12 studi di vaccinati vs. non vaccinati sono in Tab. 4 di *Hulscher N et al*. [autism report]

Study (Author, Year)	Sample Size	Design Type	Unvaccinated Control?	Autism Verification Method	Vaccination Status Verification Method	Key Findings	Rates of NDD, Measures of Association
Enriquez et al., 2005[286]	1,177 children (515 never-vaccinated; 423 partially; 239 fully)	Cross-sectional mailed survey to NVIC member households	Yes	Survey	Survey	Parents who refuse vaccinations reported less asthma and allergies in their unvaccinated children	NR
Lyons-Weiler and Thomas[287]	3,324 pediatric patients born into one practice (2,763 variably vaccinated; 561 unvaccinated)	Cohort	Yes (561 unvaccinated)	ICD-coded diagnoses in the EMR	EMR/billing records (practice database)	Overall results indicate that the unvaccinated pediatric patients in this practice are healthier overall than the vaccinated. Noted "0 of 561" unvaccinated with ADHD	ASD overall in cohort: 8.4 per 1,000 (0.84%). ADHD among unvaccinated: 0 per 1,000 (0/561)
Mawson et al., 2017[288]	666 homeschooled children (261 unvaccinated; 405 vaccinated); 7.7% preterm	Cross-sectional Survey	Yes	Survey	Survey	Vaccination associated with higher odds of NDD in preterm births (OR 2.7, 95% CI 1.2–6.0); preterm+vaccinated had higher odds vs term+vaccinated (OR 5.4, 2.5–11.9) and vs term+unvaccinated (OR 14.5, 5.4–38.7). No NDD observed in preterm-unvaccinated subgroup (n=12)	NDD: 104 per 1,000 (vaccinated 10.4%) vs 31 per 1,000 (unvaccinated 3.1%). ASD: 46.9 per 1,000 vs 11.5 per 1,000. Preterm-unvaccinated subgroup: 0 per 1,000 (0/12; note very small n)
Hooker and Miller, 2021[290]	1,565 children (from 1,929 surveys; post-exclusions) across 3 US practices	Voluntary Survey	Yes	Parent report; subset confirmed via EMR chart review	Parent report; diagnoses confirmation subset via EMR; some analyses restricted to patients in participating practices	Higher ORs were observed within the fully and partially vaccinated groups versus the unvaccinated multiple conditions	Autism: OR 5.03 (1.64–15.5). ADHD: OR 20.8 (4.74–91.2). GI disorders: OR 1[illegible] (5.85–32.[illegible] Asthma: O[illegible] (0.94–14. Chronic ear infections: OR 27.8 (9.56–80.8).
Joy Garner, 2020[291]	1,482 entirely unvaccinated participants	Cross-sectional, self-selected survey of only post-birth unvaccinated people	No (all participants unvaccinated; compared only to U.S. average)	Survey	Survey	Unvaccinated individuals reported dramatically lower lifetime rates of chronic illness, disability, and death compared with national U.S. averages. Authors emphasized absence of autism, ADHD, diabetes, heart disease, and chronic allergy/asthma among surveyed unvaccinated participants, and proposed a national follow-up study	Vaccinated U.S. children (ages 3–17): 47.6 per 1,000 vs. Unvaccinated (all ages): 1.3 per 1,000; relative risk reduction ≈ 97%
Nederlandse Vereniging Kritisch Prikken, 2006[292]	231 unvaccinated and 312 vaccinated children analyzed	National Survey	Yes	Survey	Survey	Autism reported in 8/312 vaccinated vs 0/231 unvaccinated	Vaccinated: 8/312 = 2.6%; Unvaccinated: 0/231 = 0%
Joy Garner, 2022[293]	1,482 unvaccinated	Cross-sectional survey of unvaccinated	Yes (unvaccinated controls vs. vaccine-exposed U.S.	Survey	Survey	Unvaccinated Americans were "incommensurably healthier" than vaccinated counterparts.	Post-birth unvaccinated, all ages: 1.3 per 1,000
					population, 99.74%)		Chronic disease risk 5–6% in unvaccinated vs. ~60% in vaccinated. Autism prevalence 0% among those with no post-birth, pre-birth, or vitamin K exposure; 0.13% overall (2/1,482) limited to K-shot/maternal vaccine–exposed subgroup. Exposure to maternal vaccines and vitamin K shot associated with 4–10× higher risk of chronic disorders.
Hooker and Miller, 2020[294]	4,821	Retrospective chart/EMR study with vaccinated vs unvaccinated groups	Yes	NR	EMR-documented vaccination (ICD/CPT in records)	Higher odds in vaccinated vs unvaccinated for developmental delay (OR 2.18), asthma (OR 4.49), and ear infection (OR 2.13); GI disorder OR 3.10 (NS)	Developmental delays OR 2.18 (95% CI 1.47–3.24) for vaccination before age 1; sensitivity (≥5 y): OR 2.36 (95% CI 1.29–4.31).
Mawson A R, 2025[295]	47,155 nine-year-old children in Florida Medicaid	Cross-sectional (NDD odds by vaccination/preterm) and retrospective cohort	Yes	Claims-based diagnosis codes (ICD[illegible]) for ASD/NDD	[illegible] captured vi[illegible] CPT/ICD-[illegible] c[illegible] # vaccination visits derived from claims	Preterm, vaccinated children had 39.9% NDD vs 15.7% in preterm, unvaccinated (adjusted OR 3.58). ASD risk rose with vaccination visits: RR 1.7 (95% CI 1.21–2.35) for 1 visit and RR 4.4 (95% CI 2.85–6.84) for ≥11 visits vs 0	ASD: 28.1 per 1,000 (vaccinated 2.81%) vs 10.5 per 1,000 (unvaccinated 1.05%). By vaccination-visit count: 15 per 1,000 (1 visit), 24 per 1,000 (≥5 visits), 40 per 1,000 (11+ visits) vs 9 per 1,000 (unvaccinated)
Gallagher, [illegible] 2008[illegible]202	1,824 children (NHANES 1999–2000)	Cross-sectional analysis	Yes (children with vs without HepB triple-series)	ASD not assessed; NDD proxied by EIS status	Parental report of HepB doses (NHANES immunization data)	NHIS 1999–2000 analysis of U.S. boys: adjusted odds of receiving Early Intervention Services ≈9× higher in vaccinated vs unvaccinated	EIS (boys): OR = 8.63 (2.08–35.8); White boys: OR = 9.24 (2.08–41.0)
Gallagher CM, Goodman MS, 2010[263]	79,883	Cross-sectional analysis of national survey data	Yes (neonatal HepB vs later/never)	Parent report of clinician diagnosis of autism via NHIS condition checklist	Vaccination timing determined from the record	Boys vaccinated as neonates had ~3-fold higher adjusted odds of autism diagnosis vs boys vaccinated later/never (adjusted OR 3.00; 95% CI 1.11–8.13).	4.32 per 1,000 boys and 2.42 per 1000 children
Lamerato L, Chatfield A, Tang A, Zervos M. 2025[297]	18,468 children total (16,511 with ≥1 vaccine; 1,957 unvaccinated)	Retrospective birth cohort	Yes	Diagnosis codes from healthcare encounters (ICD-9-CM/ICD-10-CM); NDDs (incl. autism) evaluated from age ≥2	HFHS/HAP electronic medical/claims data supplemented by Michigan State Immunization Registry; providers required to report vaccines to the state registry within 72 hours	Vaccination exposure associated with higher risk of any chronic health condition (adjusted HR 2.54, 95% CI 2.16–2.97); significantly higher risk for neurodevelopmental disorders (adjusted HR 5.53, 95% CI 2.91–10.51).	Vaccinated: 0.0011 per 1,000, unvaccinated: 0.0009 per 1,000.

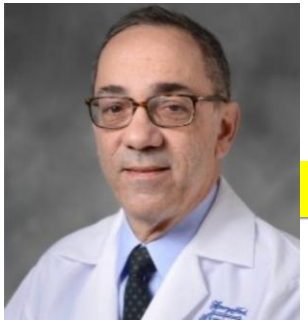
Table 4. Comparative Studies of Vaccinated Versus Unvaccinated Populations Evaluating ASD, Neurodevelopmental and Health Outcomes

... e tutti mostrano lo stesso andamento: i bambini vaccinati sono significativamente più malati rispetto ai diversi esiti esaminati. Ma sono soprattutto *sondaggi*, solo 3 sono studi di *coorte*, quasi tutti con autori critici verso le vaccinazioni. Lo *studio di Zervos* cambia tutto.

Inside the Henry Ford vaccine controversy

Del Bigtree – (Film)An Inconvenient Study (2025)

Diversi precedenti studi di confronto "vaccinati vs. non vaccinati« erano stati respinti non per la debolezza dei dati, ma perché non graditi, sostenendo che non provenivano da istituzioni di alto livello o non apparivano sulle maggiori riviste mediche.



Ciò ha spinto Bigtree a rivolgersi al Dott. Marcus Zervos per questo studio. Il Dott. Zervos era uno dei maggiori infettivologi USA, Direttore di ricerca per trial clinici e Direttore malattie infettive dell'Henry Ford Health, centro medico stimato, con uno dei più grandi database di pazienti USA.

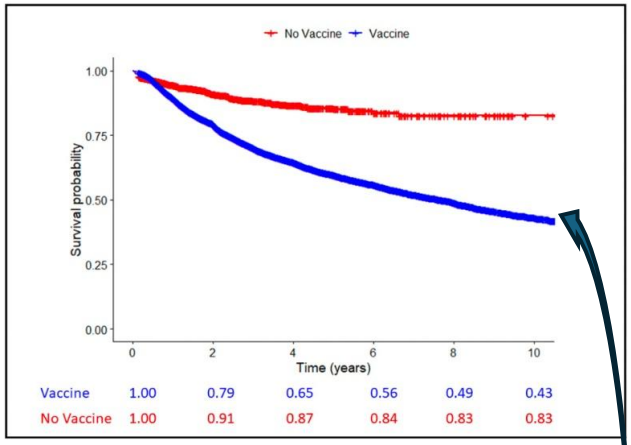
Bigtree disse a Zervos che questa era l'opportunità per dimostrare che i no-vax si sbagliavano, e ciò lo convinse ad accettare lo studio, che fu completato nel 2020. Come previsto da Bigtree, i risultati furono devastanti per i vaccinati, ma c'era un problema: il Dott. Zervos scelse di non pubblicarlo.

Nel 2022, Bigtree convinse il Dott. Zervos a spiegare il perché. Consapevole dell'importanza del momento, registrò la conversazione con una telecamera nascosta.

Il Dott. Zervos ammise su nastro il perché, senza mezzi termini: "Se pubblicassi una cosa del genere, tanto vale che mi ritiri. Sarebbe la mia fine".

Ecco cosa ha rivelato lo studio. I bambini vaccinati avevano:

- una probabilità 4,3 volte maggiore di soffrire di asma
- 3 volte maggiore di malattie atopiche (come l'eczema)
- quasi 6 volte maggiore di malattie autoimmuni, (che comprendono oltre 80 malattie diverse)
- 5,5 volte più disturbi dello sviluppo neurologico
- 2,9 volte più disabilità motorie
- 4,5 volte più disturbi del linguaggio
- 3 volte più ritardi nello sviluppo
- 6 volte più infezioni acute/croniche dell'orecchio.



Kaplan-Meyer: 10 y. chronic-free

- In circa 2.000 bambini non vaccinati, non si sono verificati casi di ADHD, diabete, problemi comportamentali, difficoltà di apprendimento, disabilità intellettive, tic o altri disturbi psicologici.

La **conclusione** dello studio: «Contrariamente alle nostre aspettative, abbiamo scoperto che l'esposizione alla vaccinazione era associata in modo indipendente a un **aumento complessivo di 2,5 volte della probabilità di una condizione di salute cronica** rispetto ai bambini non esposti alla vaccinazione».

Non vaccinati nei 10 anni **17%** di probabilità di malattia cronica, vaccinati **57%**

Tentativi falliti di screditare studio di Zervos

Solo ampio RCT pragmatico potrà chiudere il discorso

Scott ha detto che:

- *i vaccinati sono in partenza più malati*. Dall'epidemiologia, non sembra vero, e comunque i tassi di cancro (controllo negativo) erano paragonabili.

- *il disegno di studio era sbagliato*. Ma aveva seguito le linee guida CDC, e approvato dall'Henry Ford Inst., finanziatore. Perché poi Scott non ha detto come si sarebbe dovuto fare, secondo lui?

- *le coorti erano differenti*. Ma Zervos ha correttamente aggiustato per sesso, razza; peso, distress respiratorio e traumi alla nascita, prematurità.

- *Il tempo medio di misurazione dell'esordio di malattia era più corto nei non vaccinati*. Vero, media 1,3 anni vs 2,7. Ma le analisi di sensibilità hanno mostrato risultati coerenti per i seguiti almeno 1 anno, 3 anni, 5 anni, anzi sempre più alti!

- *Il 75% è stato seguito solo fino a 3 aa*. Ma CDC mostrano che molti più bambini hanno diagnosi di malattie croniche entro 2 anni, anziché da 3 a 8!

Quali sono secondo voi le quattro cose più gravi di questa storia?
(in ordine, a mio avviso, di crescente gravità)

1) Che Zervos e gli altri coautori, e l'Henry Ford Health abbiano **deciso tutti di tacere**, preferendo carriera, fondi di ricerca e tranquillità alla salute dei bambini

2) Che **i critici in Senato** (l'infettivologo Scott e l'epidemiologo Morris) **non abbiano** detto come avrebbero fatto *loro* lo studio, né **chiesto di ripeterlo subito**

3) Che l'**intera Comunità scientifica non l'abbia ancora preteso** (e non abbia chiesto di far partire studi clinici randomizzati che sciolgano finalmente ogni dubbio)

4) (*con auspicio che ciò non si verifichi…)* Se - quando renderemo pubblici questi dati - medici, scienziati, politici, ecc. italiani non pretenderanno che uno studio come questo sia al più presto replicato…
togliendo nel frattempo l'obbligo vaccinale!

In ogni caso **il messaggio che il mondo scientifico sta inviando è spaventoso**: «se i dati e le informazioni che ne derivano non sono allineati alla narrazione dominante, è lecito, accettabile, *normale* ignorare questi dati, o persino occultarli».

Dovete *fidarvi* della Scienza! Oppure no?!

***TTE: Trust the Evidence,* not «The Science» → Fida-tevi delle *Prove*, non de 'La Scienza'**

Tom Jefferson, MD
Oxford Group - Cochrane

Medscape Canada *Hoption Cann*, March 30, 2026 - **Ibuprofen and Empyema**

Study	Study design	Population (age range)	Condition	Findings: OR/RR (95% CI)
Byington et al (2002)	Case-control	Utah (< 19 years)	Community-acquired bacterial pneumonia	Empyema: Outpatient treatment with ibuprofen: OR, 7.8 (95% CI, 2.2-32.8) Preadmission ibuprofen: OR, 4.0 (95% CI, 2.5-6.5)
François et al (2010)	Case-control	France (28 days to 15 years)	Community-acquired pneumonia	Complicated pneumonia (empyema or lung abscess): Preadmission ibuprofen: OR, 2.6 (95% CI, 1.51-4.35)
Voiriot et al (2011)	Case-control	France (17-80 years)	Community-acquired pneumonia	Pleuropulmonary complications (empyema or lung cavitation): Preadmission NSAIDs: OR, 8.1 (95% CI, 2.3-28)

Messika et al (2014)	Case-control	France (adults)	Pneumococcal community-acquired pneumonia	Pleural effusion: Preadmission NSAIDs: OR, 8.8 (95% CI, 2.20-35.14)
Elemraid et al (2015)	Case-control	UK (≤ 16 years)	Community-acquired pneumonia	Empyema: Preadmission ibuprofen: OR, 1.94 (95% CI, 0.80-3.18)
Le Bourgeois et al (2016)	Case-control	France (3 months to 15 years)	Acute viral infections	Empyema[a]: NSAID use ≥ 3 days: OR, 2.67 (95% CI, 1.37-5.18) Acetaminophen use ≥ 3 days: OR, 2.57 (95% CI, 1.39-4.77)
Kotsiou et al (2016)	Cohort	Greece (adults)	Community-acquired pneumonia	Empyema: Preadmission NSAIDs: OR, 2.0; 95% CI, 0.65-6.11) Parapneumonic effusion: Preadmission NSAIDs: 1.17 *ns*

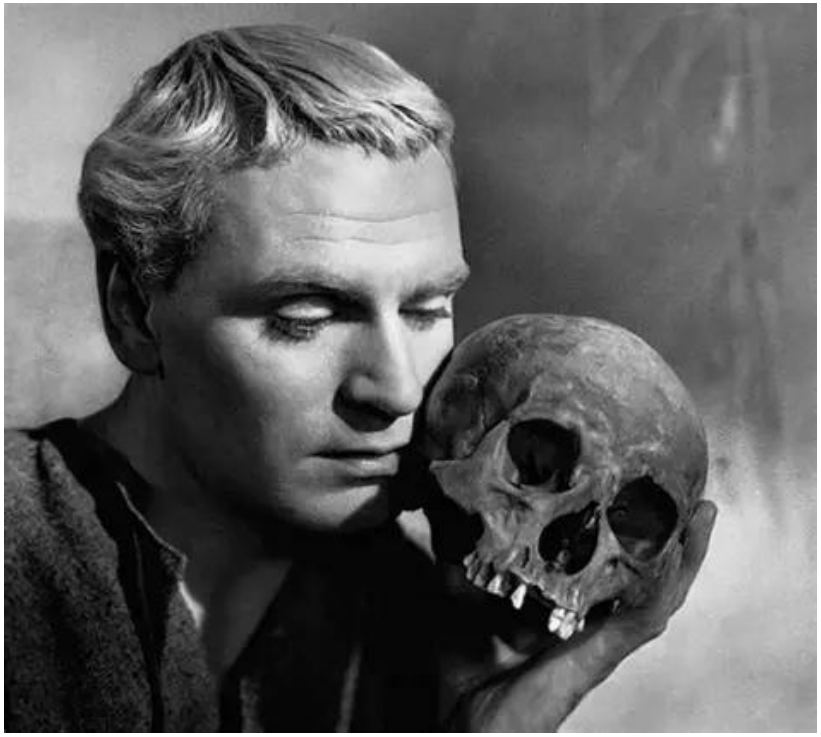
[a]Drug exposure that began within 72 hours of the onset of the acute viral infection

Study	Study design	Population (age range)	Condition	Findings: OR/RR (95% CI)
Basille et al (2017)	Cohort	France (all ages)	Community-acquired pneumonia	Pleuroparenchymal complications[b]: Preadmission NSAIDs: OR, 2.57 (95% CI, 1.02-6.64)
Krenke et al (2018)	Cohort	Poland (2 months to 17 years)	Community-acquired pneumonia	Complicated pneumonia[c]: Preadmission ibuprofen: OR, 3.27 (95% CI, 1.11-9.65) Preadmission acetaminophen: OR, 2.79 (95% CI,1.32-5.88)
Meganatha and Awasthi (2019)	Case-control	India (2-59 months)	Community acquired pneumonia	Parapneumonic effusion/empyema: Ibuprofen intake: OR, 6.8 (95% CI, 1.07-43.6)
Lund et al (2020)	Cohort	Denmark (≥ 40 years)	Bacterial pneumonia	Pleuropulmonary complications[d]: Recently started NSAID use: RR, 3.67 (95% CI, 1.95-6.91) Long-term NSAID use: RR, 1.87 (95% CI, 1.13-3.09)
Pokorska-Spiewak et al (2024)	Cohort	Poland (0-17 years)	Varicella complicated by bacterial superinfection	Complications after treatment[e]: Preadmission ibuprofen: OR, 4.07 (2.50-6.60) Necessary surgical intervention: Preadmission ibuprofen: OR, 2.87 (1.39-5.89)

«Non può essere, perché sappiamo molto bene dalla fisiopatologia…»

“Ci son più cose in cielo e in terra, Orazio, di quante ne sogni la tua filosofia”

(*William Shakespeare, Hamlet*)



I prodotti o principi attivi oggetto di questa presentazione, ampliano il ventaglio di cure disponibili per la COVID-19, anche a domicilio, **sempre di intesa con il curante** (che valuterà anche interazioni e fattori individuali…)


Dott. A. Donzelli

Sono stati scelti e inseriti con questi criteri di massima:

- prodotti o principi attivi di efficacia molto promettente, in base a studi randomizzati controllati (RCT) favorevoli e di discreta/sufficiente validità, integrati da studi osservazionali coerenti.

