

Anti-Coronavirus Therapies (ACT) trials

Colchicine and Aspirin in community patients with COVID-19

An open-label, factorial, randomized trial

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on behalf of the ACT Trials Steering Committee and Investigators

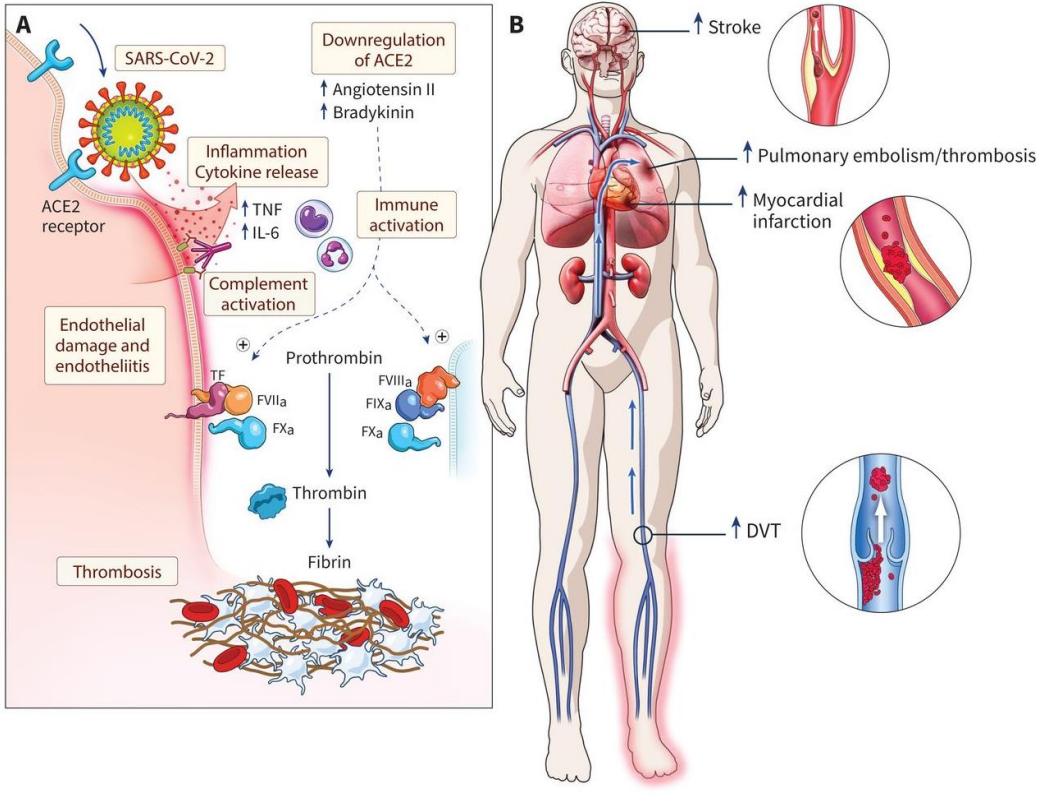
Monday August 29, 2022

NCT04324463

The problem

- Estimated 3.8 billion people infected and 18 million deaths by end 2021
 - Health care systems overwhelmed
 - Existing treatments incompletely effective, often expensive
 - Vaccination not readily accessible in many countries
- ➔ ***Widely-applicable treatments needed for patients with mild, moderate, severe disease***

