectin, compared with placebo, did not significantly improve time to recovery. These findings do not support the use of ivermectin in patients with mild to moderate COVID-19.

TRIAL REGISTRATION ClinicalTrials.gov Identifier: NCT04885530

Visual Abstract
Supplemental content

Author Affiliations: Author affiliations are listed at the end of this article.

Group Information: The Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV-6) Study Group and Investigators appear in Supplement 4.

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JAMA

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A Randomized Clinical Trial

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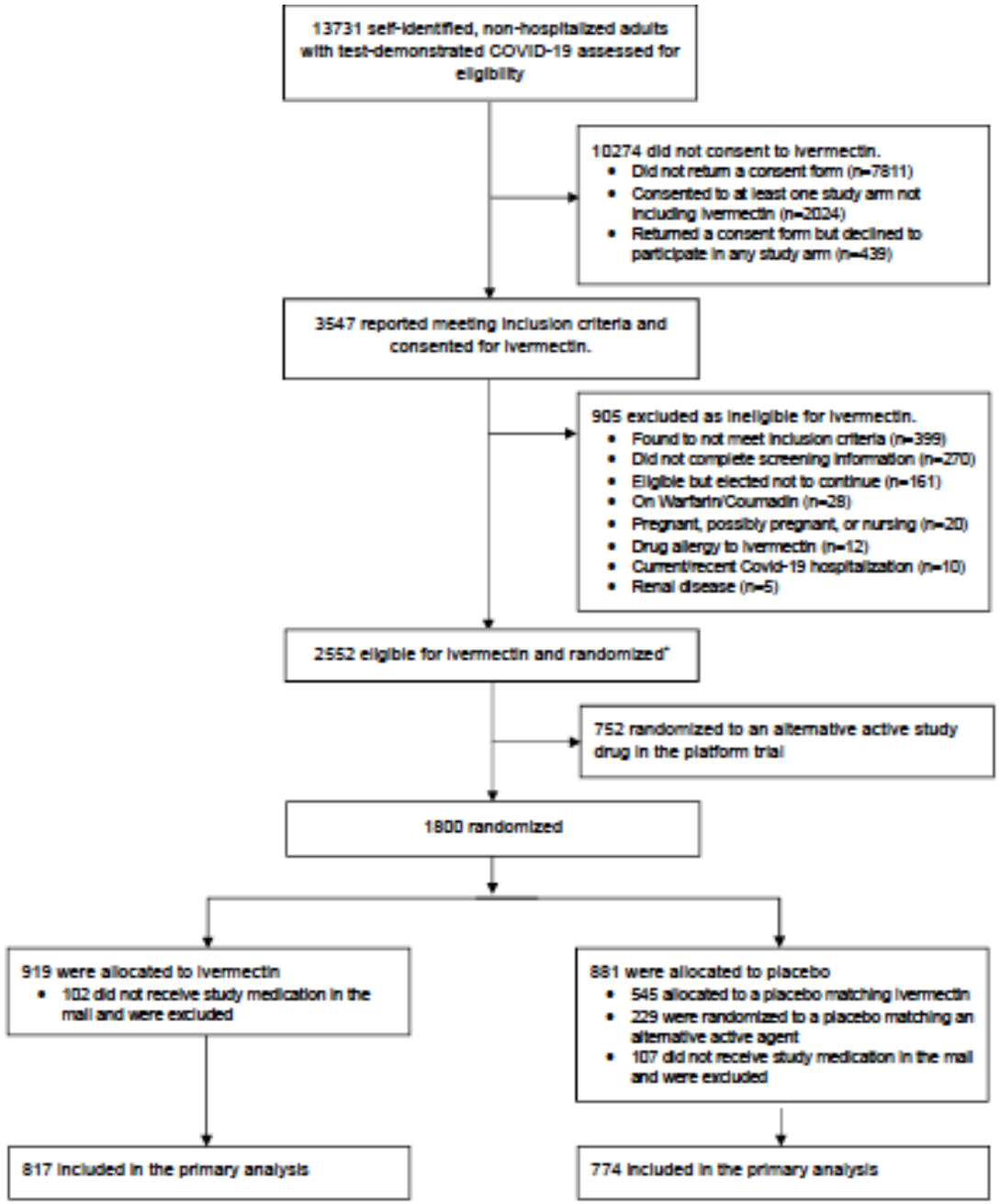
Questions