Anche dove le prove non siano definitive, curanti e assistiti informati li possono considerare nella misura in cui, insieme, siano anche:

- sicuri (primum non nocere!), allo stato conoscenze, a dosi e tempi testati in RCT
- biologicamente plausibili
- economici (con un costo-opportunità molto favorevole)
- accessibili (o che possano rapidamente diventarlo)
- senza megasponsor commerciali né ricercatori con grandi conflitti d'interessi

Ciò non esaurisce certo il numero di terapie efficaci contro la Covid-19 (incluse terapie approvate o in corso di approvazione), che tuttavia al momento non rispondono a una o più delle condizioni-filtro qui utilizzate.

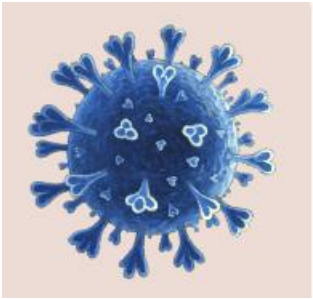
Criteri di massima di selezione di prodotti e principi attivi:

Sicurezza
(x stato conoscenze)
+
No megasponsor
commerciali né forti
COI primi ricercatori

Sufficienti
Prove d'efficacia
+
Plausibilità biologica

Economicità
+
Accessibilità
(potenziale)

COVID-19 involves the interplay of 500+ viral and host proteins and factors, providing many therapeutic targets. c19early analyzes **6,500+ studies for 216 treatments**—over 17 million hours of research. **Only three high-profit early treatments are approved in the US**. In reality, many treatments reduce risk, with 24 low-cost treatments approved across 163 countries.



Naso/oropharyngeal treatment

Direct treatment to the primary source of initial infection reduces progression and transmission. **2) efficaci**

Healthy lifestyles

Exercise, sunlight, a healthy diet, and good sleep all reduce risk.

1) protettivi

Immune support

Vitamins A, C, D, and zinc show reduced risk, as with other viruses.

Thermotherapy

Methods for increasing internal body temperature, comparable to natural fever, enhancing immune system function.

3) rispettare febbre

Systemic agents

Many systemic agents reduce risk, and may be required when infection progresses beyond the upper respiratory tract. **4) efficaci**

High-profit systemic agents

High-profit systemic agents are also effective, but have greater access and cost barriers.

[5) condizionati]

Monoclonal antibodies

Highly effective for matching variants but rarely used, with high cost, variant dependence, and IV/SC administration.

[6) costosi e utilità limitata ed effimera]

Acetaminophen

Acetaminophen increases the risk of severe outcomes and mortality.

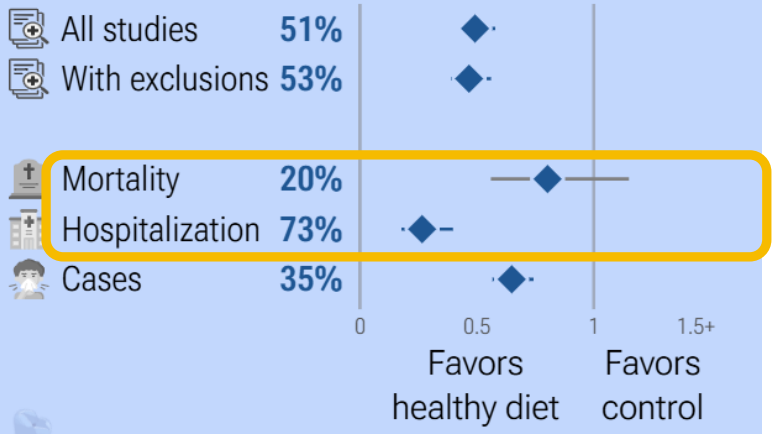
Remdesivir

Studies show increased mortality with longer followup.

Diet for COVID-19

30 studies with >600,000 patients

	Serious Outcome Risk
Control	
Healthy diet	



Significantly lower risk for **ICU**, **hospitalization**, **progression**, **recovery**, **cases**, and **viral clearance**.

73% lower **hospitalization** in **4** studies CI 60-82%

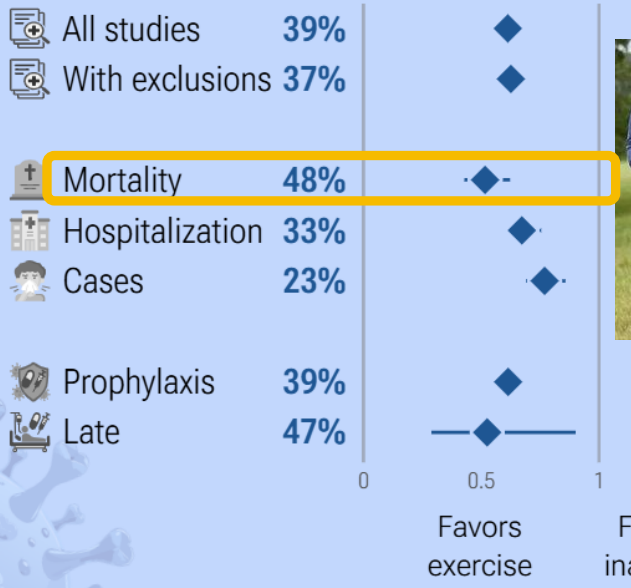
Studies analyze diet quality before infection.

COVID-19 DIET STUDIES. APR 2026. C19EARLY.ORG

Exercise for COVID-19

68 studies with >1,900,000 patients

	Serious Outcome Risk
Control	
Exercise	



Significantly lower risk for **mortality**, **ventilation**, **ICU**, **hospitalization**, **progression**, **recovery**, and **cases**.

48% lower **mortality** in **19** studies CI 38-57%

Most studies analyze exercise before infection.

COVID-19 EXERCISE STUDIES. APR 2026. C19EARLY.ORG

Sleep for COVID-19

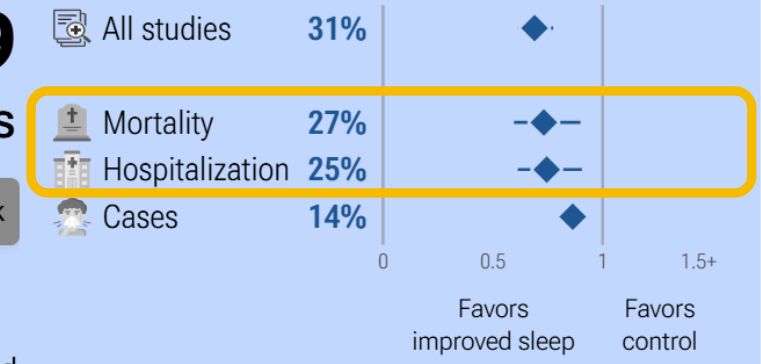
16 studies with >400,000 patients

	Serious Outcome Risk
Control	
Improved sleep	

Significantly lower risk for **mortality**, **hospitalization**, and **cases**.

13 studies from 13 independent teams in 6 countries show significant benefit.

COVID-19 SLEEP STUDIES. APR 2026. C19EARLY.ORG



Sunlight for COVID-19

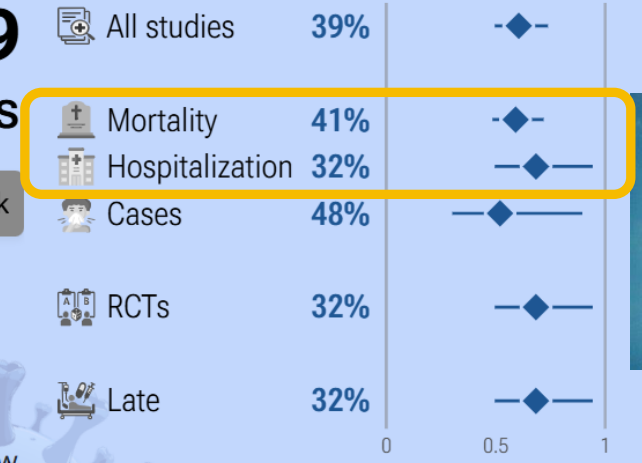
6 studies with >19,000 patients

	Serious Outcome Risk
Control	
Sunlight	

Significantly lower risk for **mortality**, **hospitalization**, **recovery**, and **cases**.

6 studies from 6 independent teams in 4 countries show significant benefit.

COVID-19 SUNLIGHT STUDIES. APR 2026. C19EARLY.ORG



Curcumin for COVID-19

28 studies with >15,000 patients

Control — Serious Outcome Risk

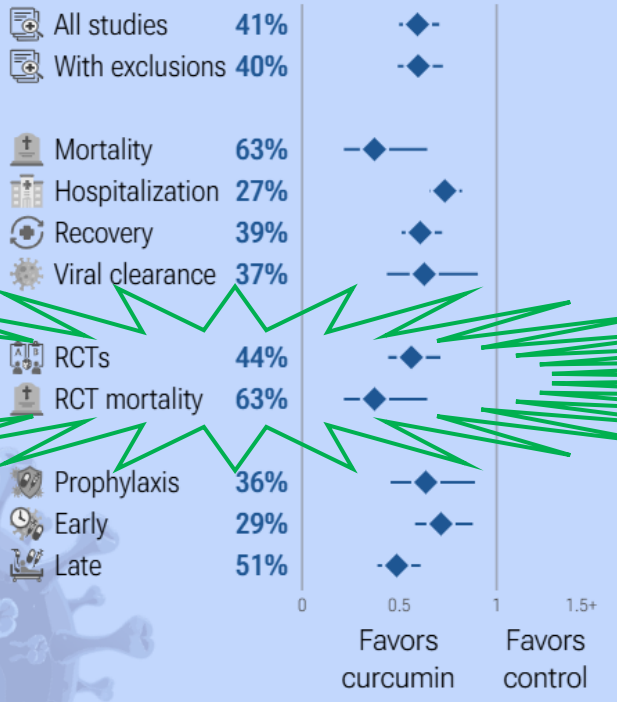
Curcumin

Significantly lower risk for **mortality**, **ventilation**, **hospitalization**, **progression**, **recovery**, and **viral clearance**.

44% lower risk in **21 RCTs** CI 29-56%

Studies typically use advanced formulations for greatly improved bioavailability.

COVID-19 CURCUMIN STUDIES. APR 2026. C19EARLY.ORG



Studies typically use advanced formulations for greatly improved bioavailability. *Recent: Ataya Grüneberg Marzouk.*

Curcumina è ~10% in peso di **curcuma**, ma poco assorbita.

(Integratori: rischi x calcoli e stasi biliare, se farmaci anticoagulanti, gravidanza, iperacidità gastrica...)

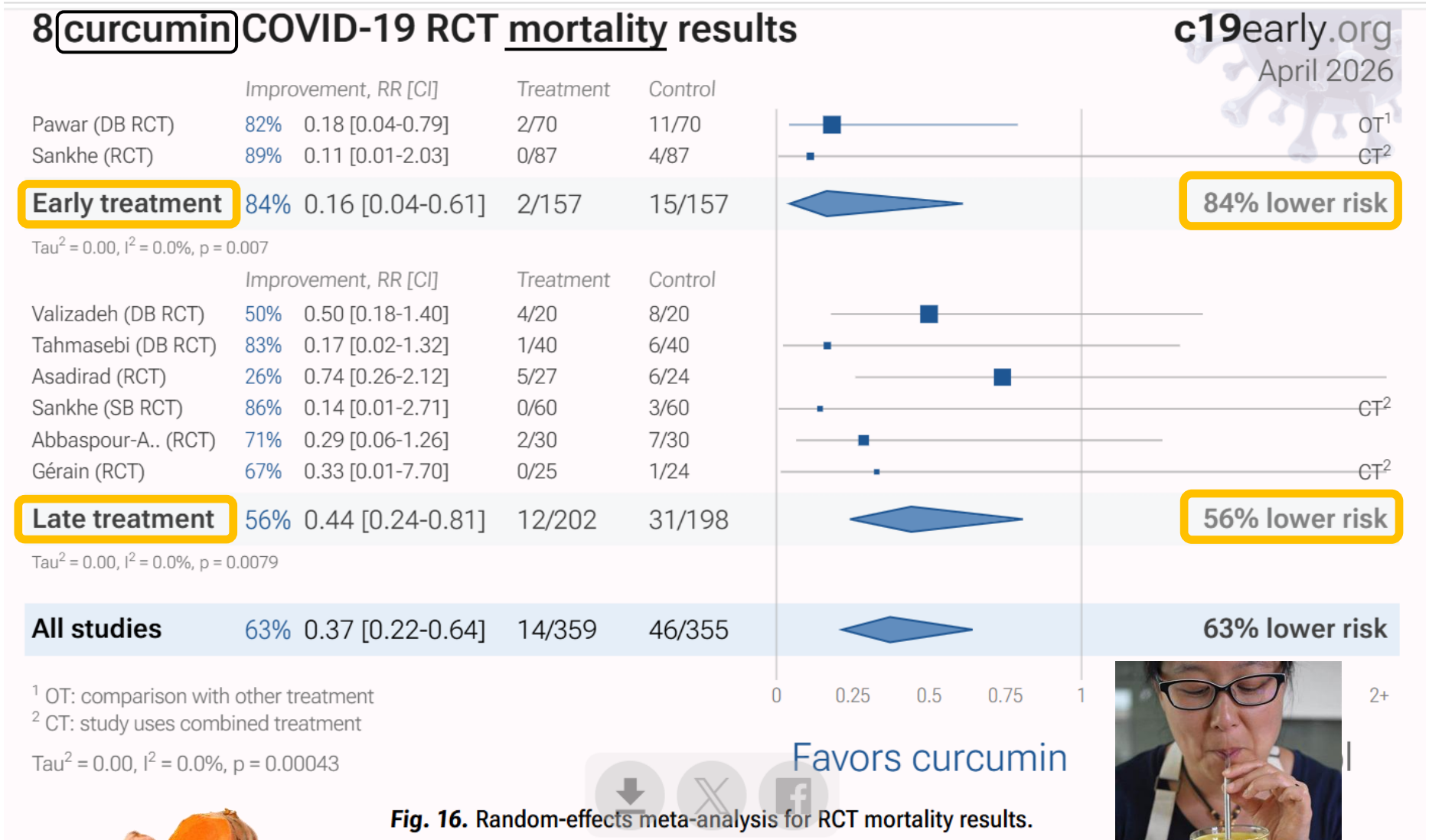


Fig. 16. **Random-effects meta-analysis for RCT mortality results.**

8 RCT riportano esito *mortalità, sempre a favore*

Beve *golden milk*

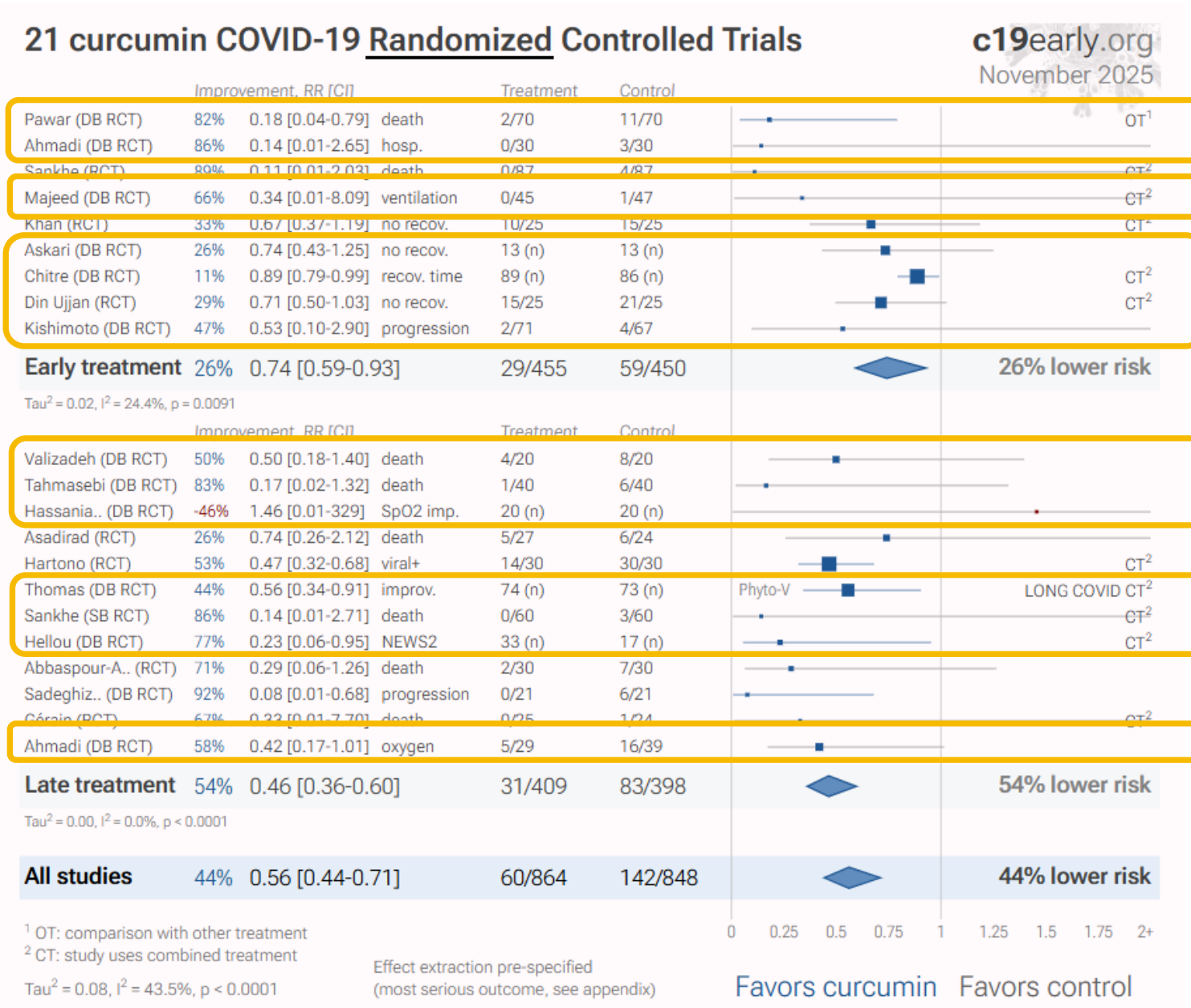


***Fig. 15.* Random effects meta-analysis for all Randomized Controlled Trials.** This plot shows pooled effects, see the specific outcome analyses for individual outcomes. Analysis validating pooled outcomes for COVID-19 can be found below. Effect extraction is pre-specified, using the most serious outcome reported. For details see the appendix.

tanti RCT doppio cieco, di alta validità

frontiers in Pharmacology

REVIEW
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Curcumin as a Potential Treatment for COVID-19

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Coronavirus disease 2019 (COVID-19) is an infectious disease that rapidly spread throughout the world leading to high mortality rates. Despite the knowledge of previous diseases caused by viruses of the same family, such as MERS and SARS-CoV, management and treatment of patients with COVID-19 is a challenge. One of the best strategies around the world to help combat the COVID-19 has been directed to drug repositioning; however, these drugs are not specific to this new virus. Additionally, the pathophysiology of COVID-19 is highly heterogeneous, and the way of SARS-CoV-2 modulates the different systems in the host remains unidentified, despite recent discoveries. This complex and multifactorial response requires a comprehensive therapeutic approach, enabling the integration and refinement of therapeutic responses of a given single compound that has several action potentials. In this context, natural compounds, such as Curcumin, have shown beneficial effects on the progression of inflammatory diseases due to its numerous action mechanisms: antiviral, anti-inflammatory, anticoagulant, antiplatelet, and cytoprotective. These and many other effects of curcumin make it a promising target in the adjuvant treatment of COVID-19. Hence, the purpose of this review is to specifically point out how curcumin could interfere at different times/points during the infection caused by SARS-CoV-2, providing a substantial contribution of curcumin as a new adjuvant therapy for the treatment of COVID-19.