Targets: inflammation & hypercoagulability



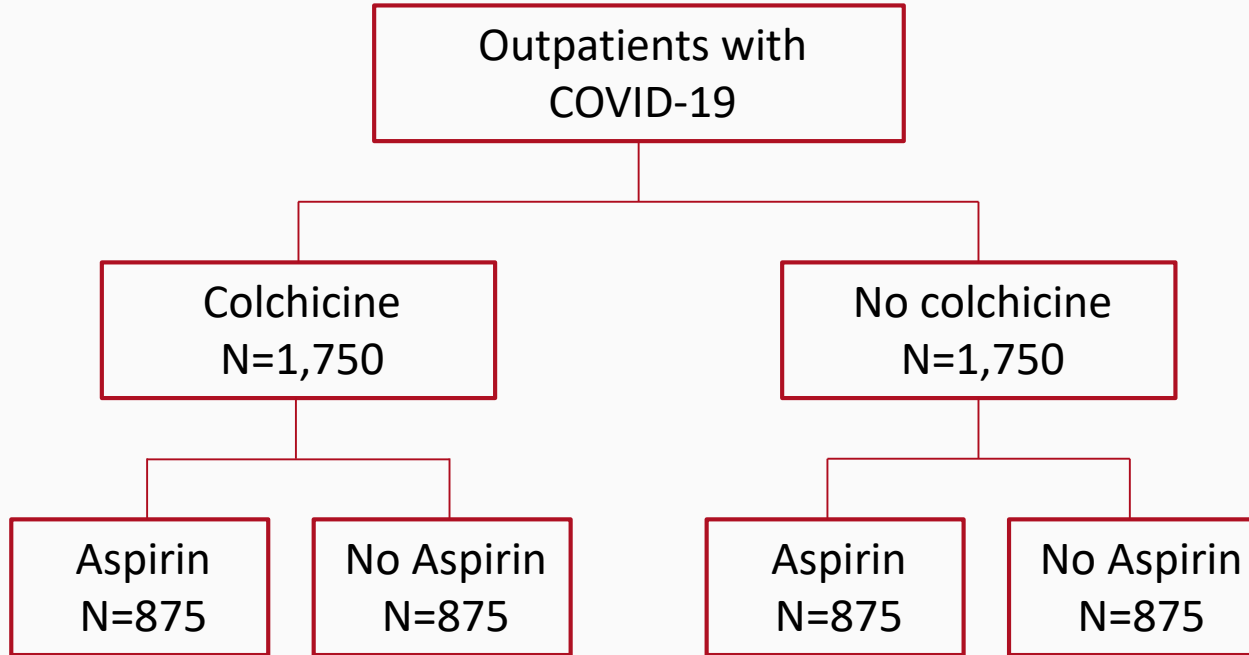
Objectives of the **ACT trial program**

To determine in patients with symptomatic, laboratory confirmed COVID-19 whether:

1. Anti-inflammatory therapy with colchicine
2. Antithrombotic therapy with aspirin (mild disease) or the combination of rivaroxaban and aspirin (moderate or severe disease)

can prevent disease progression or death *across the spectrum of disease severity*.

Outpatient trial design (mild disease)



Primary outcomes

Colchicine: hospitalization or death

Aspirin: Major thrombosis, hospitalization or death

Eligibility

Inclusion

- Symptomatic, laboratory-confirmed COVID-19
- Age ≥ 30 years
- High risk*
- Within 7 days of diagnosis or worsening clinically

Exclusion:

- Advanced kidney or liver disease
- Pregnancy (known or potential) or lactation.
- Allergy or planned use of study interventions

*One or more of age ≥ 70 , male, BMI ≥ 30 , chronic disease, active cancer, diabetes

Country recruitment (n=3,917)

Region	Country	N
Middle East	Egypt	1,971
	UAE	70
Eurasia	Russia	614
North America	Canada	354
South Asia	Nepal	317
	Philippines	129
	India	77
	Pakistan	8
South America	Colombia	181
	Brazil	122
	Ecuador	74

Baseline characteristics

Characteristic	Colchicine (n=3,917)		Aspirin (n= 3,917)	
Randomized, n	1,956	1,961	1,964	1,953
Age, mean (SD)	45.0 (13.7)	45.0 (13.3)	45.2 (13.5)	44.9 (13.4)
Males, n (%)	1,173 (60.5%)	1,177 (60.6%)	1,195 (61.4%)	1,155 (59.7%)
Diabetes, n (%)	256 (13.2%)	264 (13.6%)	247 (12.7%)	273 (14.1%)
Hypertension, n (%)	435 (22.4%)	422 (21.7%)	440 (22.6%)	417 (21.5%)
Fully vaccinated	419 (21.6%)	402 (20.7%)	425 (21.9%)	396 (20.5%)