Additional questions can be sent to the ACTIV-6 inbox: DCRI-ACTIV6@dm.duke.edu

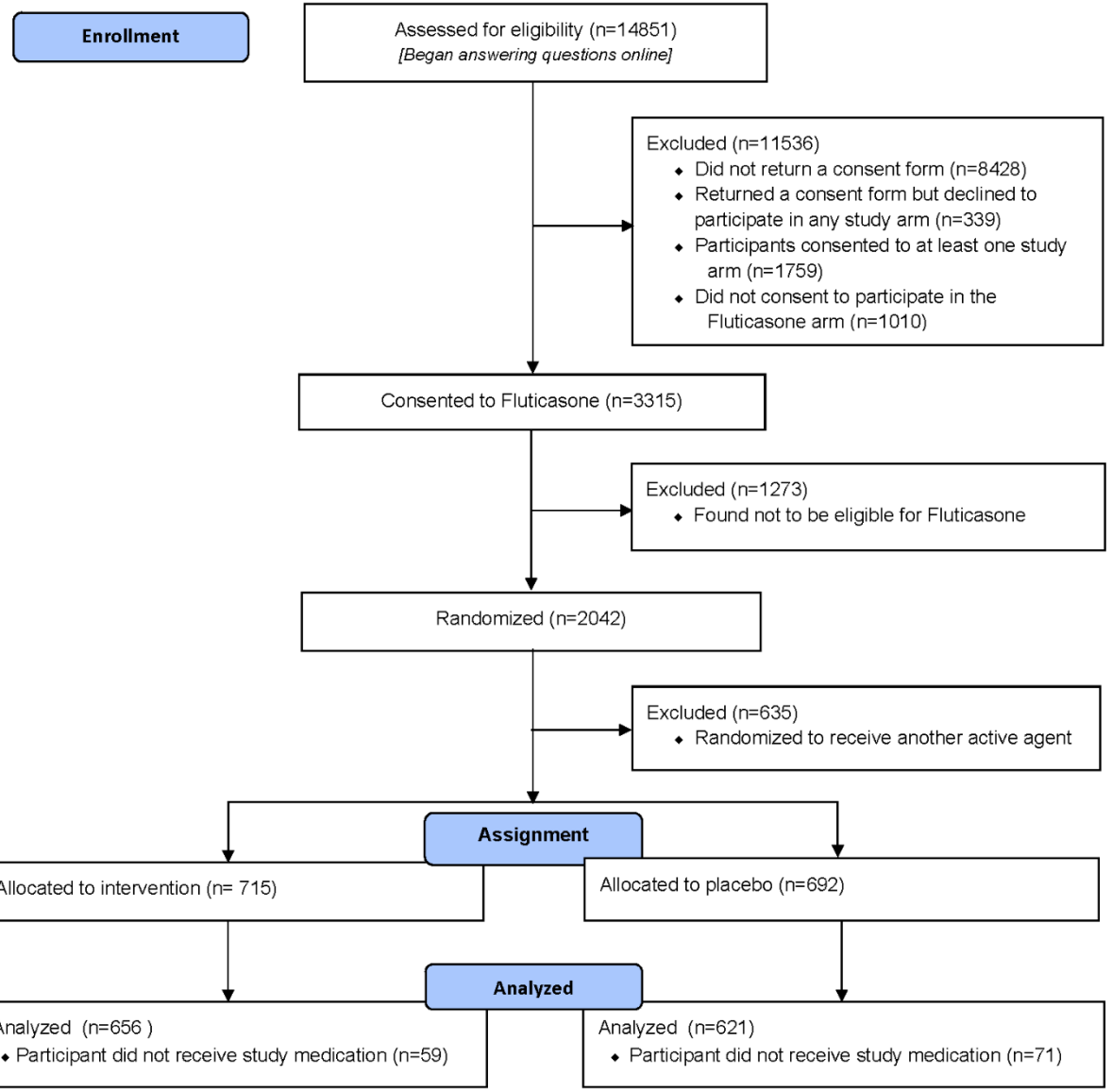
Enrollment



Ivermectin 400
n=(817)