Keywords: curcumin, COVID-19, SARS-CoV-2, new therapies, ACE2

OPEN ACCESS

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INTRODUCTION

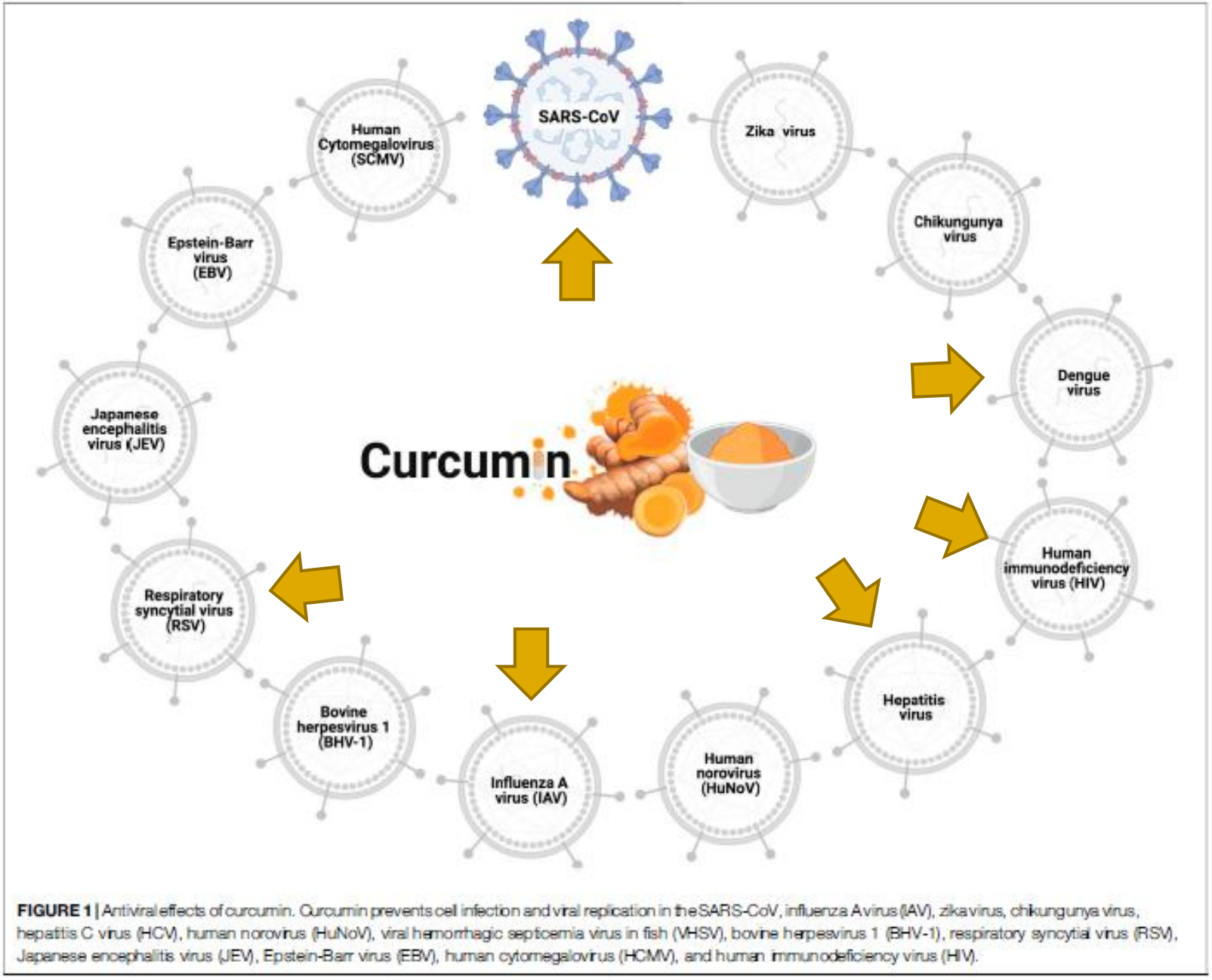


FIGURE 1 | Antiviral effects of curcumin. Curcumin prevents cell infection and viral replication in the SARS-CoV, influenza A virus (IAV), zika virus, chikungunya virus, hepatitis C virus (HCV), human norovirus (HuNoV), viral hemorrhagic septicemia virus in fish (VHSV), bovine herpesvirus 1 (BHV-1), respiratory syncytial virus (RSV), Japanese encephalitis virus (JEV), Epstein-Barr virus (EBV), human cytomegalovirus (HCMV), and human immunodeficiency virus (HIV).

Nigella Sativa for COVID-19

14 studies with >3,000 patients

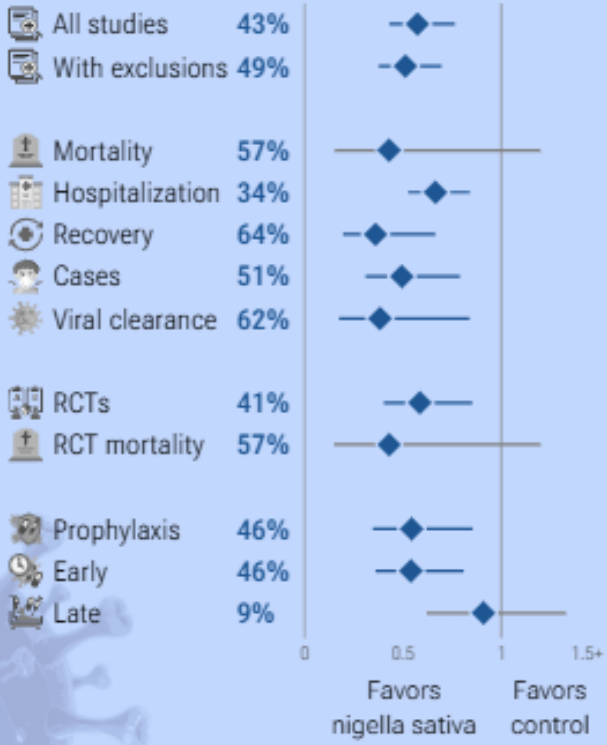
Control — Serious Outcome Risk

Nigella Sativa

Significantly lower risk for **ventilation**, **hospitalization**, **recovery**, **cases**, and **viral clearance**.

41% lower risk in **10 RCTs** CI 15-60%

COVID-19 NIGELLA SATIVA STUDIES. APR 2026. C19EARLY.ORG



(Integratori: cautela se farmaci anticoagulanti, antidiabetici; no in gravidanza; possibili problemi gastrointestinali...)

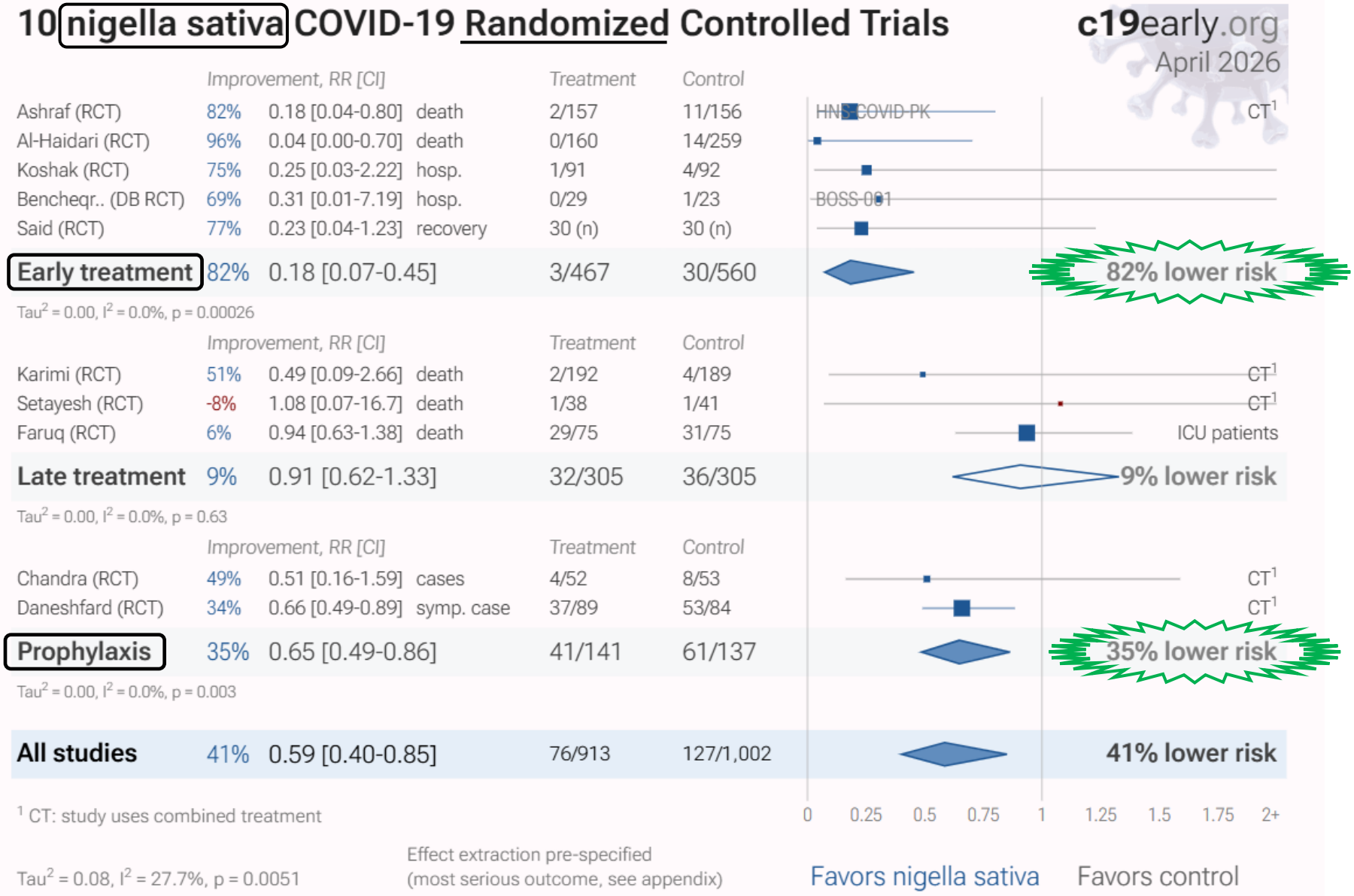


***Fig. 14.* Random-effects meta-analysis for all Randomized Controlled Trials.** This plot shows pooled effects, see the specific outcome analyses for individual outcomes. Analysis validating pooled outcomes for COVID-19 can be found below. Effect extraction is pre-specified, using the most serious outcome reported. For details see the appendix.

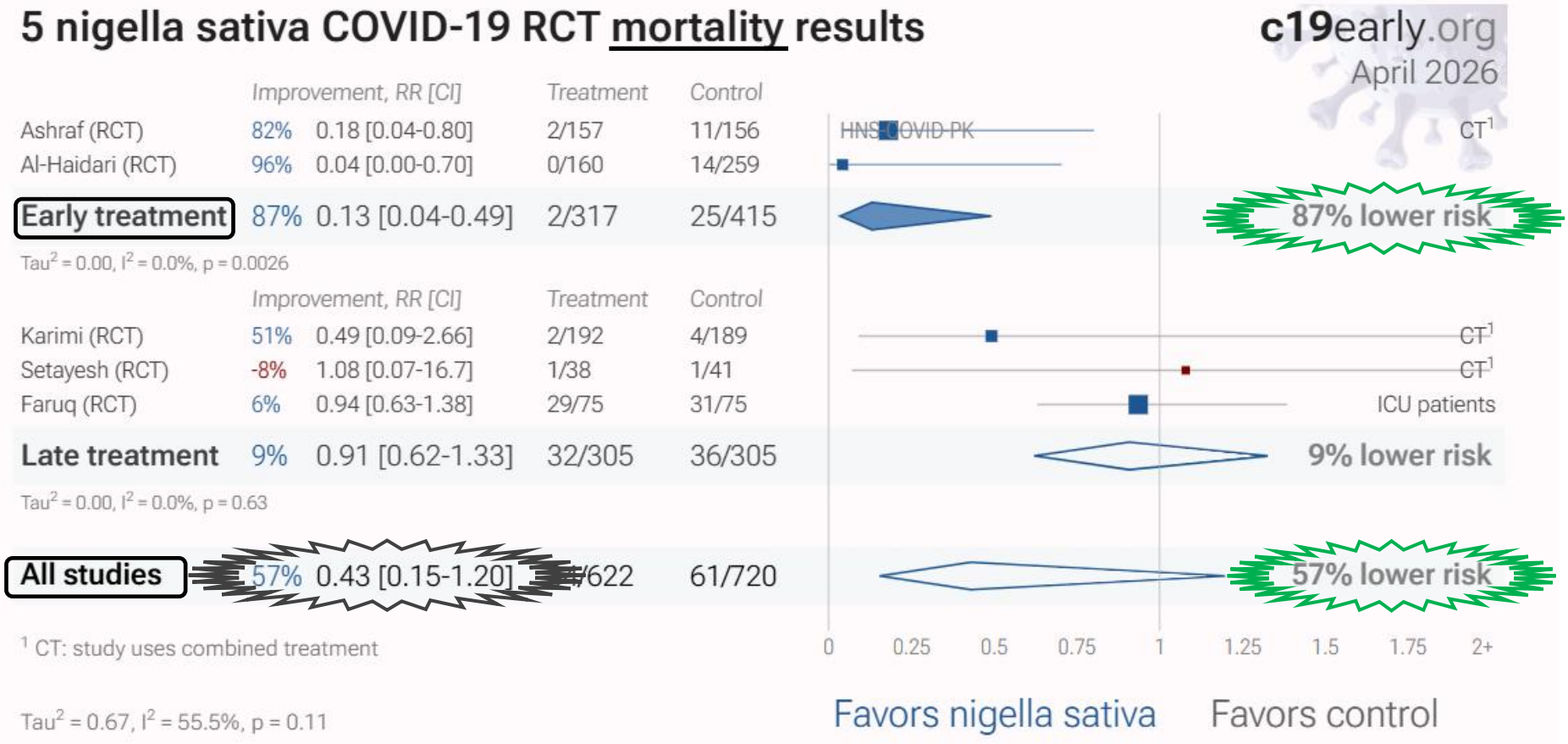
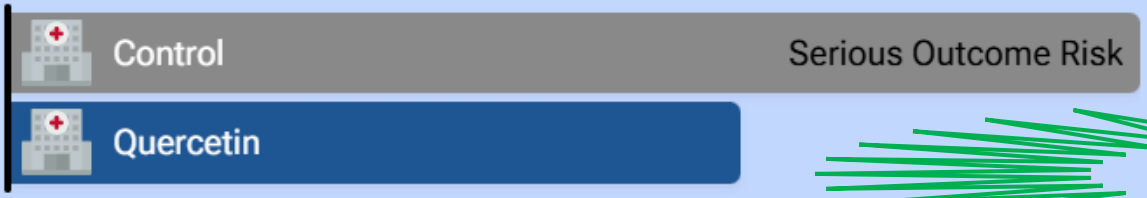


Fig. 15. **Random-effects meta-analysis for RCT mortality results.**

Quercetin for COVID-19

9 studies with >800 patients

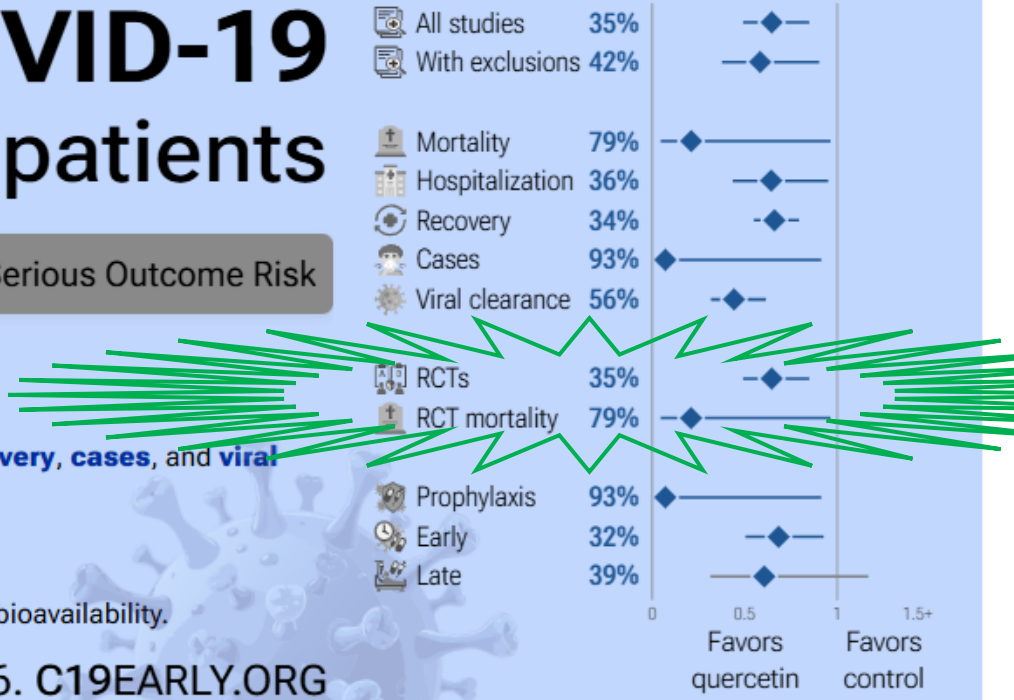


Significantly lower risk for **mortality**, **ICU**, **hospitalization**, **recovery**, **cases**, and **viral clearance**.

35% lower risk in **9 RCTs** CI 15-51%

Studies typically use advanced formulations for greatly improved bioavailability.

COVID-19 QUERCETIN STUDIES. APR 2026. C19EARLY.ORG



(Quercetin Phytosome®, QP)

(se Integratori, possibili disturbi gastrointestinali...)

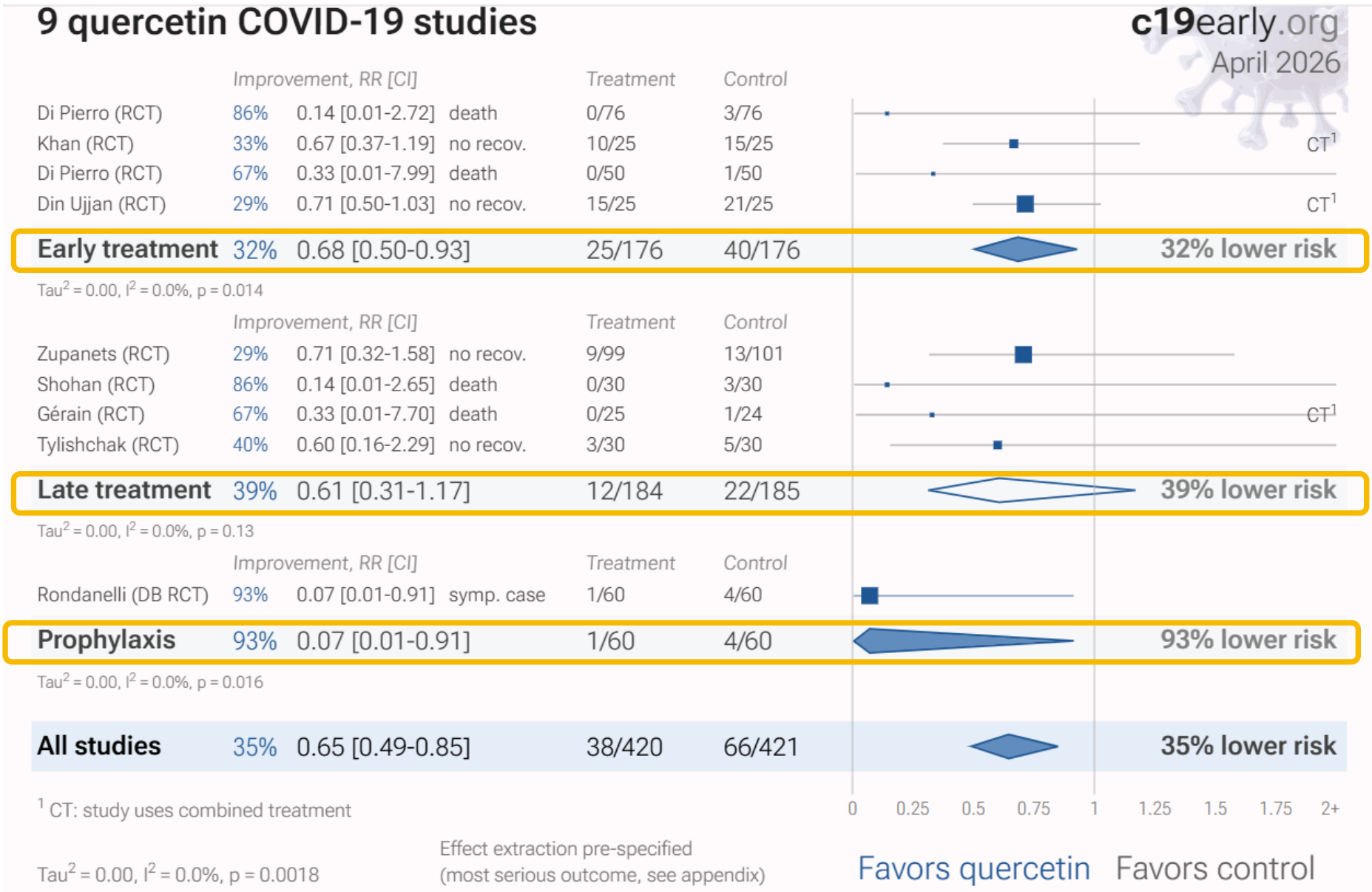


***Fig. 5.* Random-effects meta-analysis for all studies.** This plot shows pooled effects, see the specific outcome analyses for individual outcomes. Analysis validating pooled outcomes for COVID-19 can be found below. Effect extraction is pre-specified, using the most serious outcome reported. For details see the appendix.