Adherence and completeness of follow-up

Adherence = take $\geq 80\%$ of interventions at 45 days

Follow up = for primary outcome

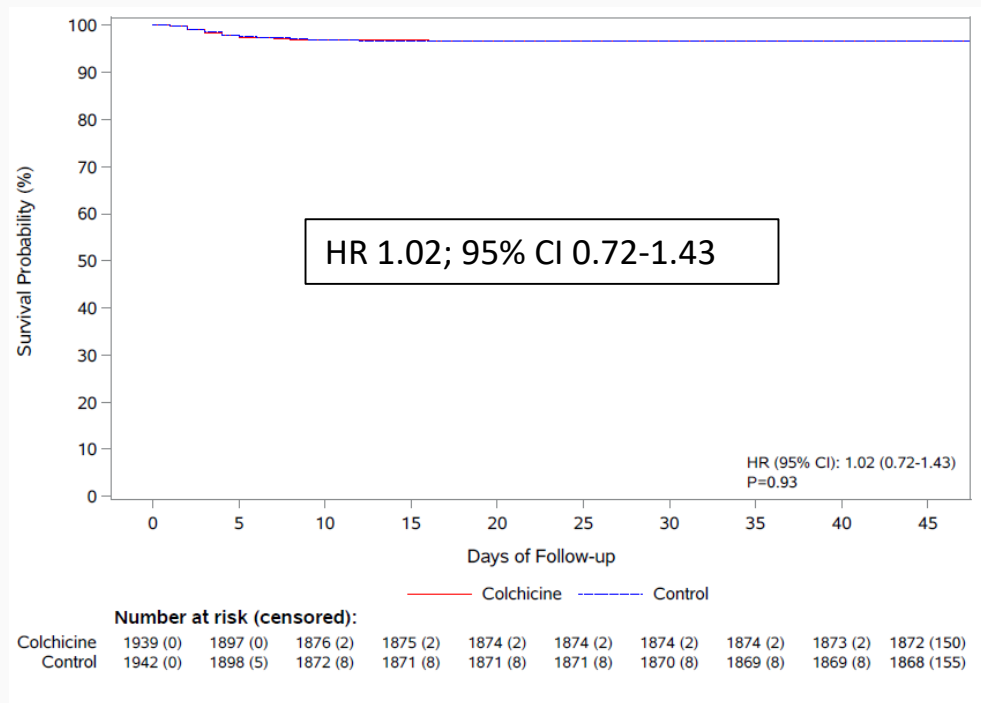
Colchicine:

- Adherence: 89.1%
- Follow up: 99.7%

Aspirin:

- Adherence: 90.0%
- Follow up: 99.7%

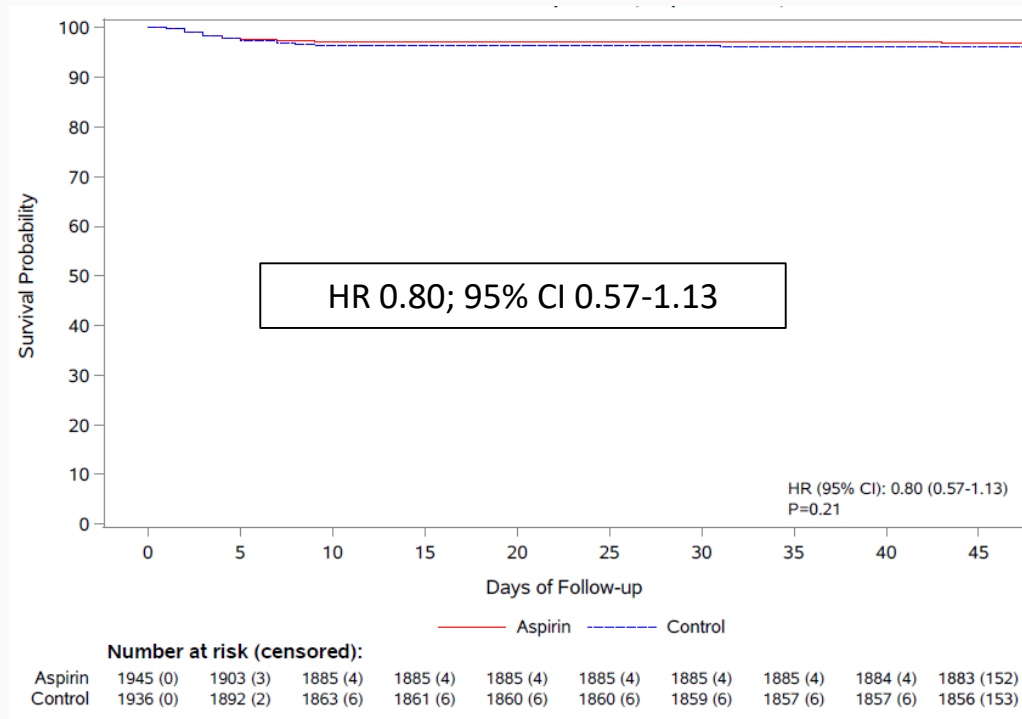
Colchicine: hospitalization or death



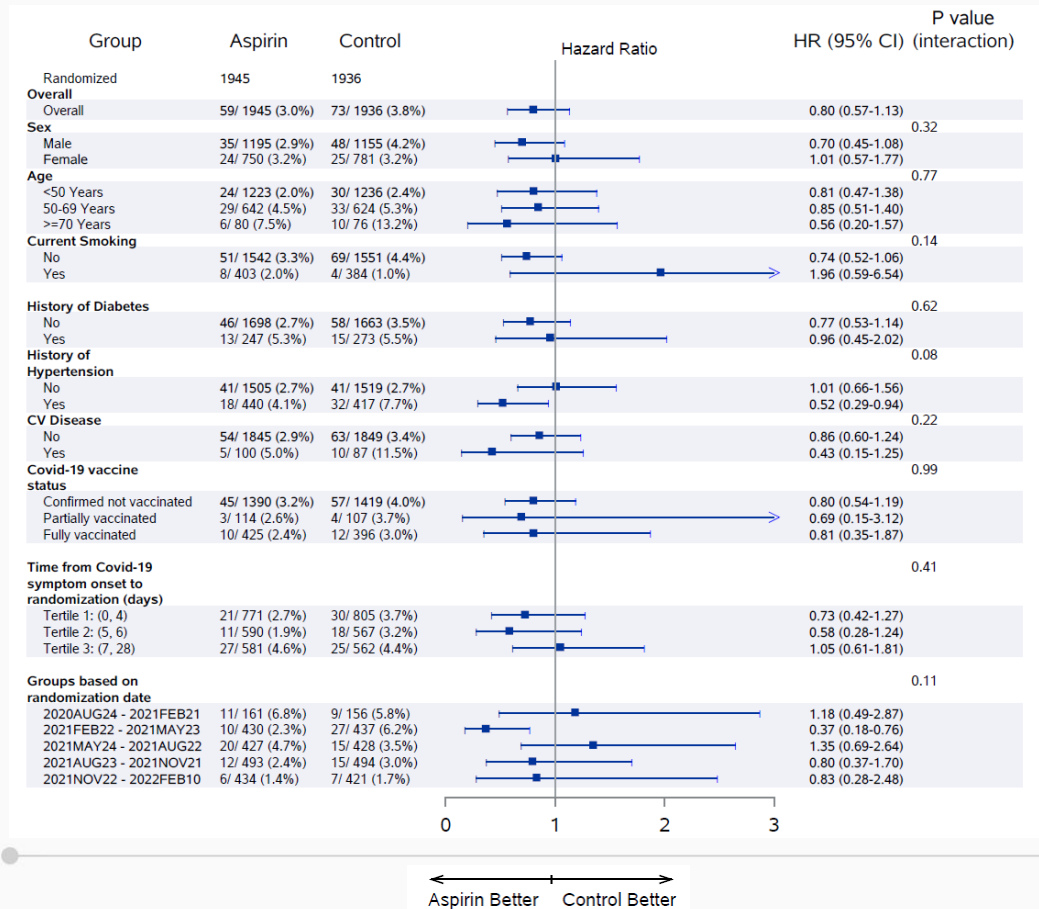
Colchicine: other outcomes

Outcome	Colchicine (n=1,956)	Control (n=1,961)	HR (95% CI)	p-value
Hospitalization or death	66 (3.4%)	65 (3.3%)	1.02 (0.72-1.43)	0.93
Hospitalization or resp. death	65 (3.4%)	65 (3.3%)	1.00 (0.71-1.41)	0.99
Hospitalization	62 (3.2%)	61 (3.1%)	1.02 (0.71-1.45)	0.92
Death	12 (0.6%)	11 (0.6%)	1.09 (0.48-2.47)	0.84
Respiratory death	10 (0.5%)	7 (0.4%)	1.43 (0.54-3.75)	0.47