Placebo
n=(774)

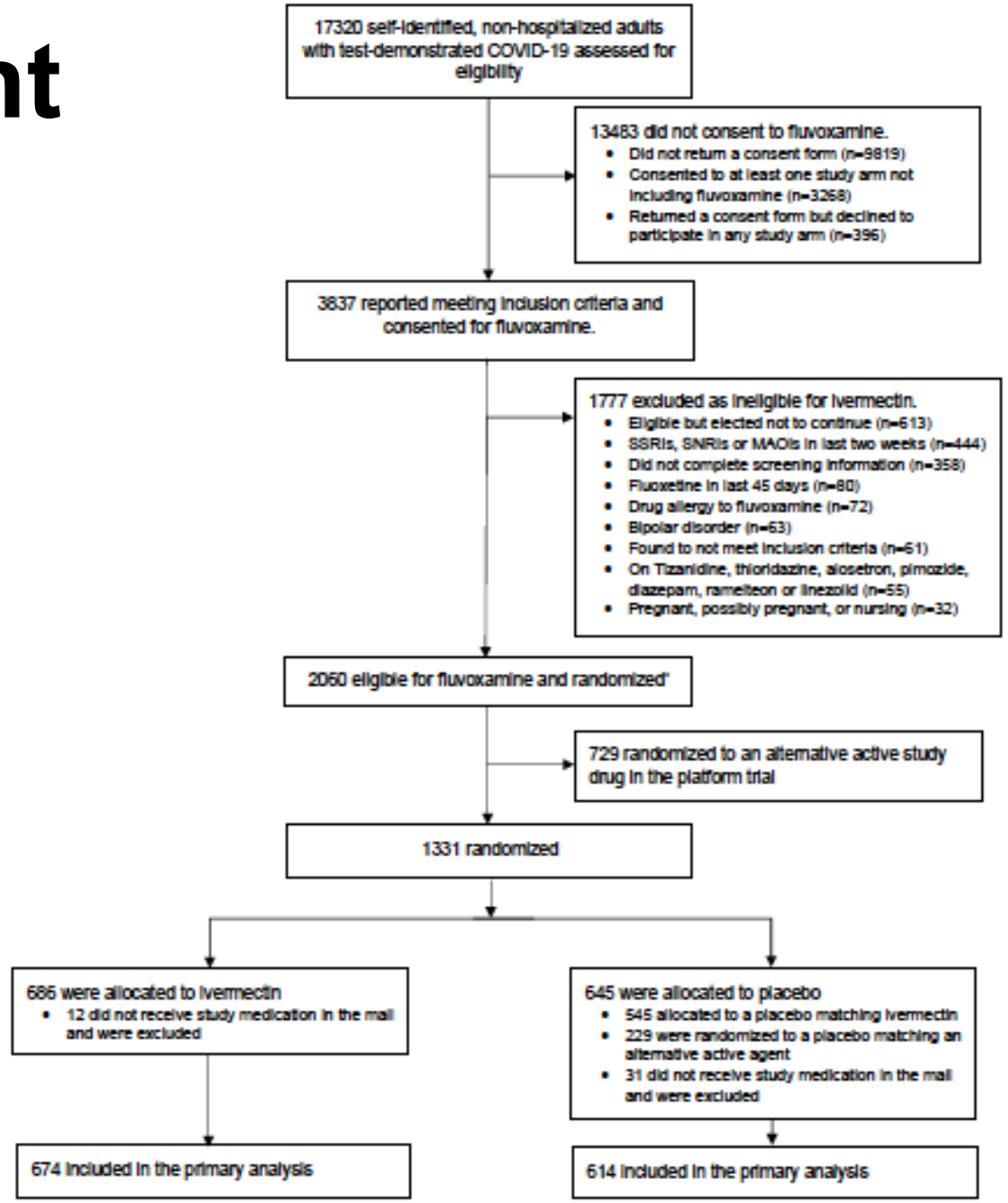
Enrollment



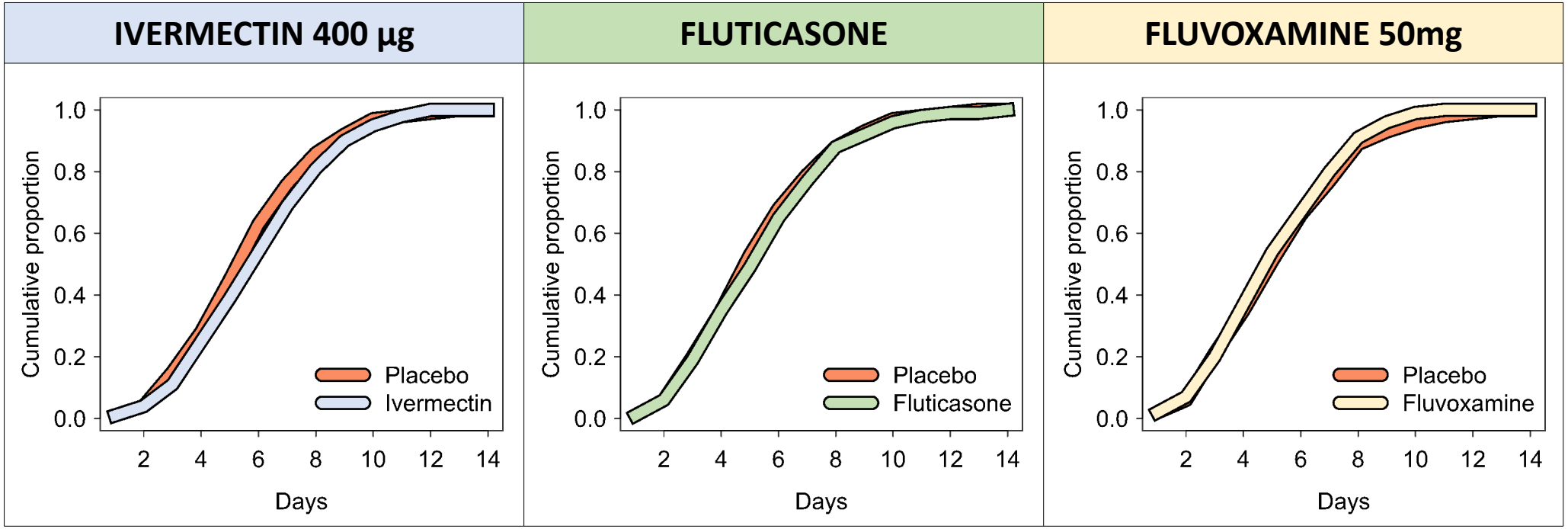
Fluticasone Furoate n=(656)

Placebo n=(621)

Enrollment


17320 self-identified, non-hospitalized adults with test-demonstrated COVID-19 assessed for eligibility
13483 did not consent to fluvoxamine.
Did not return a consent form (n=9819)
Consented to at least one study arm not including fluvoxamine (n=3268)
Returned a consent form but declined to participate in any study arm (n=396)
3837 reported meeting inclusion criteria and consented for fluvoxamine.
1777 excluded as ineligible for ivermectin.
Eligible but elected not to continue (n=613)
SSRIs, SNRIs or MAOIs in last two weeks (n=444)
Did not complete screening information (n=358)
Fluoxetine in last 45 days (n=80)
Drug allergy to fluvoxamine (n=72)
Bipolar disorder (n=63)
Found to not meet inclusion criteria (n=61)
On Tizanidine, thioridazine, alosetron, pimozide, diazepam, ramelteon or linezolid (n=55)
Pregnant, possibly pregnant, or nursing (n=32)
2060 eligible for fluvoxamine and randomized*
729 randomized to an alternative active study drug in the platform trial
1331 randomized
686 were allocated to ivermectin
12 did not receive study medication in the mail and were excluded
645 were allocated to placebo
545 allocated to a placebo matching ivermectin
229 were randomized to a placebo matching an alternative active agent
31 did not receive study medication in the mail and were excluded
674 included in the primary analysis
614 included in the primary analysis