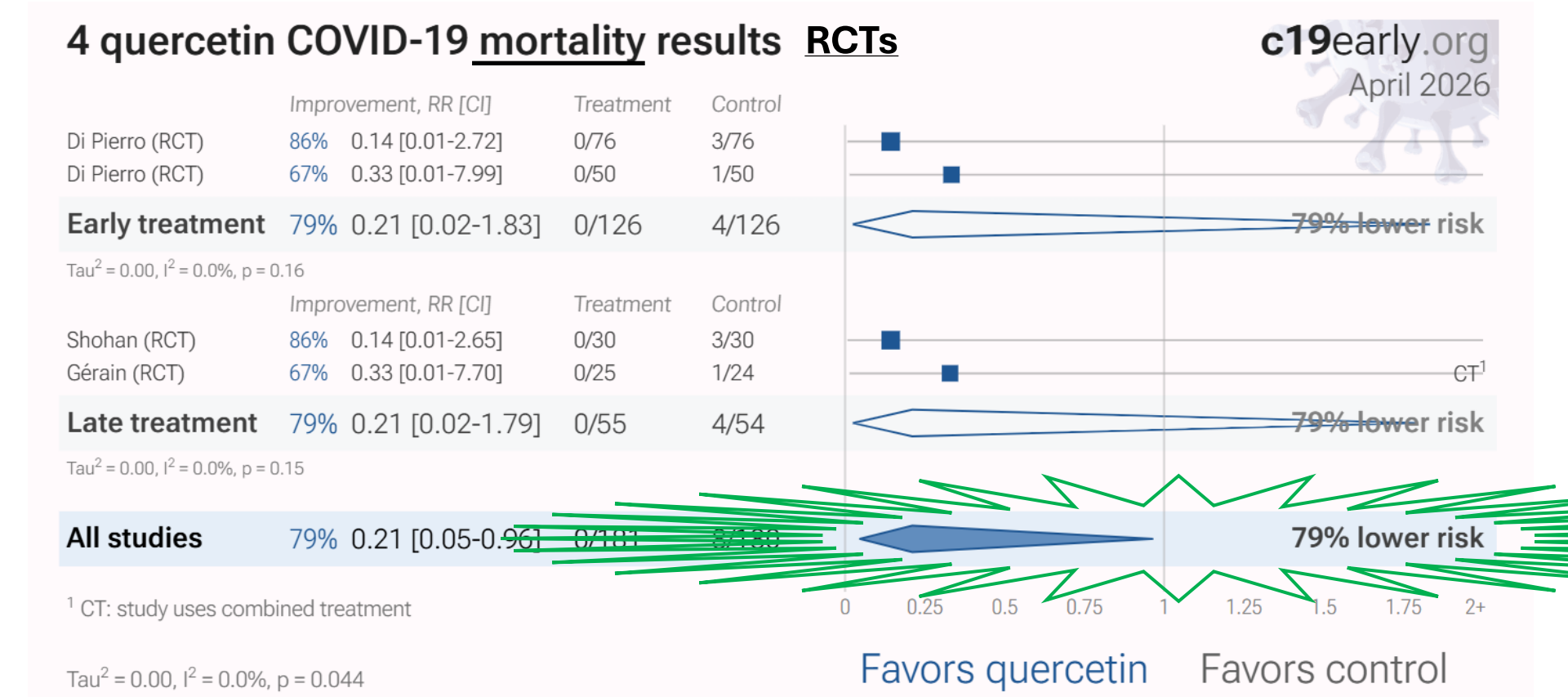


Fig. 6. Random-effects meta-analysis for mortality results.

(se Integratori, possibili disturbi gastrointestinali...)

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REVIEW Cheema HA, et al. Rev Med Virol. 2023 Mar;33(2):e2427.

WILEY

Quercetin for the treatment of COVID-19 patients: A systematic review and meta-analysis

Huzaifa Ahmad Cheema[1] | Aruba Sohail[2] | Areej Fatima[2] | Abia Shahid[1] | Muhammad Shahzil[1,3] | Mohammad Ebad Ur Rehman[4] | Rehmat Ullah Awan[5] | Sampath Chinnam[6,7] | Abdulqadir J. Nashwan[8]

5.4 with odds ratio (OR) as the effect measure. Quercetin decreased the risk of intensive care unit admission (OR = 0.31; 95% confidence interval (CI) 0.10–0.99) and the incidence of hospitalisation (OR = 0.25; 95% CI 0.10–0.62) but did not decrease the risk of all-cause mortality and the rate of no recovery. Quercetin may

Ma in tendenza sì: **0,39** (0,10-1,54)

e **0,55** (0,28-1,07)

Maggiori fonti alimentari di quercetina

(Quercetin Phytosome®, QP)

pesto di foglie di ravanelli

coriandolo fresco

10 melatonin COVID-19 mortality results

c19early.org
April 2026

	Improvement, RR [CI]	Treatment	Control	Dose (1d)
Sánchez-González	54% 0.46 [0.28-0.71]	24/224	53/224	varies
Mousavi (RCT)	67% 0.33 [0.04-3.09]	1/48	3/48	3mg
Hasan (RCT)	93% 0.07 [0.01-0.53]	1/82	13/76	10mg
Bologna	50% 0.50 [0.13-1.86]	3/40	6/40	2mg
Sánchez-Rico	19% 0.81 [0.61-1.08]			2mg
Karimpour-.. (ICU)	39% 0.61 [0.21-1.76]	5/12	13/19	15mg
Alizadeh (DB RCT)	4% 0.96 [0.80-1.16]	28/33	30/34	21mg
Ameri (RCT)	29% 0.71 [0.62-0.82]	73/109	110/117	10mg
Tian (ICU)	47% 0.53 [0.34-0.83]	301 (n)	301 (n)	
Sánchez-Gar.. (ICU)	42% 0.58 [0.32-0.94]	42/202	48/133	varies
Late treatment	33% 0.67 [0.56-0.81]	177/1,051	276/992	
All studies	33% 0.67 [0.56-0.81]	177/1,051	276/992	

ICU patients
Intubated patients
ICU patients
ICU - ramelteon
ICU patients

33% lower risk

$Tau^2 = 0.04$, $I^2 = 61.5\%$, $p < 0.0001$

33% lower risk

0 0.25 0.5 0.75 1 1.25 1.5 1.75 2+

$Tau^2 = 0.04$, $I^2 = 61.5\%$, $p < 0.0001$

Favors melatonin Favors control

Fig. 6. **Random-effects meta-analysis for mortality results.**

(cautela se antiaggreganti e anticoagulanti, gravidanza e anziani; no bambini; antidiabetici: alza glicemia...)

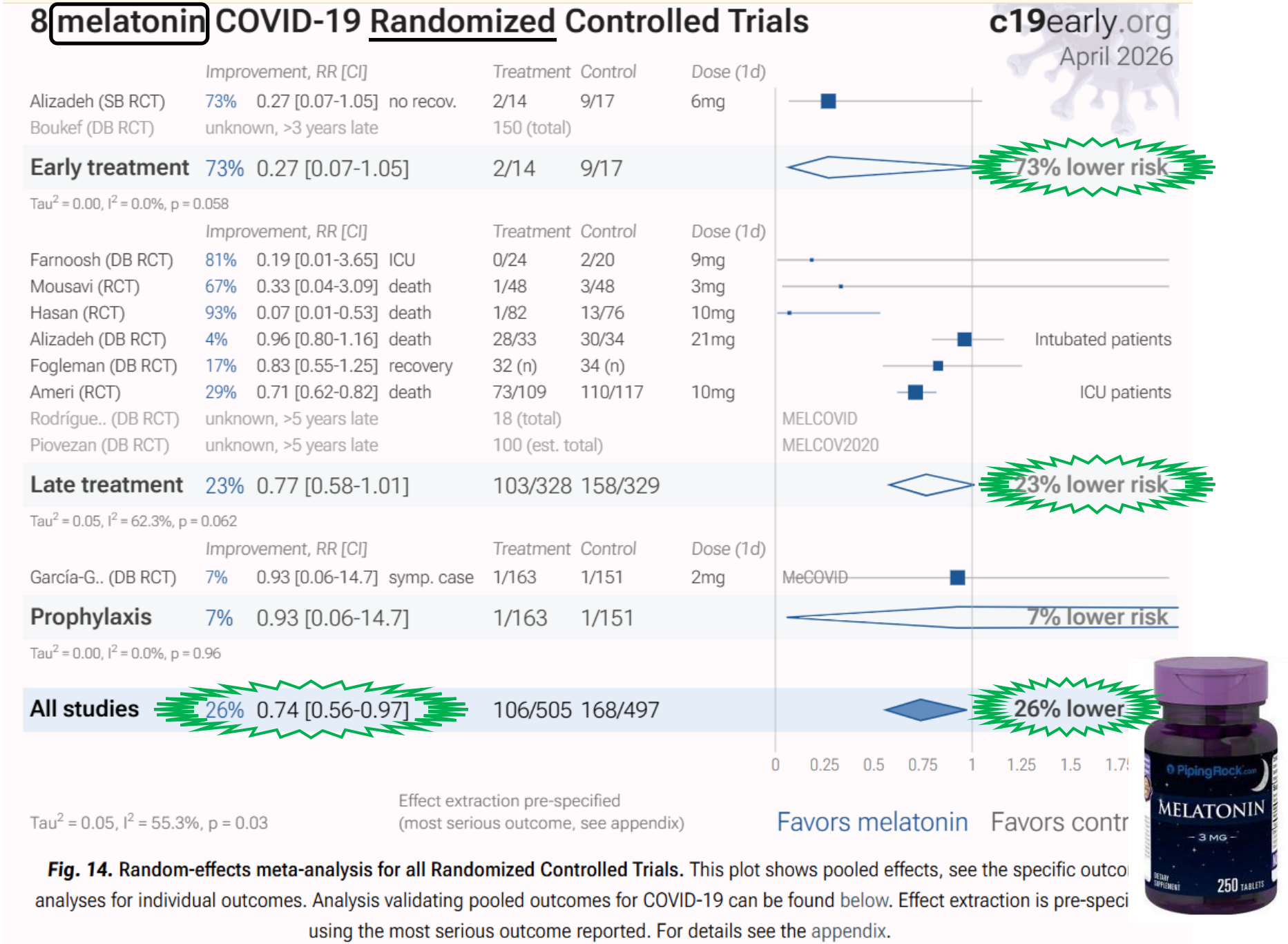


***Fig. 14.* Random-effects meta-analysis for all Randomized Controlled Trials.** This plot shows pooled effects, see the specific outco analyses for individual outcomes. Analysis validating pooled outcomes for COVID-19 can be found below. Effect extraction is pre-speci using the most serious outcome reported. For details see the appendix.

Contents lists available at ScienceDirect 2021-genn '22

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Perspective

The Effect of Melatonin on Thrombosis, Sepsis and Mortality Rate in COVID-19 Patients

Studio clinico randomizzato controllato, in aperto

Zainab Thanon Hasan [1,*], Dr. Mohammed Qasim Yahya Mal Allah Al Atrakji [2], Dr. Ahmed Kayes Mehuaiden [3]

Effect of melatonin on thrombosis in COVID-19 patients. ricoverati, gravi

	All patients (n=158)	Melatonin group (n=82)	Control group (n=76)	df	P-value
Day 5	1 (0.6%)	1 (1.2%)	0 (0.0%)	1	1.000
Day11	6 (3.8%)	3 (3.7%)	3 (3.9%)	1	1.000
Day17	27 (17.1%)	9 (11.0%)	18 (23.7%)		0.037*

n, number of patients; df, degree of freedom

Effect of melatonin on mortality in COVID-19 patients.

	All patients (n=158)	Melatonin group (n=82)	Control group (n=76)	df	P-value
Death	14 (8.9%)	1 (1.2%)	13 (17.1%)	1	0.000*

EClinicalMedicine 40 (2021) 101125

Contents lists available at ScienceDirect

EClinicalMedicine

journal homepage: https://www.journals.elsevier.com/eclinicalmedicine

Research paper

Effects of adding L-arginine orally to standard therapy in patients with COVID-19: A randomized, double-blind, placebo-controlled, parallel-group trial. Results of the first interim analysis

Giuseppe Fiorentino[a,1], Antonietta Coppola[a,1], Raffaele Izzo[b], Anna Annunziata[a], Mariano Bernardo[a], Angela Lombardi[c,d], Valentina Trimarco[e], Gaetano Santulli[b,c,f,g,*], Bruno Trimarco[b,g]

[a] COVID-19 Division, A.O.R.N. Ospedali dei Colli, Naples, Italy ....

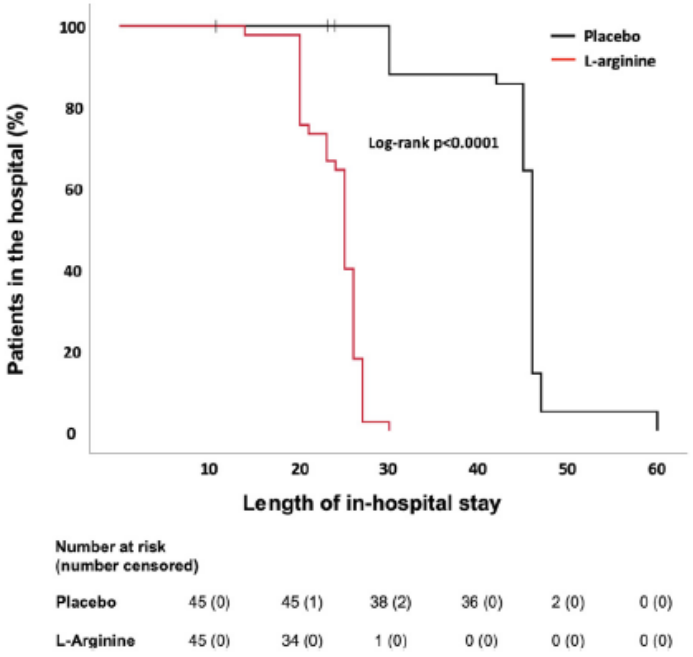
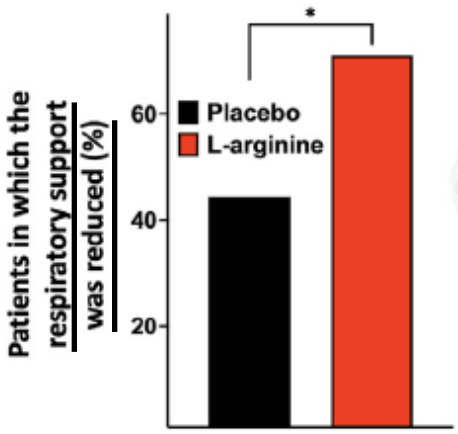


Fig. 3. Kaplan-Meier curves assessing in the per-protocol analysis the length of in-hospital stay.



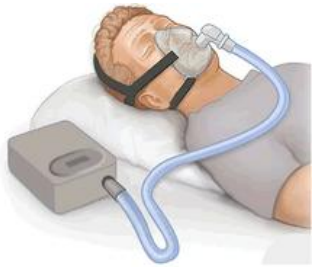


Fig. 2. Respiratory support at baseline and at day 10 (A) and percentage of patients in which the respiratory support was reduced, evaluated 10 days after randomization (B) in the per-protocol analysis; *: $p < 0.01$.

CPAP: continuous positive airway pressure; HFNC: high-flow nasal cannula; LTOT: long-term oxygen therapy; NIV: non-invasive ventilation.

Pharmacological Research 183 (2022) 106360

Contents lists available at ScienceDirect

Pharmacological Research

journal homepage: www.elsevier.com/locate/yphrs

870 pz trattati con L-Arginina + Vit. C, verso 520 del gruppo di controllo con multivitaminico

Combining L-Arginine with vitamin C improves long-COVID symptoms: The LINCOLN Survey

Raffaele Izzo [a,1], Valentina Trimarco [b,1], Pasquale Mone [c], Teresita Aloè [d], …

Table 2
Survey results in the two groups of patients.

		Alternative Treatment (N=521)	L-Arginine + Vitamin C (N=8	p
Asthenia	Absent (%)	0.4	94.9	<0.0001
	Mild (%)	5.2	4.0	
	Severe (%)	94.4	1.1	
Dyspnea	Absent (%)	5.4	74.2	<0.0001
	Mild (%)	55.1	25.4	
	Severe (%)	39.5	0.4	
Chest tightness	Absent (%)	26.3	86.1	<0.0001
	Mild (%)	50.9	13.4	
	Severe (%)	22.8	0.5	
Dizziness	Absent (%)	66.6	87.3	<0.0001
	Mild (%)	25.9	11.6	
	Severe (%)	7.5	1.1	
Gastrointestinal disorders	Absent (%)	63.3	87.7	<0.0001
	Mild (%)	26.7	11.7	
	Severe (%)	10.0	0.6	
Headache	Absent (%)	39.2	81.8	<0.0001
	Mild (%)	44.1	16.8	
	Severe (%)	16.7	1.4	
Anosmia	Absent (%)	52.0	87.2	<0.0001
	Mild (%)	34.0	11.0	
	Severe (%)	14.0	1.8	
Concentration difficulty	Absent (%)	32.8	79.1	<0.0001
	Mild (%)	46.8	19.4	
	Severe (%)	20.4	1.5	
Sleeplessness	Absent (%)	39.5	80.7	<0.0001
	Mild (%)	42.6	17.5	
	Severe (%)	17.9	1.8	

nutrients

MDPI

2022, 14, 4984. https://doi.org/10.3390/nu14234984

Article

Effects of L-Arginine Plus Vitamin C Supplementation on Physical Performance, Endothelial Function, and Persistent Fatigue in Adults with Long COVID: A Single-Blind Randomized Controlled Trial

Matteo Tosato [1], Riccardo Calvani [1,*], Anna Picca [1,2], Francesca Ciciarello [1], Vincenzo Galluzzo [1], Hélio José Coelho-Júnior [1,3], Angela Di Giorgio [1], Clara Di Mario [4], Jacopo Gervasoni [1], Elisa Gremese [1,3,4], Paolo Maria Leone [1], Antonio Nesci [1], Anna Maria Paglionico [1], Angelo Santoliquido [1,5], Luca Santoro [1], Lavinia Santucci [6], Barbara Tolusso [4], Andrea Urbani [1,7], Federico Marini [8], Emanuele Marzetti [1,3] and Francesco Landi [1,3] on behalf of the Gemelli against COVID-19 Post-Acute Care Team

[1] Fondazione Policlinico Universitario A. Gemelli IRCCS, 00168 Rome, Italy

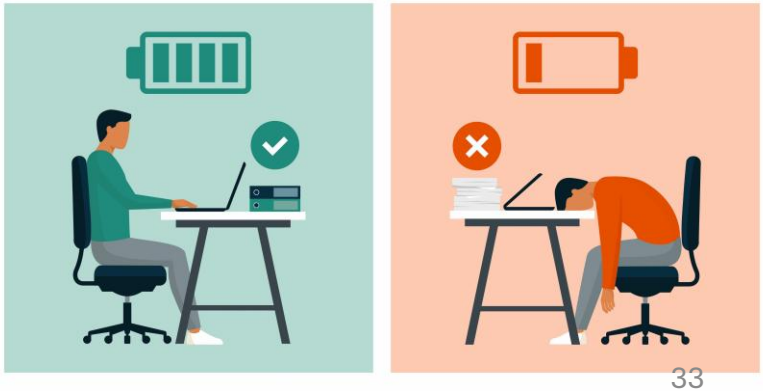
- 23 partecipanti L-Arginina 1,66 g + Vit. C 500 mg 2 volte al dì x 28 gg
- 23 partecipanti multivitaminico 2 volte al dì x 28 gg (età media 51 aa.)