Aspirin: major thrombosis, hospitalization, death



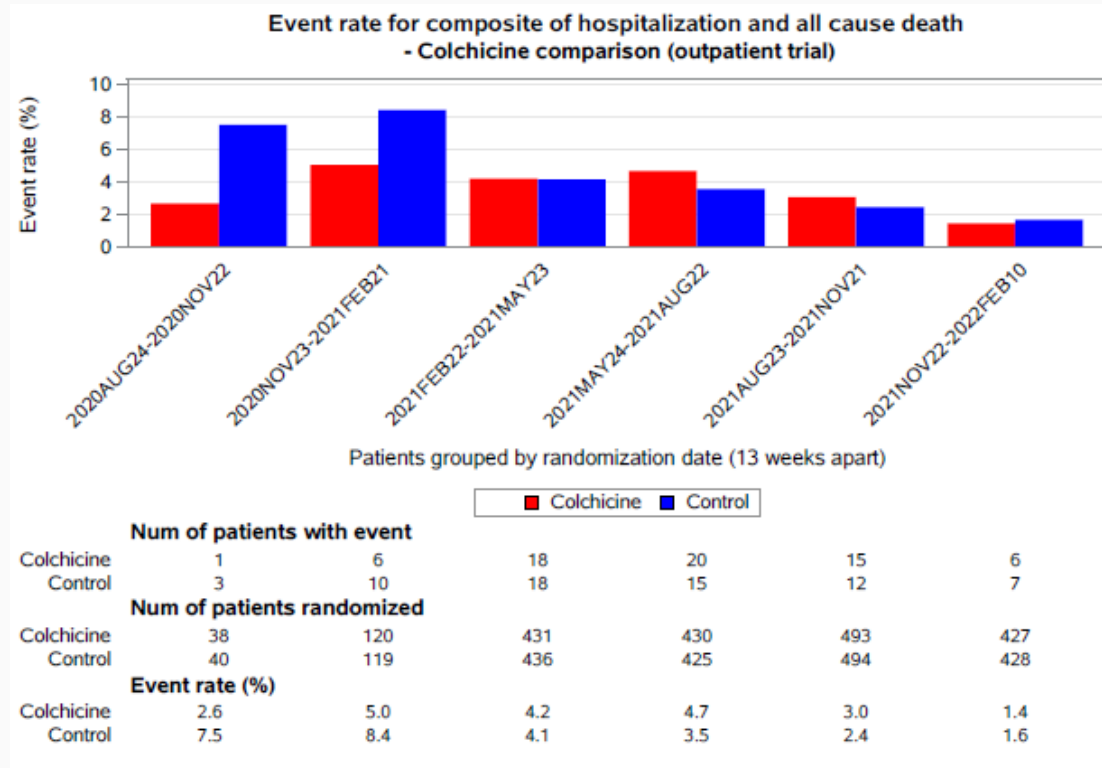
Aspirin: key subgroups



Aspirin: other outcomes

Outcome	Aspirin N=1,964	Control N=1,953	HR (95% CI)	P-value
Major thrombosis, hospitalization, or death*	59 (3.1%)	73 (3.7%)	0.80 (0.57-1.13)	0.21
Any thrombosis	2 (0.1%)	5 (0.3%)	0.40 (0.08-2.06)	0.27
Death	12 (0.6%)	11 (0.6%)	1.09 (0.48-2.46)	0.84
Respiratory death	10 (0.5%)	7 (0.4%)	1.42 (0.54-3.73)	0.48
Hospitalization	56 (2.9%)	67 (3.4%)	0.83 (0.58-1.19)	0.31

Hospitalization or death event rates over time



Conclusions

- Colchicine and aspirin appear to provide no benefits in outpatients with COVID-19 (supported by the results of an updated meta-analysis to be presented by next speaker)
- Severity of COVID-19 appears to be diminishing (but patients will continue to have severe disease and die)
- The world *still* needs additional inexpensive, widely-applicable treatments for COVID-19



PROOF
(not for distribution)

Colchicine and aspirin in community patients with COVID-19 (ACT): an open-label, factorial, randomised, controlled trial



John WEikelboom, Sanjit S Jolly, Emilie P Belley-Cote, Richard PWhitlock, Sumathy Rangarajan, Lizhen Xu, Laura Heenan, Shrikant I Bangdiwala, Wade M Tarhuni, Mohamed Hassany, Anna Kontsevaya, William Harper, Sanjib Kumar Sharma, Patricio Lopez-Jaramillo, Antonio L Dans, Lia M Palileo-Villanueva, Alvaro Avezum, Prem Pais, Denis Xavier, Camilo Felix, Afzalhussein Yusufali, Renato D Lopes, Otavio Berwanger, Zeeshan Ali, Sean Wasserman, Sonia S Anand, Jackie Bosch, Shurjeel Choudhri, Michael E Farkouh, Mark Loeb, Salim Yusuf

Summary

Background The large number of patients worldwide infected with the Sars-CoV-2 virus has overwhelmed health-care systems globally. The Anti-Coronavirus Therapies (ACT) outpatient trial aimed to evaluate anti-inflammatory therapy with colchicine and antithrombotic therapy with aspirin for prevention of disease progression in community patients with COVID-19.

Lancet Respir Med 2022

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