Days between onset of symptoms and drug delivery



Appendix	Arm	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Ivermectin 400	Placebo	0.01	0.04	0.15	0.28	0.45	0.63	0.76	0.86	0.92	0.97	0.98	0.99	1.00	1
	Active	0.01	0.04	0.11	0.25	0.39	0.54	0.69	0.81	0.90	0.95	0.98	1.00	1.00	1
Fluticasone	Placebo	0.01	0.06	0.20	0.35	0.53	0.68	0.79	0.88	0.93	0.97	0.98	0.99	1.00	1
	Active	0.01	0.06	0.19	0.35	0.49	0.65	0.77	0.88	0.92	0.96	0.98	0.99	0.99	1
Fluvoxamine 50	Placebo	0.02	0.06	0.21	0.35	0.51	0.66	0.77	0.89	0.93	0.96	0.98	0.99	1.00	1
	Active	0.02	0.07	0.20	0.37	0.54	0.67	0.80	0.91	0.96	0.99	1.00	1.00	1.00	1

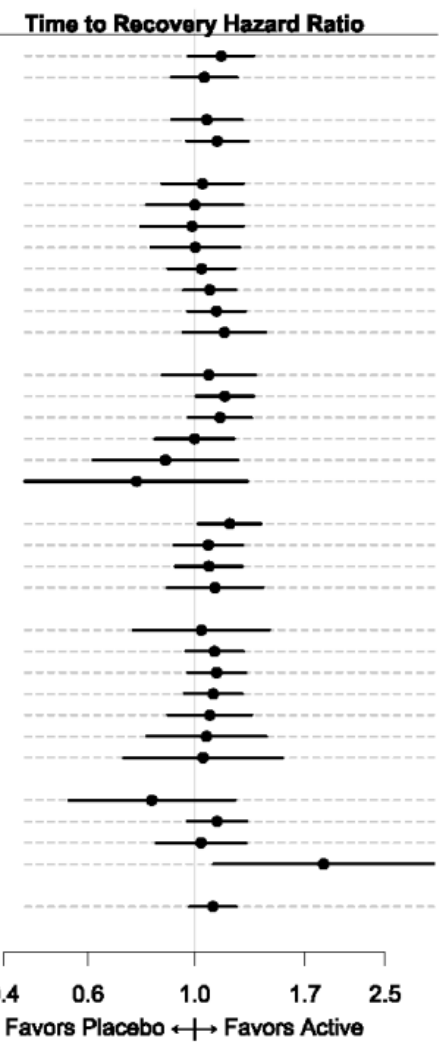
Concomitant Treatments for COVID-19

	Ivermectin 400 µg/kg		Fluticasone		Fluvoxamine 50 mg	
	Active (n=817)	Placebo (n=774)	Active (n=656)	Placebo (n=621)	Active (n=674)	Placebo (n=614)
Remdesivir (%)	2 (0.2)	2 (0.3)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.16)
Monoclonal antibodies (%)	22 (2.7)	25 (3.2)	17 (2.6)	13 (2.1)	11 (1.6)	10 (1.6)
Paxlovid (%)	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.2)	8 (1.2)	5 (0.81)
Molnupiravir (%)	0	0	0	0	1 (0.15)	1 (0.16)