Al termine: migliorata distanza camminata in 6', forza stretta di mano, funzione endoteliale ed estremo affaticamento (fatigue)

In particolare, la fatigue è stata riportata da:

- 2 partecipanti nel gruppo L-Arginina (8,7%)
- 21 nel gruppo placebo (80,1%);

differenza altamente significativa $p < 0.0001$).



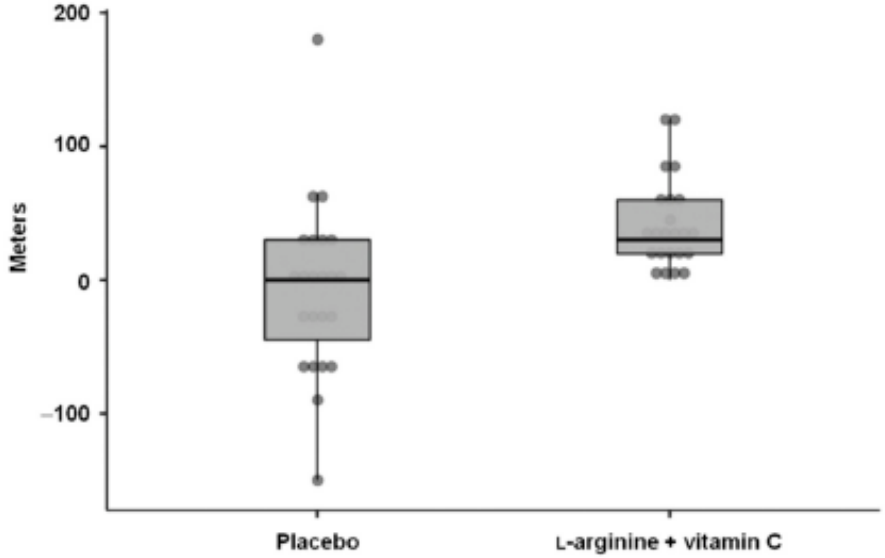
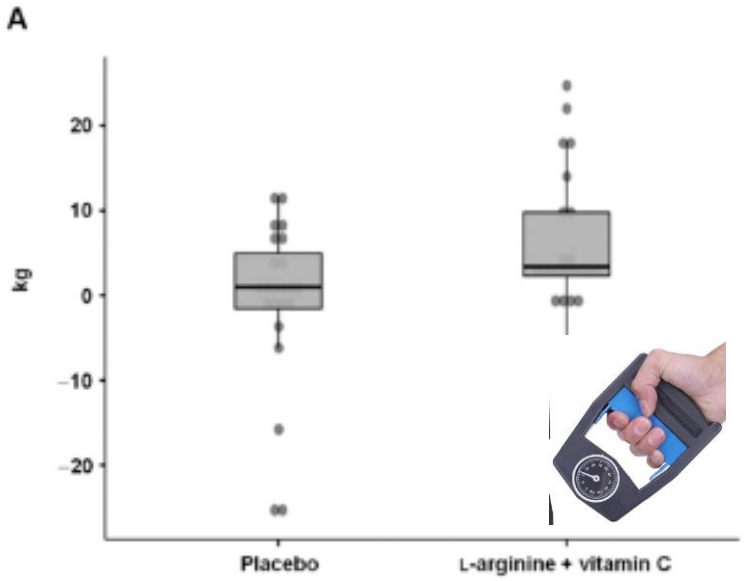


Figure 3. Changes from baseline to day 28 in the 6 min walk test distance in the two intervention groups.



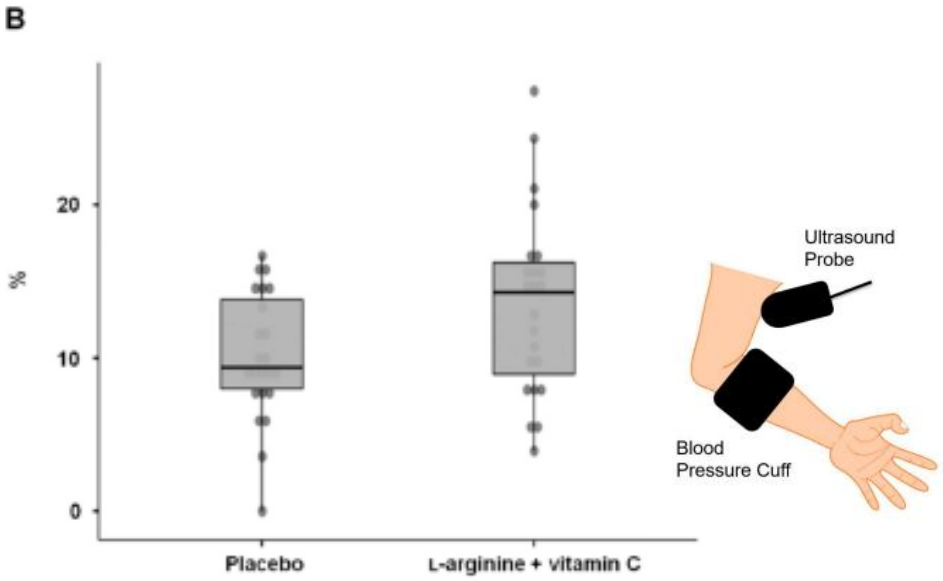


Figure 4. Changes from baseline to day 28 in (A) handgrip strength and (B) flow-mediated dilation in the two intervention groups.

~1,6 g di arginina si trovano anche in:

~25 g

~45 g

~70 g

~70-80 g

Sono fonti buone e salutari di arginina anche **legumi** e **semi**

Sono fonti buone e salutari di Vit. C anche **frutta** e **verdura** fresche. mg Vit. C/100 g →

→

Viral clearance as a surrogate of clinical efficacy for COVID-19 therapies in outpatients: a systematic review and meta-analysis

https://doi.org/10.1016/S2666-5247(23)00398-1

Karen M Elias, Shanchita R Khan, Eva Stadler, Timothy E Schlub, Deborah Cromer, Mark N Polizzotto, Stephen J Kent, Tari Turner, Miles P Davenport, David S Khoury

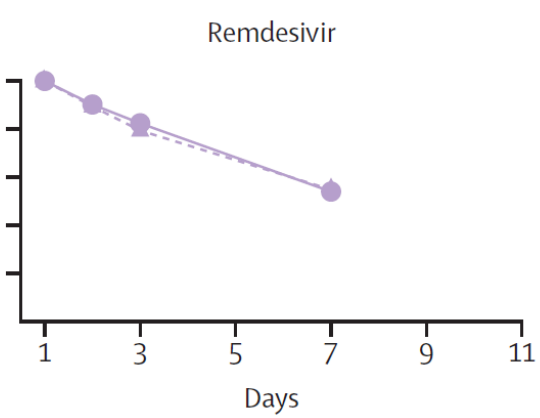
Summary

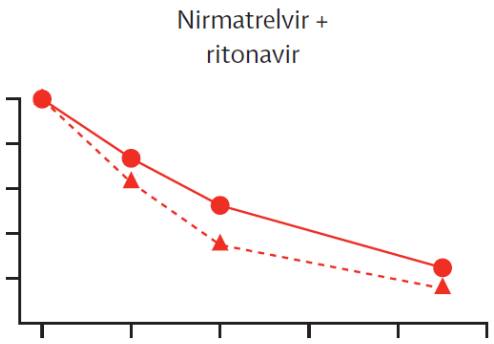
Background Surrogates of antiviral efficacy are needed for COVID-19. We aimed to investigate the relationship between the virological effect of treatment and clinical efficacy as measured by progression to severe disease in outpatients treated for mild-to-moderate COVID-19.

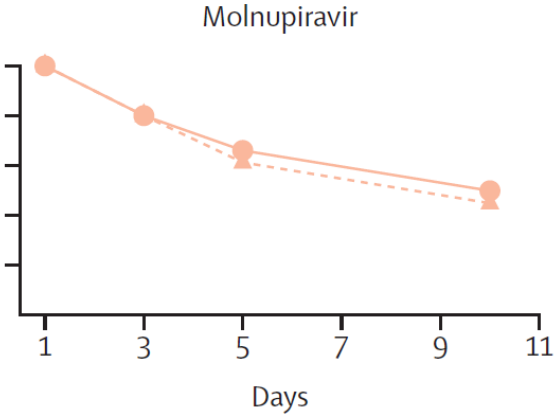
Lancet Microbe 2024
Published Online
https://doi.org/10.1016/S2666-5247(23)00398-1

Agent

- Adintrevimab
- Bamlanivimab
- Bamlanivimab + etesevimab
- Bebtelovimab
- Bebtelovimab + bamlanivimab + etesevimab
- BGB-DXP593
- Convalescent plasma
- Hydroxychloroquine
- Molnupiravir
- Nitazoxanide
- Nirmatrelvir + ritonavir
- Regdanvimab
- Casirivimab + imdevimab
- Remdesivir
- Sotrovimab
- Tixagevimab + cilgavimab







Viral clearance as a surrogate of clinical efficacy for COVID-19 therapies in outpatients: a systematic review and meta-analysis

https://doi.org/10.1016/S2666-5247(23)00398-1 Lancet Microbe 2024

Questa revisione sistematica (*Elias, Lancet 2024*) comprende 22 ricerche per studiare la relazione tra l'effetto virologico di un trattamento e la sua **efficacia clinica, misurata dalla progressione verso la malattia grave** in pazienti con COVID-19 da lieve a moderato.
La conclusione è che

> l'accelerazione dell'eliminazione virale entro i primi 5 giorni dopo il trattamento è un potenziale surrogato dell'efficacia clinica per prevenire il ricovero ospedaliero da COVID-19 e **potenzialmente altri virus del tratto respiratorio superiore**

Il trattamento comprende 14 **anticorpi monoclonali** (efficacia complessiva **63%**), plasma convalescente e alcune **piccole molecole antivirali** (efficacia complessiva **60%**).

I risultati sono importanti ma, con l'eccezione dell'**idrossiclorochina** e la parziale eccezione del **plasma convalescente** (**efficacia bassa**), i trattamenti antivirali o con Ac monoclonali sono costosi e non adatti a un uso estensivo.

Es.: Tixagevimab + Cilgavimab (*Evusheld*, Astra Zeneca, prezzo listino € 2359)

iodopovidone

PVP-I for COVID-19

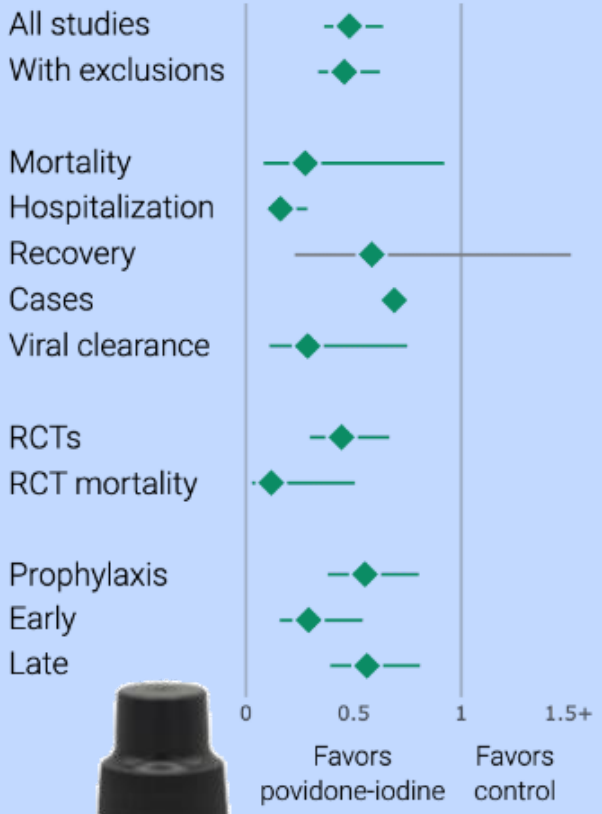
12 studies from 125 scientists
2,549 patients in 8 countries

Statistically significant improvement for **mortality**, **hospitalization**, **cases**, and **viral clearance**.

6 studies from 4 countries show statistically significant improvements.

56% improvement in **10 RCTs** CI [33-70%]
72% lower **mortality** in **2** studies CI [8-92%]

COVID-19 PVP-I STUDIES. JAN 5 2022. C19PVPI.COM



21 povidone-iodine COVID-19 studies

c19early.org
April 2025

	Improvement, RR [CI]			Treatment	Control
Mohamed (RCT)	86%	0.14 [0.01-2.21]	viral+	0/5	3/5
Choudhury (RCT)	88%	0.12 [0.03-0.50]	death	2/303	17/303
Guenezan (RCT)	63%	0.37 [0.06-1.63]	viral load	12 (n)	12 (n)
Elzein (DB RCT)	89%	0.11 [0.01-1.00]	viral load	25 (n)	9 (n)
Arefin (RCT)	79%	0.21 [0.08-0.54]	viral+	4/27	19/27
Pablo-Marcos	29%	0.71 [0.32-1.56]	viral load	31 (n)	40 (n)
Sulistyani (SB RCT)	6%	0.94 [0.45-1.96]	viral load	15 (n)	15 (n)
Elsersy (DB RCT)	91%	0.09 [0.01-1.62]	hosp.	0/100	5/100
Sevinç Gül (RCT)	99%	0.01 [0.00-439]	viral load	21 (n)	20 (n)
Natto (RCT)	74%	0.26 [0.03-2.76]	viral load	12 (n)	12 (n)
Sirijatuphat	33%	0.67 [0.17-2.67]	viral load	12 (n)	12 (n)
Karaaltin (RCT)	83%	0.17 [0.05-0.62]	viral load	30 (n)	30 (n)
Matsuyama (RCT)	69%	0.31 [0.10-0.93]	viral+	4/139	13/140
Friedland (DB RCT)	60%	0.40 [0.18-0.93]	viral load	10 (n)	13 (n)
Early treatment	64%	0.36 [0.24-0.54]		10/742	57/738

$Tau^2 = 0.14$, $I^2 = 26.1\%$, $p < 0.0001$

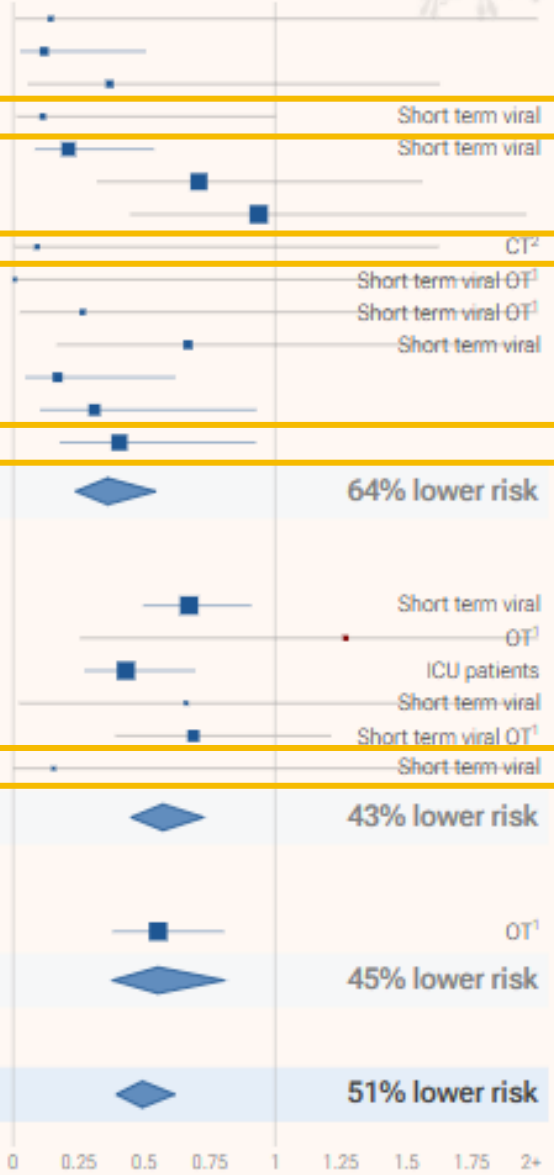
	Improvement, RR [CI]			Treatment	Control
Seneviratne (RCT)	33%	0.67 [0.50-0.91]	viral load	4 (n)	2 (n)
Zarabanda (RCT)	-27%	1.27 [0.26-6.28]	no recov.	3/13	2/11
Jamir (ICU)	57%	0.43 [0.27-0.69]	death	39/163	62/103
Ferrer (RCT)	34%	0.66 [0.02-19.0]	viral load	9 (n)	12 (n)
Fantozzi (RCT)	31%	0.69 [0.39-1.21]	viral+	5/8	10/11
Graves (DB RCT)	85%	0.15 [0.00-454]	viral load	16 (n)	16 (n)
Late treatment	43%	0.57 [0.45-0.73]		47/213	74/155

$Tau^2 = 0.01$, $I^2 = 11.7\%$, $p < 0.0001$

	Improvement, RR [CI]			Treatment	Control
Seet (CLUS. RCT)	45%	0.55 [0.38-0.80]	symp. case	42/735	64/619
Prophylaxis	45%	0.55 [0.38-0.80]		42/735	64/619

$Tau^2 = 0.00$, $I^2 = 0.0\%$, $p = 0.002$

All studies	51%	0.49 [0.39-0.62]		99/1,690	195/1,512



[1] OT: comparison with other treatment
[2] CT: study uses combined treatment

$Tau^2 = 0.05$, $I^2 = 24.6\%$, $p < 0.0001$

Effect extraction pre-specified
(most serious outcome, see appendix)

Povidone-Iodine reduces COVID-19 risk: real-time meta analysis of 21 studies

@CovidAnalysis, April 2025, Version 38

PDF | All Studies | All Treatments | Feedback

Abstract

Significantly lower risk is seen for mortality, hospitalization, recovery, cases, and viral clearance. 11 studies from 11 independent teams in 9 countries show significant benefit.

Meta analysis using the most serious outcome reported shows 51% [38-61%] lower risk. Results are similar for Randomized Controlled Trials, higher quality studies, and peer-reviewed studies. Early treatment is more effective than late treatment.

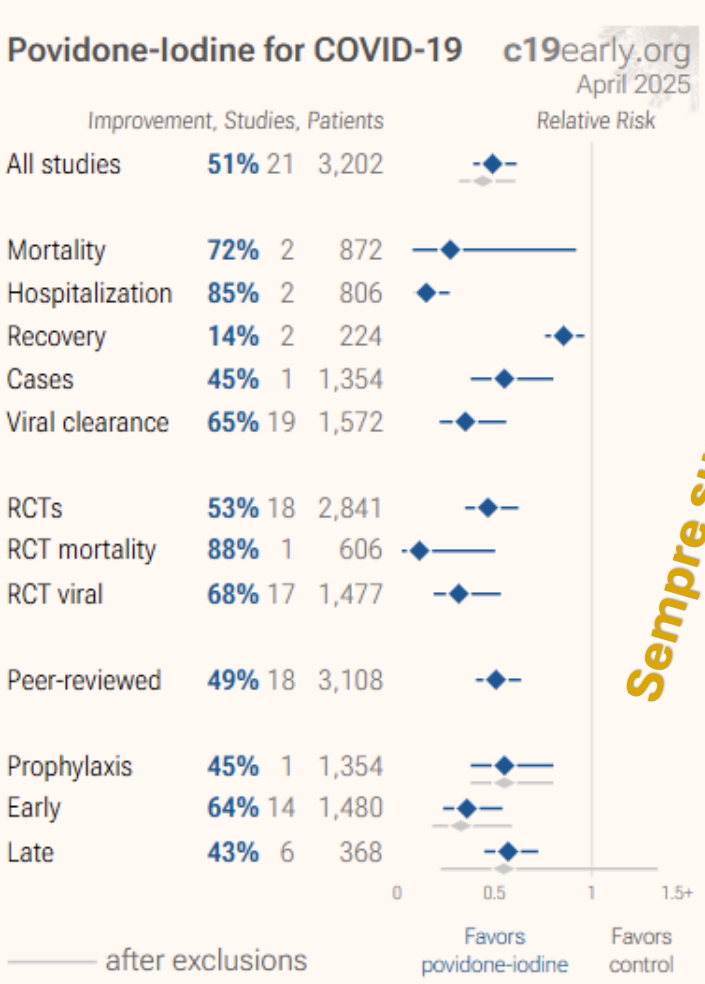
Results are very robust — in exclusion sensitivity analysis 17 of 21 studies must be excluded to avoid finding statistically significant efficacy in pooled analysis.