ACTIV-6

Heterogeneity of Treatment Effect: Ivermectin 400 µg/d

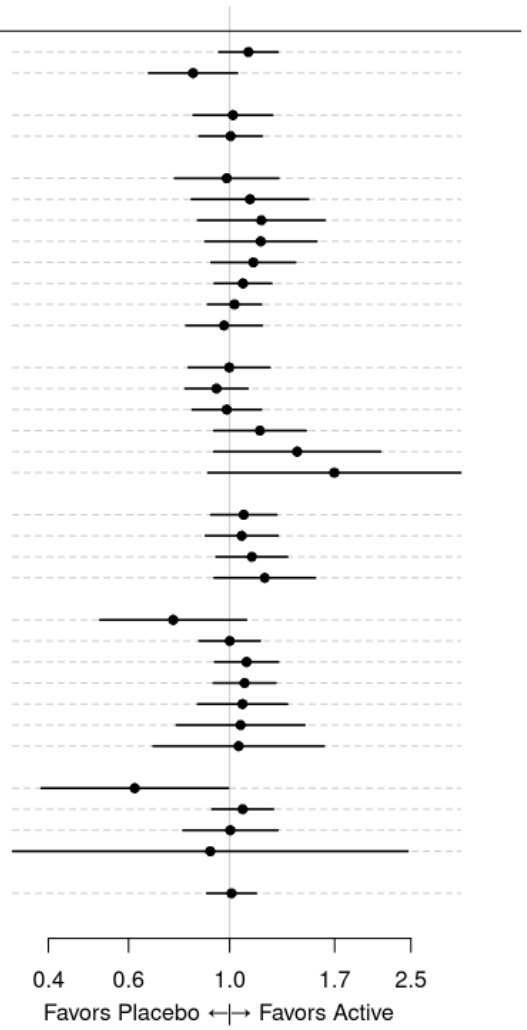
Characteristic	Subgroup	Ivermectin N	Placebo N	HR (95% CI)	HTE p-value
Vaccination status	Vaccinated	397	380	1.14 (0.97, 1.33)	0.474
	Not vaccinated	420	394	1.05 (0.90, 1.23)	
Sex	Male	309	350	1.06 (0.90, 1.26)	0.663
	Female	508	424	1.12 (0.96, 1.30)	
Calendar time	2021-10-15			1.04 (0.85, 1.27)	0.667
	2021-11-01			1.00 (0.79, 1.26)	
	2021-11-15			0.99 (0.77, 1.27)	
	2021-12-01			1.00 (0.81, 1.24)	
	2021-12-15			1.03 (0.88, 1.22)	
	2022-01-01			1.08 (0.95, 1.22)	
	2022-01-15			1.11 (0.97, 1.28)	
	2022-02-01			1.16 (0.95, 1.41)	
Symptom onset, days	3			1.07 (0.86, 1.34)	0.386
	5			1.16 (1.01, 1.33)	
	7			1.13 (0.97, 1.32)	
	9			1.00 (0.83, 1.21)	
	11			0.87 (0.61, 1.23)	
	13			0.76 (0.44, 1.29)	
Age, years	40			1.18 (1.02, 1.38)	0.953
	50			1.07 (0.91, 1.26)	
	60			1.07 (0.91, 1.26)	
	70			1.10 (0.88, 1.39)	
Body mass index, kg/m²	20			1.03 (0.75, 1.43)	0.911
	25			1.10 (0.96, 1.26)	
	30			1.11 (0.97, 1.28)	
	35			1.09 (0.95, 1.26)	
	40			1.08 (0.88, 1.32)	
	45			1.06 (0.79, 1.41)	
	50			1.04 (0.71, 1.53)	
Symptoms on study day 1	None	53	54	0.82 (0.55, 1.22)	0.101
	Mild	491	433	1.11 (0.97, 1.29)	
	Moderate	224	247	1.03 (0.83, 1.28)	
	Severe	49	40	1.86 (1.10, 3.16)	
Overall mITT population		817	774	1.09 (0.98, 1.22)	