3 RCTs with 424 patients have not reported results (up to 3 years late).

Excessive use of PVP-I could affect thyroid function.

No treatment is 100% effective. Protocols combine safe and effective options with individual risk/benefit analysis and monitoring. Povidone-Iodine may be detrimental to the natural microbiome, raising concern for side effects, especially with prolonged or excessive use. All data and sources to reproduce this analysis are in the appendix.

Other meta analyses show significant improvements with povidone-iodine for viral load[1,2] and viral clearance[1].



Sempre superiore alle alternative! Per tutti gli esiti!!

Iodopovidone

	Improvement, RR [CI]	Treatment	Control	
Mohamed (RCT)	86% 0.14 [0.01-2.21] viral+	0/5	3/5	
Choudhury (RCT)	88% 0.12 [0.03-0.50] death	2/303	17/303	
Guenezan (RCT)	63% 0.37 [0.06-1.63] viral load	12 (n)	12 (n)	
Elzein (DB RCT)	89% 0.11 [0.01-1.00] viral load	25 (n)	9 (n)	Short term viral
Arefin (RCT)	79% 0.21 [0.08-0.54] viral+	4/27	19/27	Short term viral
Baxter (RCT)	-214% 3.14 [0.13-74.7] hosp.	1/37	0/42	OT[1]
Sulistyani (SB RCT)	6% 0.94 [0.45-1.96] viral load	15 (n)	15 (n)	
Elsersy (DB RCT)	91% 0.09 [0.01-1.62] hosp.	0/100	5/100	CT[2]
Sevinç Gül (RCT)	99% 0.01 [0.00-439] viral load	21 (n)	20 (n)	OT[1] Short term viral
Natto (RCT)	74% 0.26 [0.03-2.76] viral load	12 (n)	12 (n)	OT[1] Short term viral
Karaaltin (RCT)	83% 0.17 [0.05-0.62] viral load	30 (n)	30 (n)	
Matsuyama (RCT)	69% 0.31 [0.10-0.93] viral+	4/139	13/140	
Early treatment	**71% 0.29 [0.17-0.50]**	**11/726**	**57/715**	**71% lower risk**
Tau² = 0.27, I² = 31.6%, p < 0.0001				
Seneviratne (RCT)	33% 0.67 [0.50-0.91] viral load	4 (n)	2 (n)	Short term viral
Zarabanda (RCT)	-27% 1.27 [0.26-6.28] no recov.	3/13	2/11	OT[1]
Ferrer (RCT)	34% 0.66 [0.02-19.0] viral load	9 (n)	12 (n)	Short term viral
Fantozzi (RCT)	31% 0.69 [0.39-1.21] viral+	5/8	10/11	OT[1] Short term viral
Late treatment	**31% 0.69 [0.53-0.89]**	**8/34**	**12/36**	**31% lower risk**
Tau² = 0.00, I² = 0.0%, p = 0.0051				
Seet (CLUS. RCT)	45% 0.55 [0.38-0.80] symp. case	42/735	64/619	OT[1]
Prophylaxis	**45% 0.55 [0.38-0.80]**	**42/735**	**64/619**	**45% lower risk**
Tau² = 0.00, I² = 0.0%, p = 0.002				
All studies	**53% 0.47 [0.34-0.65]**	**61/1495**	**133/1370**	**53% lower risk**

[1]OT: comparison with other treatment
[2]CT: study uses combined treatment
Tau² = 0.11, I² = 35.3%, p < 0.0001

0 0.25 0.5 0.75 1 1.25 1.5 1.75 2+

Favors povidone-iodine Favors control

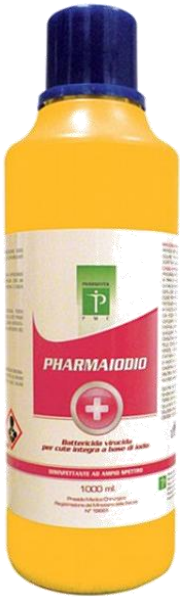
Il maggior RCT, su mortalità: **-88%**

Effect of 1% Povidone Iodine Mouthwash/Gargle, Nasal and Eye Drop in COVID-19 patient (es. Betadine)

Bioresearch Communications
Volume 7, Issue 1, January 2021
Bioresearch Communications

Md. Iqbal Mahmud Choudhury[1], Nilufar Shabnam[2], Tazin Ahsan[3], Md. Saiful kabir[4], Rashed Md. Khan[5], S.M. Abu Ahsan[6]

[1]Assistant professor, Plastic Surgery Unit, Department of Surgery, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka, Bangladesh. [2] Assistant professor, Department of Surgery, BIRDEM Hospital &



RCT classificato: «certezza prove moderata» in revisione *DepLazio*

Lo iodopovidone è un antisettico semplice, economico, ad ampio spettro in uso da 150 anni; l'OMS lo pone **tra i farmaci essenziali**, non ha resistenze note.

RCT su 606 pazienti Covid-19, in Bangladesh:

- **Gruppo A**: 303 pz. randomizzati a sciacqui/gargarismi, gocce nasali e oculari con **1% di iodopovidone** (antisettico) ogni ora x 4 settimane,
- Gruppo B: 303 pz. idem con **acqua tiepida**.
- In **gruppo A** solo 8 pz (**2,6%**) erano ancora PCR-RT^{+} in 7^{a} giornata, vs 70% in gruppo B
- Necessità di supporto di Ossigeno: **3,3% gruppo A**, 21% gruppo B
- Mortalità: **0,7% gruppo A**, 6% gruppo B (differenza significativa)

frontiers | Frontiers in Public Health 13:1462286.
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Saline nasal irrigation and gargling in COVID-19: Part II. Outcomes in Omicron and risk–benefit for self-care

S. Huijghebaert[1*†], C. Fabbris[2,3], A. L. Baxter[4], S. Parviz[5], U. S. Chatterjee[6] and D. Rabago[7†‡]

[1]Pharmaceutical Science, Non-Profit Research, Antwerp, Belgium, [2]ENT Unit, Department of Surgery, Ospedali Riuniti Padova Sud, Padova, Italy, [3]Department of Medicine DIMED, Padova University,

Rassegna sistematica di studi preclinici e clinici su esiti su Omicron di soluzioni saline. 14 studi (di cui 1 prova sperimentale di fattibilità, 8 RCT, 2 quasi sperimentali non randomizzati, 3 osservazionali).

In linea con i risultati di precedenti revisioni, l'inizio precoce di irrigazioni saline nasali (SNI)/gargarismi aiuta i pz COVID-19 lieve a sentirsi meglio, in modo indipendente dalla variante.

Se si forniscono materiali per l'irrigazione, le SNI si possono ragionevolmente raccomandare come automedicazione precoce per COVID-19 e per il comune raffreddore.

Benefici:

• l'irrigazione nasale con soluzione salina isotonica e ipertonica (SNI) ha ridotto la carica virale e ridotto la durata della diffusione virale in adulti e bambini con infezione da Omicron, se la SNI si è iniziata precocemente.

L'effetto era indipendente dallo stato vaccinale.
La durata della diffusione virale ha superato la durata dei sintomi.

• Le SNI isotoniche (9 g sale x litro d'acqua) alleviano i sintomi respiratori e aiutano a riprendere le attività quotidiane. In combinazione con i gargarismi, hanno prevenuto disturbi dell'olfatto e del gusto, se iniziate prima della loro insorgenza.
Un miglioramento dei sintomi è stato osservato anche negli studi pre-Omicron e nelle infezioni respiratorie del tratto superiore.

• Le SNI possono ridurre l'uso di farmaci.

• Oltre all'effetto principale di risciacquo (diluizione e rimozione del virus), i gargarismi x 1 minuto con soluzione isotonica si possono raccomandare per ridurre l'infettività della saliva, mentre l'SNI ripetuto può contribuire a migliorare l'efficacia neutralizzante contro Omicron nelle secrezioni nasali.

• SNI e gargarismi salini sono risultati sicuri. Non si sono osservati effetti avversi, e solo limitati effetti collaterali, a risoluzione spontanea. Nessun aggravamento.

• Negli studi sui marcatori immunitari/infiammatori, non si sono osservati effetti avversi; anzi, se la SNI si iniziava precocemente, si osservava una riduzione della diffusione virale, accompagnata da un aumento dei linfociti e da una riduzione di PCR e IL-6.

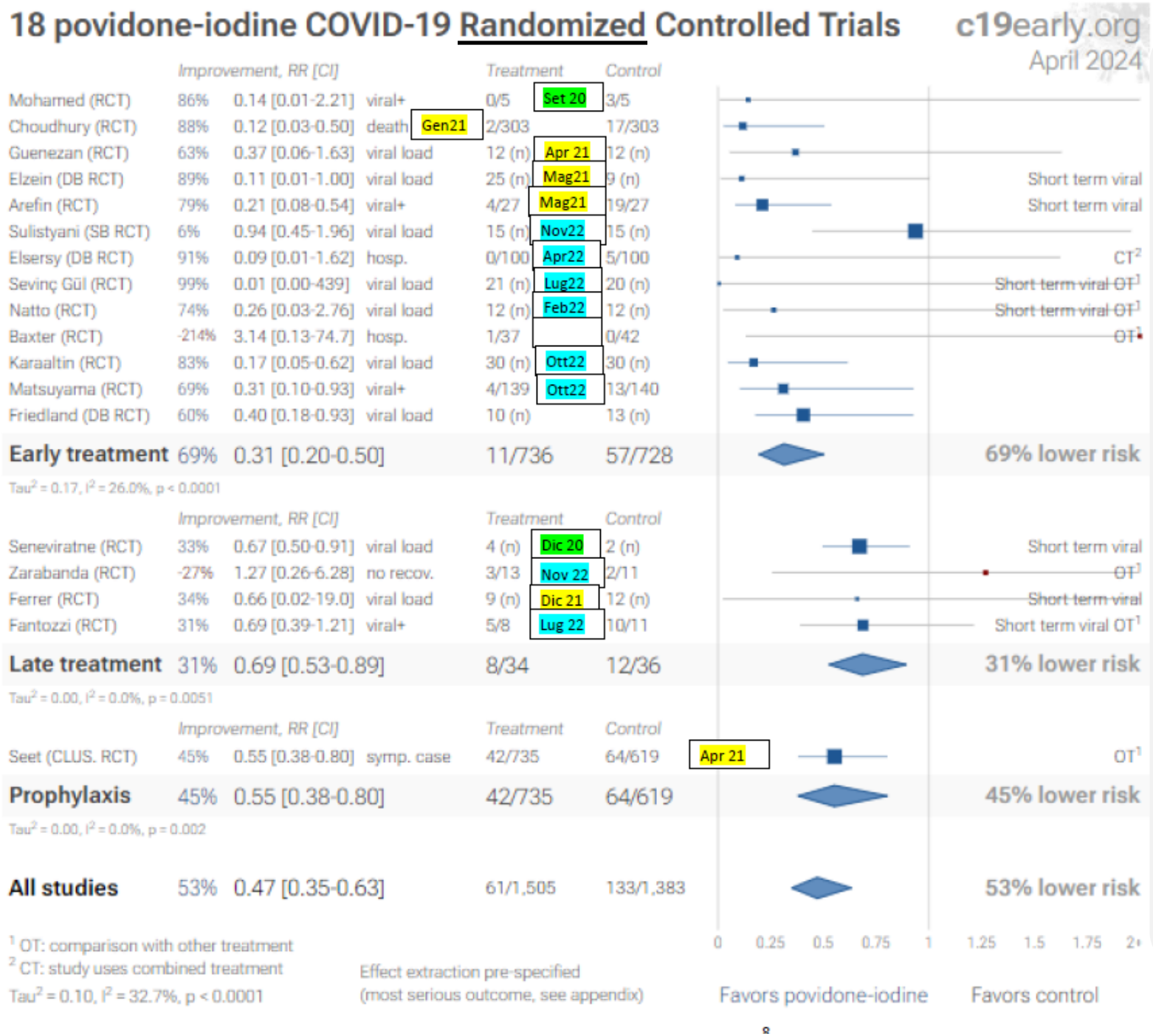
• La SNI isotonica è stata ben tollerata. L'SNI ipertonica causa occasionalmente prurito nasale, dolore o irritazione autolimitanti. L'aggiunta di antivirali (molnupiravir) o antisettici (clorexidina) si è stata associata a maggiori effetti avversi.

• Non si sono osservati rischi per l'automedicazione.

• **Conclusione**: l'SNI + gargarismi si può raccomandare in modo sicuro come pratica igienica quotidiana in caso di COVID-19, anche da Omicron.
I risultati clinici sono migliori se iniziata presto.

• Un approccio pragmatico all'automedicazione in caso di COVID-19 può includere SNI + gargarismi ai primi sintomi delle vie respiratorie superiori,

in modo simile a quanto si raccomanda (*si dovrebbe* raccomandare!) in caso di comune raffreddore e altre patologie delle vie respiratorie superiori.



RCT (cioè le ricerche più valide) indicizzati in PubMed negli anni (legenda colore):

2020

2021

2022

No colore in anni successivi

Anni in cui le Circolari MinSal erano ferme a pa-racetamolo o FANS

All. 5

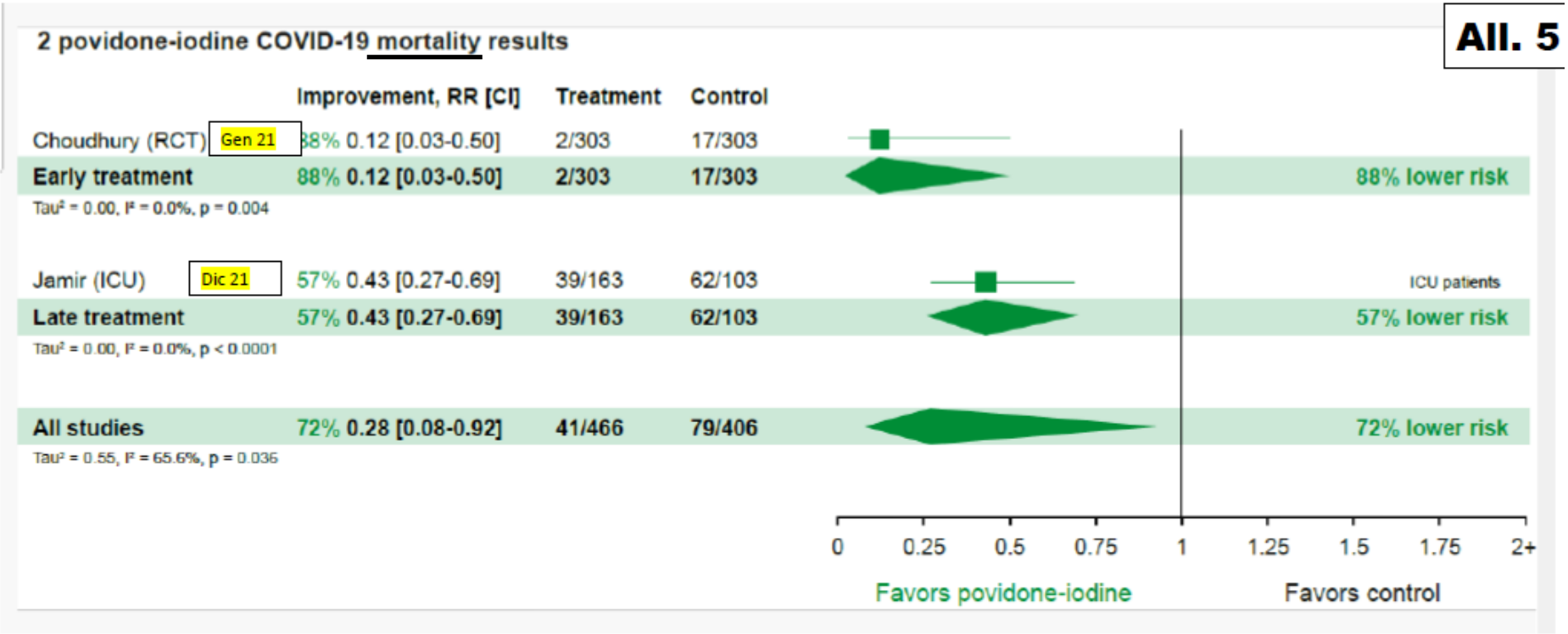


Figure 7 - Random effects meta-analysis for RCTs with mortality results about povidone-iodine in COVID-19 [100-101].

Se ci si limita ai RCT in cui si è valutata la mortalità, la riduzione media con iodopovidone è stata del 72%. Quante vite si sarebbero salvate (e risorse risparmiate per usi più produttivi in salute...) se il MinSal avesse avuto un sistema di monitoraggio continuo della letteratura scientifica mondiale (anziché lasciarsi imbeccare da Big Pharma)?

Ancora oggi gran parte dell''*area del dissenso*' ripete del tutto acriticamente e senza valide prove che, invece del paracetamolo ('non *abbastanza* antinfiammatorio'), si sarebbero dovuti usare i FANS a piene dosi e subito, senza neppure attendere l'esito dei test...! Invece, avevamo già nel 2020-'21-'22 informazioni sufficienti per curare secondo prove valide, con scelte legittime anche giuridicamente.

Quelle ricerche non sono ancora conclusive...

«Ogni lavoro scientifico è incompleto,
sia esso osservazionale o sperimentale.

Ogni lavoro scientifico è soggetto
a essere smentito o modificato
da nuove conoscenze.

**Ciò non ci autorizza a ignorare
le conoscenze che già abbiamo,
o a rimandare l'azione che esse
sembrano richiedere in un dato momento**.»

Sir Austin Bradford Hill,
Epidemiologo (1897-1991)

Antihistamine H1RAs for COVID-19

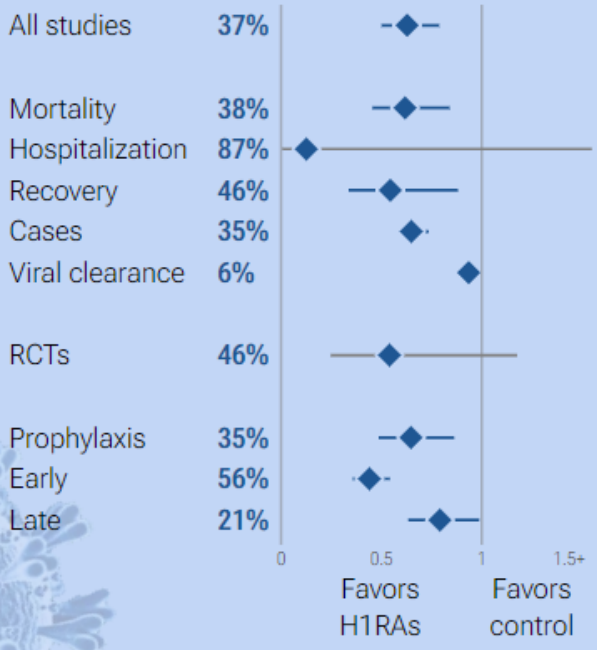
16 studies from **193** scientists

71,956 patients in **7** countries

Significantly lower risk for **mortality**, **recovery**, **cases**, and **viral clearance**.

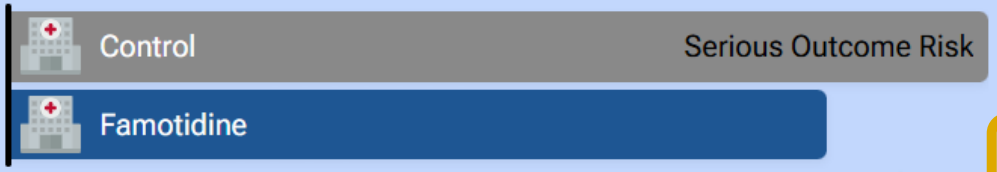
9 studies from 8 independent teams in 5 countries show significant benefit.

COVID-19 ANTIHISTAMINE H1RA STUDIES. DEC 2024. C19EARLY.ORG



Famotidine for COVID-19

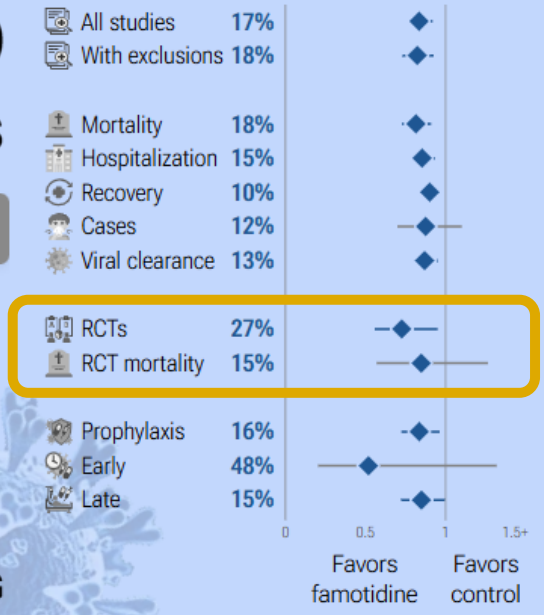
30 studies with **>110,000** patients



Significantly lower risk for **mortality**, **hospitalization**, **recovery**, and **viral clearance**.

15 studies from 15 independent teams in 7 countries show significant benefit.

COVID-19 FAMOTIDINE STUDIES. NOV 2025. C19EARLY.ORG



Accesso 28-11-'25

Antihistamine H1RAs reduce COVID-19 risk: real-time meta analysis of 16 studies

@CovidAnalysis, December 2024, Version 13

All Treatments 57% lower symptomatic PCR+ cases with HCQ/CQ, p=0.0004, COPCOV 4,652 patient RCT

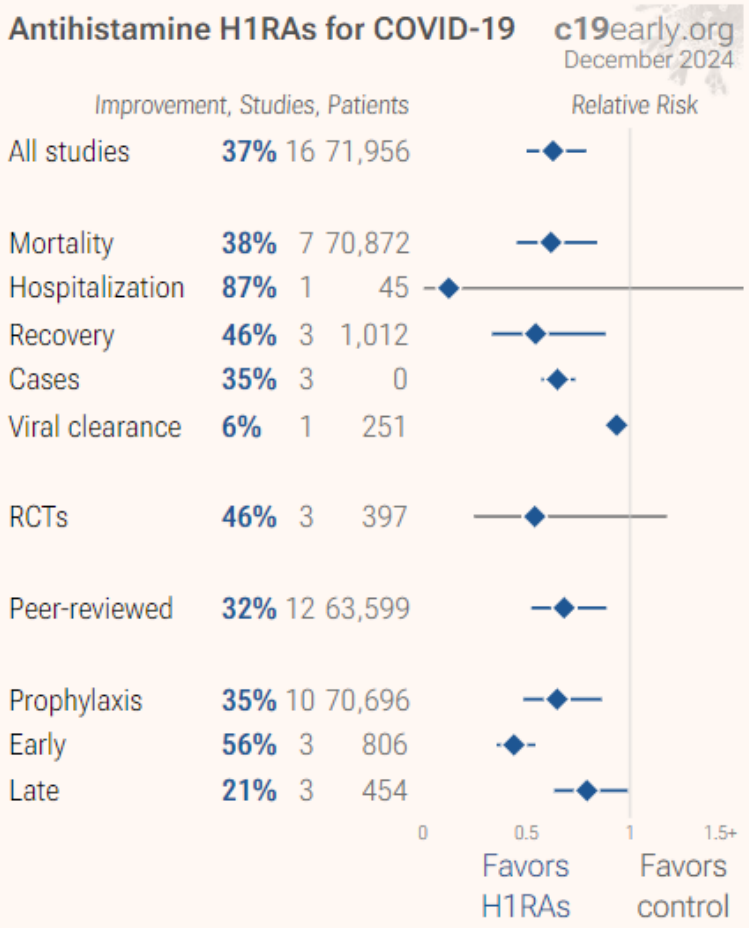
Abstract

Significantly lower risk is seen for mortality, recovery, cases, and viral clearance. 9 studies from 8 independent teams in 5 countries show significant benefit.

Meta analysis using the most serious outcome reported shows 37% [21-50%] lower risk. Results are similar for Randomized Controlled Trials and peer-reviewed studies. Early treatment is more effective than late treatment.

Results are robust — in exclusion sensitivity analysis 8 of 16 studies must be excluded to avoid finding statistically significant efficacy in pooled analysis.

No treatment is 100% effective. Protocols combine safe and effective options with individual risk/benefit analysis and monitoring. Other treatments are more effective. All data and sources to reproduce this analysis are in the appendix.



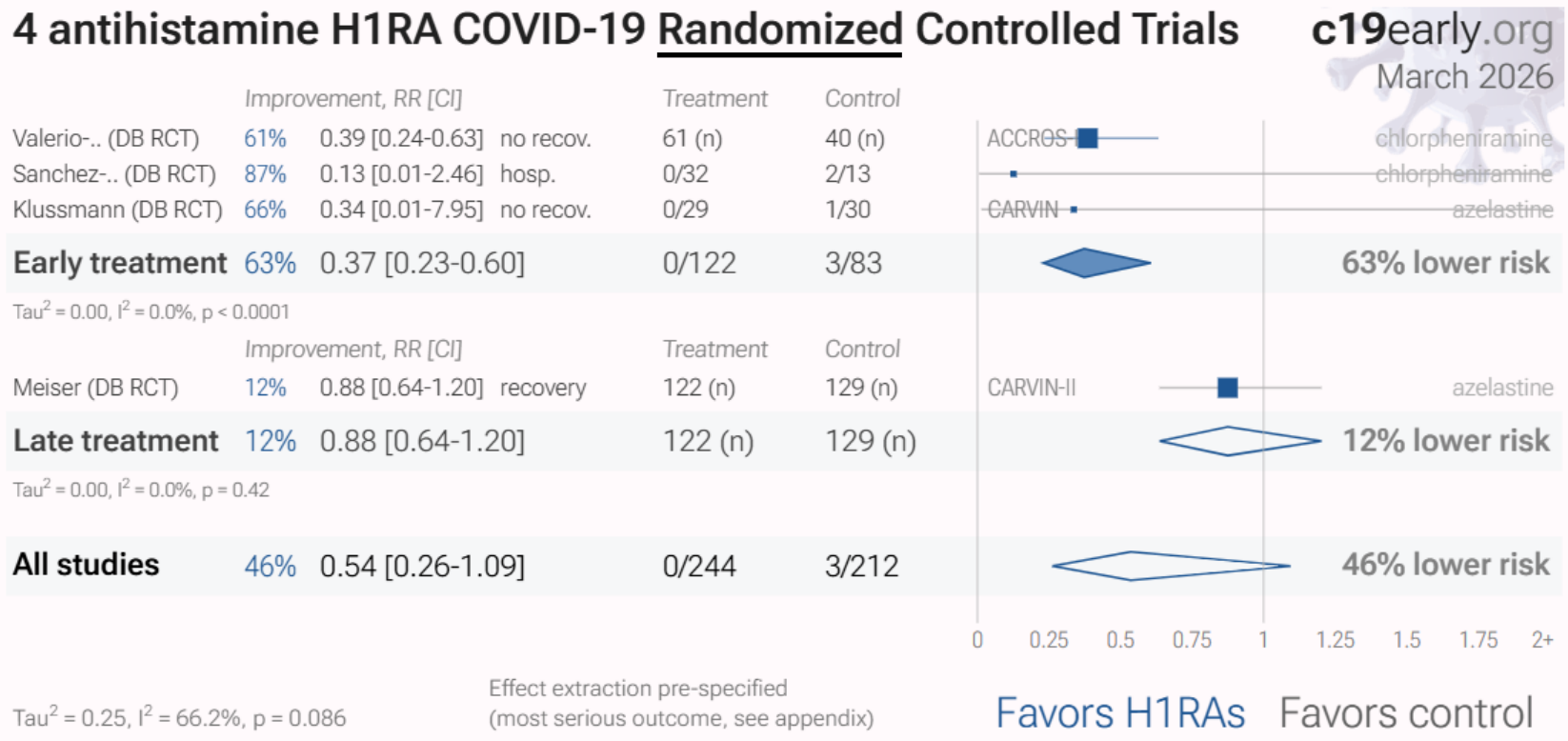


Fig. 14. **Random-effects meta-analysis for all Randomized Controlled Trials.** This plot shows pooled effects, see the specific outcome analyses for individual outcomes. Analysis validating pooled outcomes for COVID-19 can be found below. Effect extraction is pre-specified, using the most serious outcome reported. For details see the appendix.

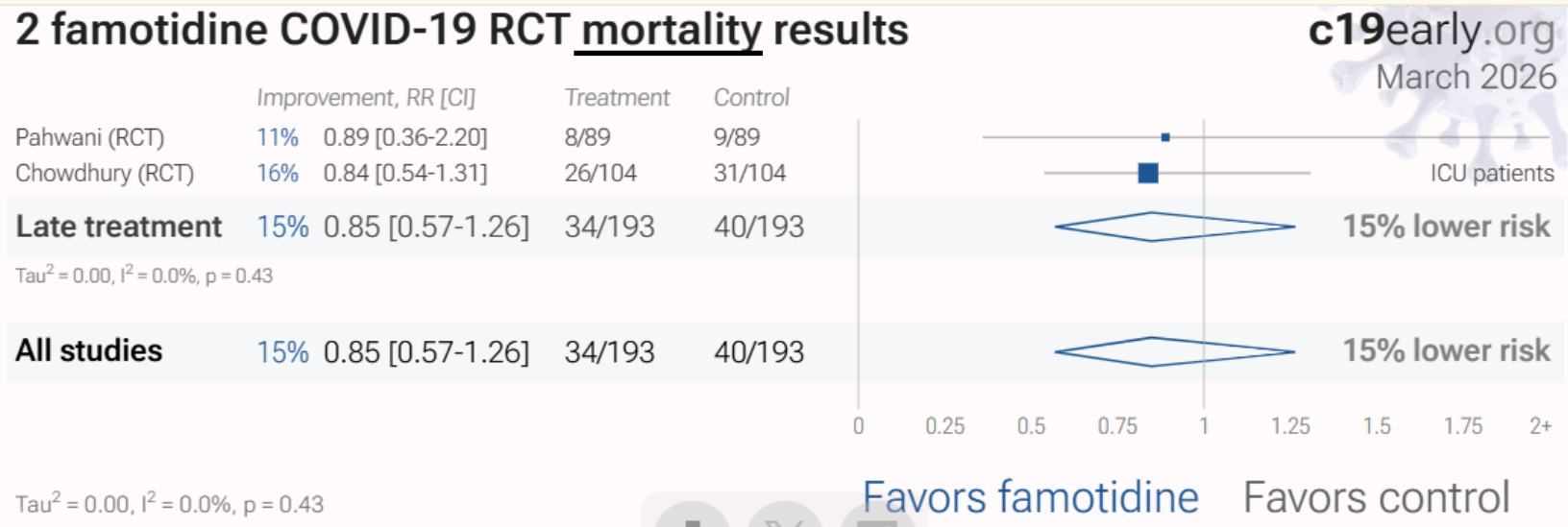


Fig. 17. **Random-effects meta-analysis for RCT mortality results.**

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Research article

Clinical efficacy of N-acetylcysteine for COVID-19: A systematic review and meta-analysis of randomized controlled trials

Ting-Hui Liu [a], Jheng-Yan Wu [b], Po-Yu Huang [c], Ya-Wen Tsai [d], Wan-Hsuan Hsu [c], Min-Hsiang Chuang [c], Hung-Jen Tang [b], Chih-Cheng Lai [e,f,*]

[a] Department of Psychiatry, Chi Mei Medical Center, Tainan City, Taiwan

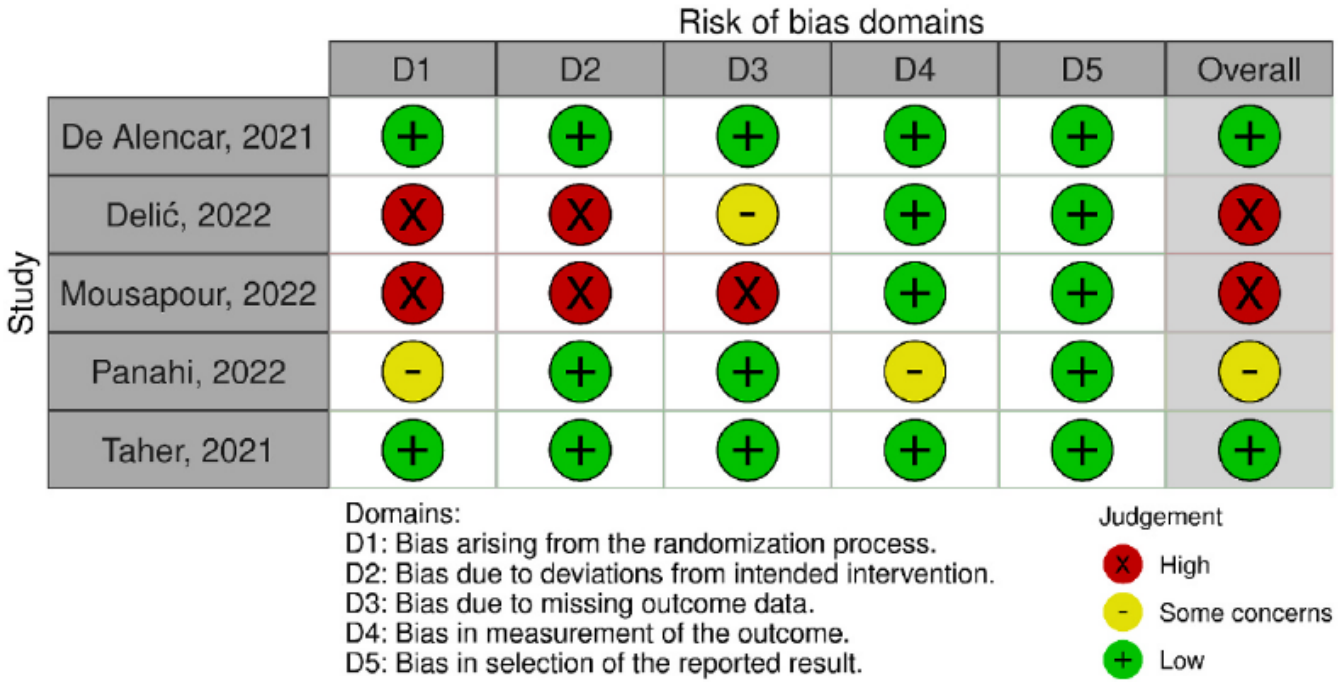


Fig. 2. Risk-of-bias assessment.

Figure 13. **Random effects meta-analysis for all Randomized Controlled Trials.** This plot shows pooled effects, see the specific outcome analyses for individual outcomes. Analysis validating pooled outcomes for COVID-19 can be found below. Effect extraction is pre-specified, using the most serious outcome reported. For details see the appendix.

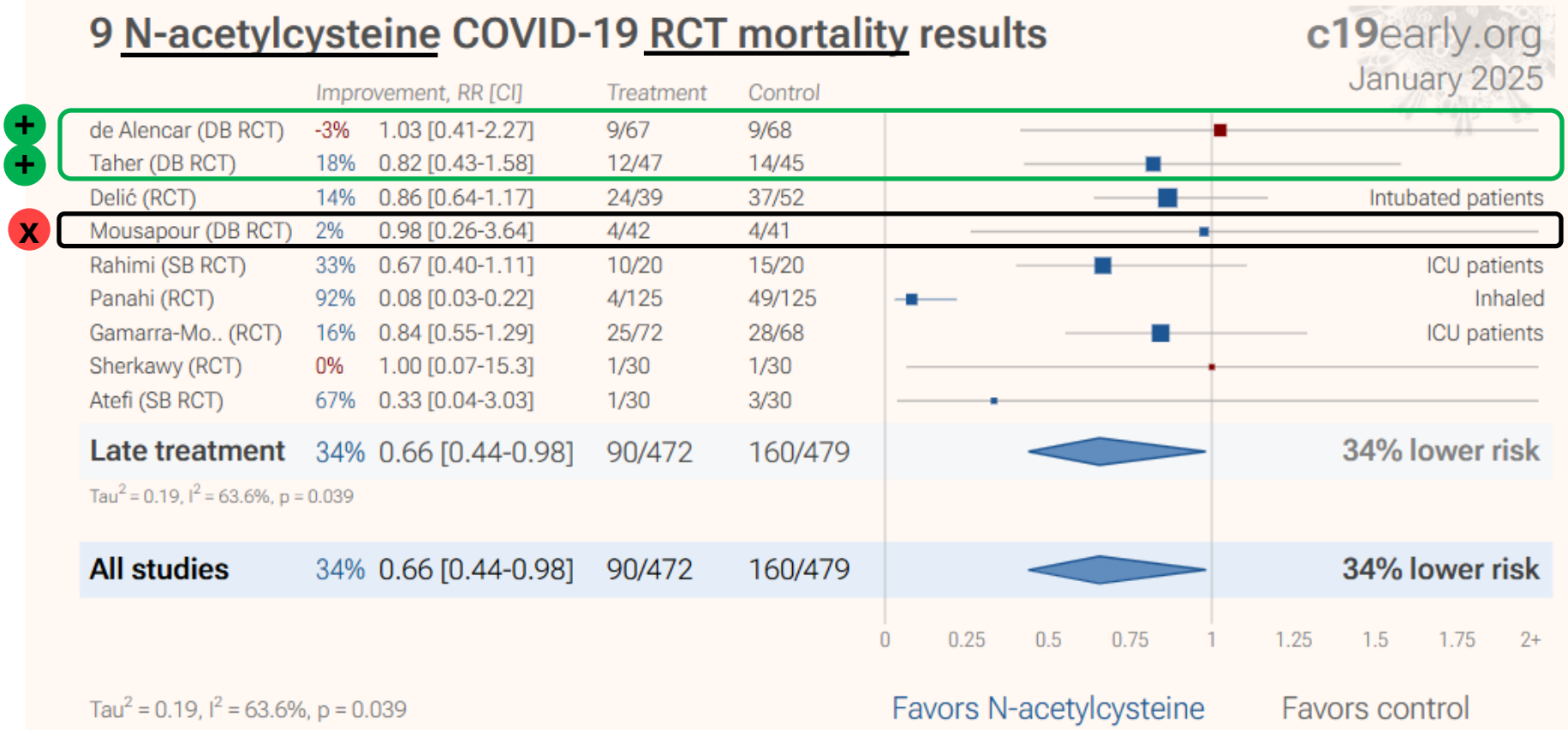


Figure 14. **Random effects meta-analysis for RCT mortality results.**

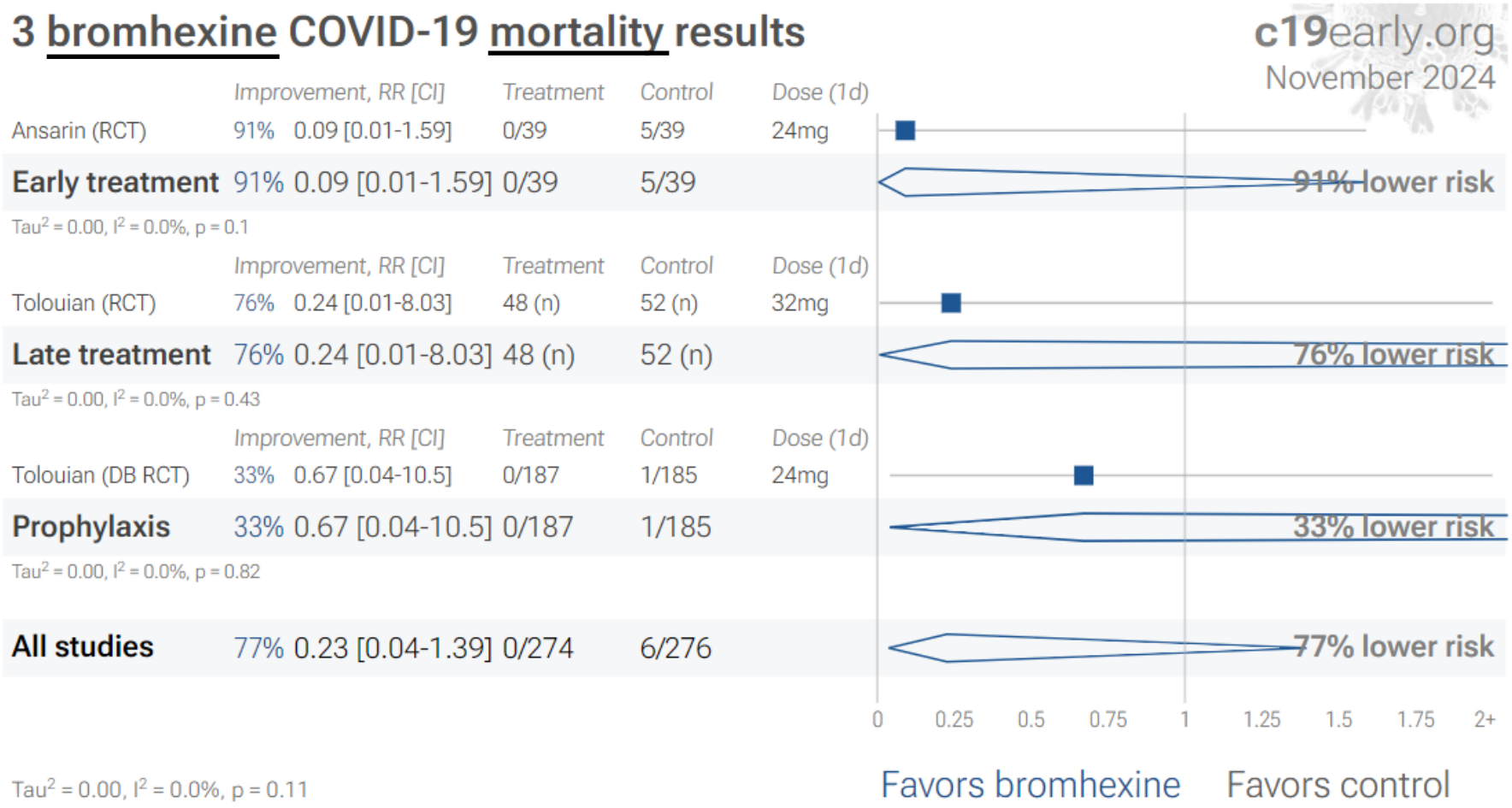


Figure 5. Random effects meta-analysis for mortality results.