[a]No subgrouping variable achieved significance

Heterogeneity of Treatment Effect: Inhaled Fluticasone

Characteristic	Subgroup	Placebo N	Active N	HR (95% CI)
Vaccination status	Vaccinated	410	436	1.10 (0.95, 1.28)
	Not vaccinated	211	220	0.83 (0.66, 1.04)
Sex	Male	245	225	1.02 (0.83, 1.24)
	Female	376	431	1.01 (0.86, 1.18)
Calendar time	2021-10-15			0.99 (0.76, 1.28)
	2021-11-01			1.11 (0.82, 1.49)
	2021-11-15			1.17 (0.85, 1.62)
	2021-12-01			1.17 (0.88, 1.55)
	2021-12-15			1.13 (0.91, 1.39)
	2022-01-01			1.07 (0.93, 1.24)
	2022-01-15			1.02 (0.89, 1.17)
	2022-02-01			0.97 (0.80, 1.18)
Symptom onset, days	3			1.00 (0.81, 1.23)
	5			0.94 (0.80, 1.10)
	7			0.99 (0.83, 1.17)
	9			1.17 (0.92, 1.47)
	11			1.41 (0.92, 2.14)
	13			1.70 (0.90, 3.21)
Age, years	40			1.07 (0.91, 1.27)
	50			1.06 (0.89, 1.28)
	60			1.12 (0.93, 1.34)
	70			1.19 (0.93, 1.54)
Body mass index, kg/m²	20			0.75 (0.52, 1.09)
	25			1.00 (0.86, 1.17)
	30			1.09 (0.93, 1.28)
	35			1.08 (0.92, 1.26)
	40			1.07 (0.85, 1.34)
	45			1.06 (0.76, 1.46)
	50			1.05 (0.68, 1.61)
Symptoms on study day 1	None	41	35	0.62 (0.39, 0.99)
	Mild	379	420	1.07 (0.92, 1.25)
	Moderate	176	190	1.00 (0.79, 1.28)
	Severe	25	11	0.91 (0.33, 2.46)
Overall mITT population		621	656	1.01 (0.89, 1.14)



Heterogeneity of Treatment Effect: Fluvoxamine 50 mg

[a]

Characteristic	Subgroup	Fluvoxamine N	Placebo N	HR (95% CI)	HTE p-value
Vaccination status	Vaccinated	464	418	0.96 (0.83, 1.12)	0.660
	Not vaccinated	210	196	0.90 (0.71, 1.14)	
Sex	Male	287	267	1.02 (0.85, 1.24)	0.246
	Female	387	347	0.88 (0.74, 1.05)	
Calendar time	2021-10-15			1.19 (0.92, 1.53)	0.114
	2021-11-01			1.07 (0.86, 1.32)	
	2021-11-15			1.00 (0.79, 1.25)	
	2021-12-01			0.96 (0.77, 1.20)	
	2021-12-15			0.95 (0.77, 1.15)	
	2022-01-01			0.93 (0.79, 1.11)	
	2022-01-15			0.92 (0.79, 1.08)	
	2022-02-01			0.91 (0.79, 1.05)	
Symptom onset, days	3			0.89 (0.72, 1.10)	0.225
	5			0.88 (0.75, 1.04)	
	7			0.96 (0.80, 1.15)	
	9			1.14 (0.89, 1.47)	
	11			1.37 (0.87, 2.18)	
	13			1.66 (0.83, 3.32)	
Age, years	40			1.05 (0.88, 1.25)	0.192
	50			0.93 (0.77, 1.13)	
	60			0.92 (0.77, 1.11)	
	70			0.94 (0.74, 1.21)	
Body mass index, kg/m²	20			0.61 (0.41, 0.90)	0.016
	25			0.88 (0.76, 1.02)	
	30			1.04 (0.88, 1.21)	
	35			1.10 (0.94, 1.29)	
	40			1.17 (0.94, 1.46)	
	45			1.24 (0.91, 1.68)	
	50			1.32 (0.88, 1.96)	
Symptoms on study day 1	None	36	37	1.19 (0.73, 1.95)	0.450
	Mild	442	396	0.88 (0.76, 1.03)	
	Moderate	182	168	1.02 (0.80, 1.32)	
	Severe	14	13	1.46 (0.54, 3.94)	
Overall mITT population		674	614	0.94 (0.83, 1.07)