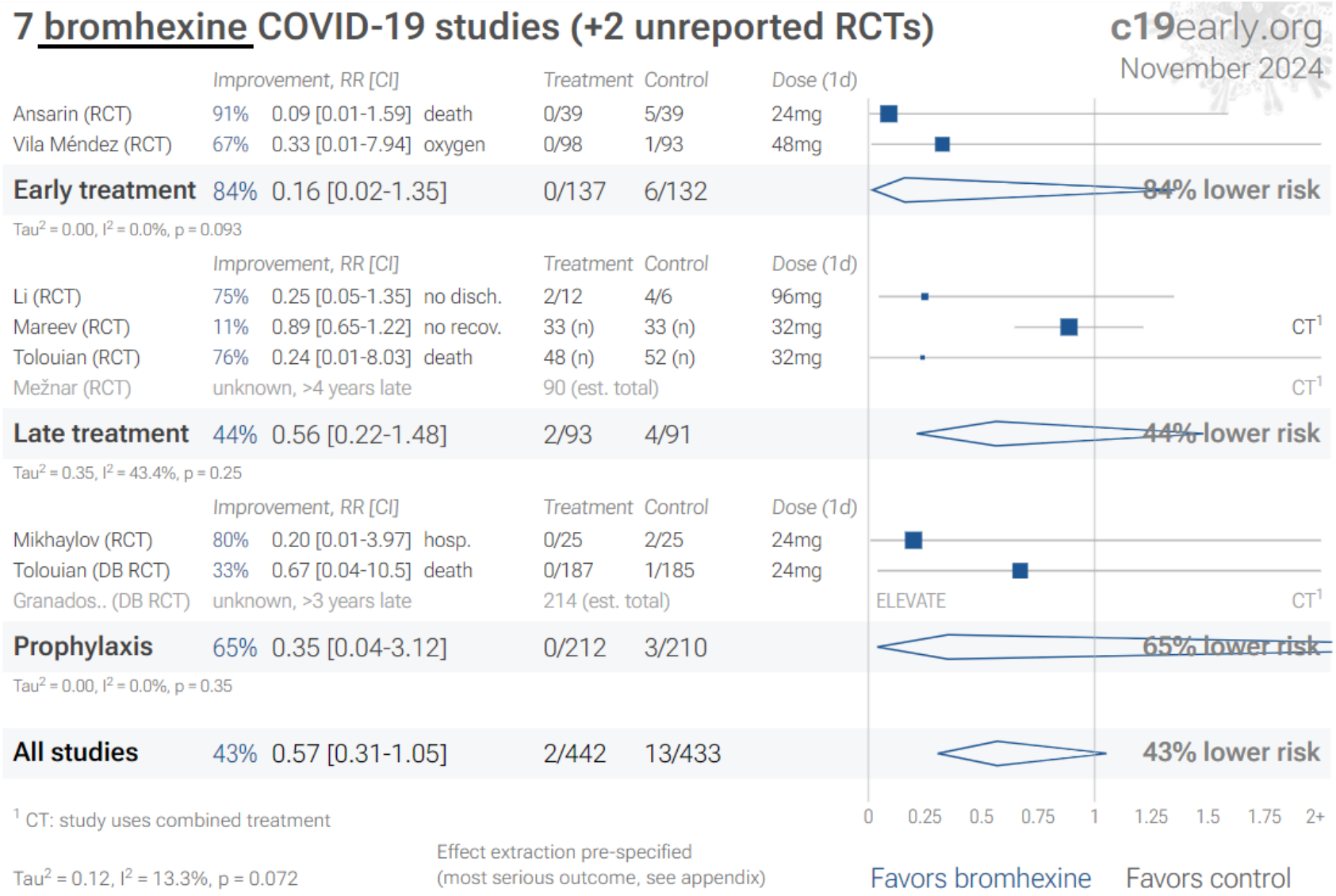


Figure 4. **Random effects meta-analysis for all studies.** This plot shows pooled effects, see the specific outcome analyses for individual outcomes. Analysis validating pooled outcomes for COVID-19 can be found below. Effect extraction is pre-specified, using the most serious outcome reported. For details see the appendix.

https://c19early.org/lfmeta.html#fig_fprd

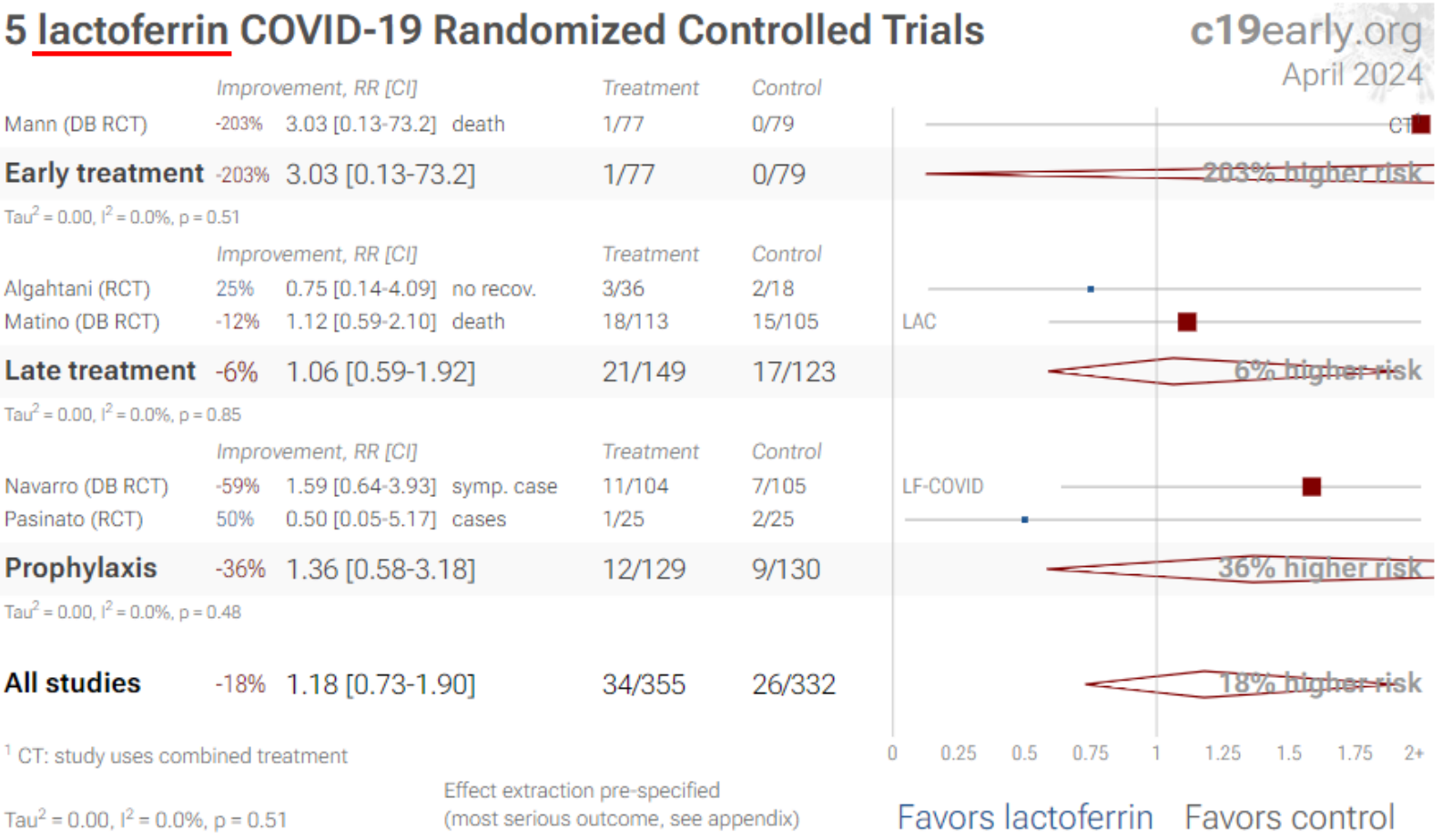


Figure 12. **Random effects meta-analysis for all Randomized Controlled Trials.** This plot shows pooled effects, see the specific outcome analyses for individual outcomes. Analysis validating pooled outcomes for COVID-19 can be found below. Effect extraction is pre-specified, using the most serious outcome reported. For details see the appendix.

~25 Euro

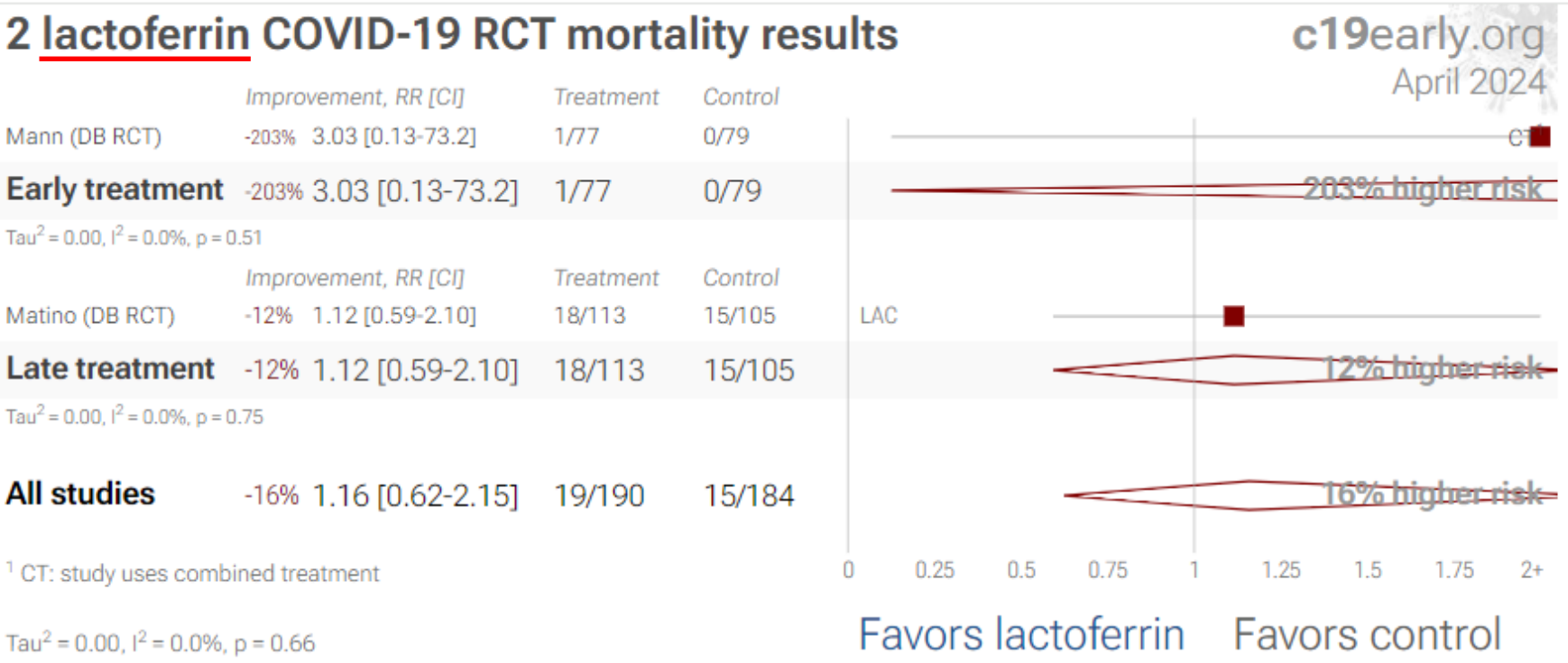
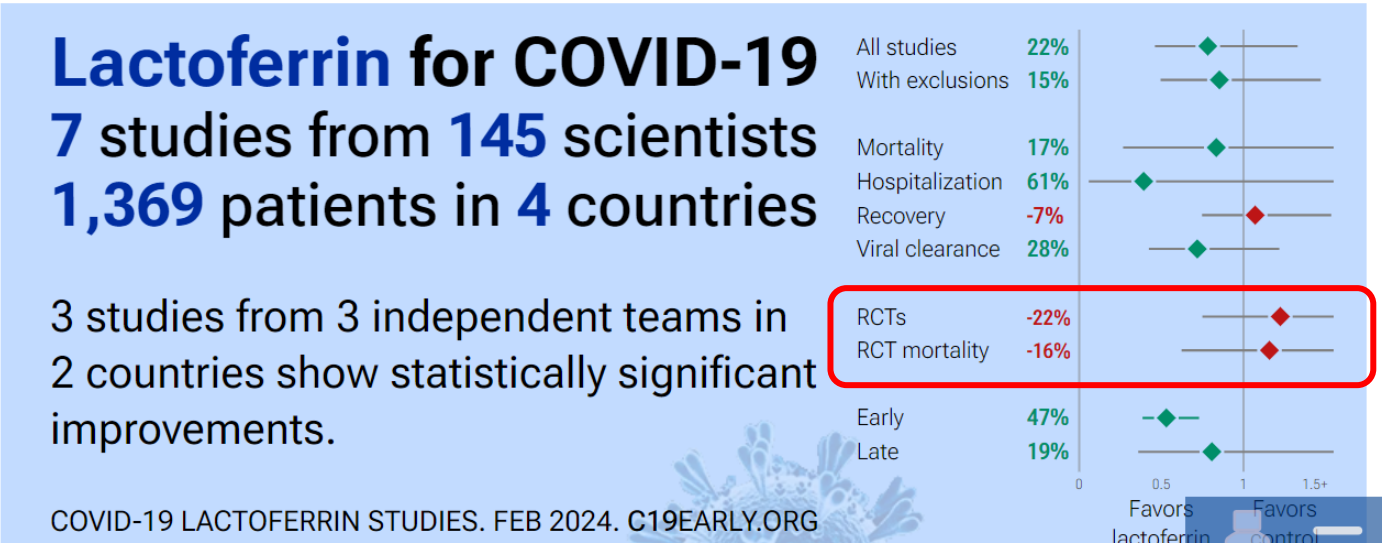


Figure 13. Random effects meta-analysis for RCT mortality results.



JAMA Network Open

Vit. C… almeno nella COVID lieve?

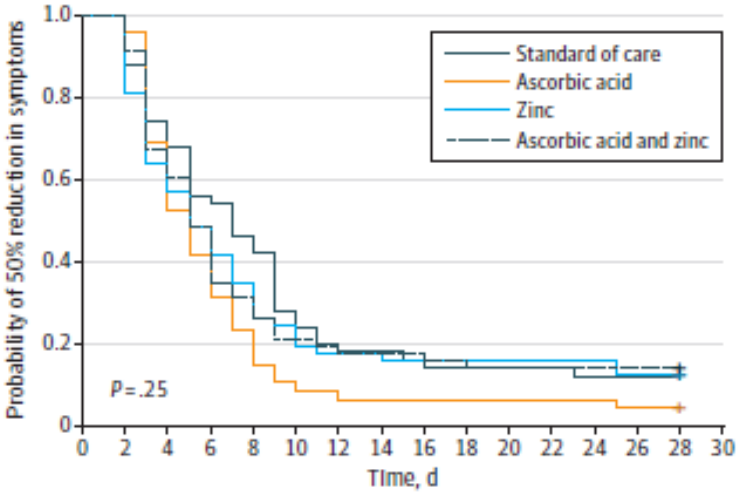
Original Investigation | Public Health

Effect of High-Dose Zinc and Ascorbic Acid Supplementation vs Usual Care on Symptom Length and Reduction Among Ambulatory Patients With SARS-CoV-2 Infection

The COVID A to Z Randomized Clinical Trial

Suma Thomas, MD, MBA; Divyang Patel, MD, MS; Barbara Bittel, BSN, RN; Kathy Wolski, MPH; Qiuqing Wang, MS; Anirudh Kumar, MD, MS; Zachary J. Il'Giovine, MD; Reena Mehra, MD, MS; Carla McWilliams, MD; Steve E. Nissen, MD; Milind Y. Desai, MD, MBA

Figure 3. Kaplan-Meier Curves for the Primary End Point by Treatment Group



No. at risk																
Standard of care	50	50	37	28	23	14	10	9	8	7	7	7	6	6	6	0
Ascorbic acid	48	48	33	20	11	5	4	3	3	3	3	3	3	2	2	0
Zinc	58	58	37	28	20	14	10	10	9	9	9	9	9	7	7	0
Ascorbic acid and zinc	58	58	39	28	18	12	11	10	10	9	8	8	8	8	8	0

JAMA Network Open. 2021;4(2):e210369. doi:10.1001/jamanetworkopen.2021.0369

End point	Mean (SD) Total	Standard of care	Ascorbic acid only	Zinc only	Ascorbic acid with zinc	P value
12-Symptom scale						
Patients meeting 50% reduction, No./total No. (%)	74/75 (98.7)	18/19 (94.7)	14/14 (100.0)	21/21 (100.0)	21/21 (100.0)	.44
Time to 50% reduction, d	6.4 (3.3)	6.2 (2.9)	6.6 (3.7)	6.6 (3.7)	6.2 (3.2)	.97
Difference, d (95% CI)	NA	[Reference]	0.40 (−1.99 to 2.80)	0.40 (−1.77 to 2.58)	0.07 (−1.94 to 2.09)	NA
Secondary end points						
Time until 4-symptom composite score is 0						
Time, d	10.6 (6.1)	9.9 (4.4)	12.1 (6.9)	10.8 (6.8)	9.7 (5.7)	.29
Difference, d (95% CI)	NA	[Reference]	2.22 (−0.58 to 5.02)	0.85 (−1.91 to 3.62)	−0.24 (−2.67 to 2.19)	NA
Composite 4-symptom score at day 5						
Score	3.2 (2.2)	3.1 (2.3)	3.3 (2.1)	3.2 (2.2)	3.3 (2.3)	.94
Difference, d (95% CI)	NA	[Reference]	0.77 (−0.64 to 1.18)	0.11 (−0.78 to 1.00)	0.20 (−0.72 to 1.12)	NA
Hospitalization, No. (%)	17 (7.9)	3 (6.0)	2 (4.2)	5 (8.6)	7 (12.1)	.50[b]
Death, No. (%)	3 (1.4)	0	1 (2.1)	0	2 (3.4)	.40[b]

I cibi non contengono le mega dosi *giuste* di Vit. C!

I 2 gruppi con Vit. C hanno 3 morti.
Negli altri 2 gruppi nessun morto

gastrointestinal intolerance, and in the current study, a significantly higher proportion of patients in the ascorbic acid subgroups reported adverse effects, including nausea, diarrhea, and stomach cramps.

British Journal of Nutrition (2012), **108**, 1235–1245
doi:10.1017/S0007114511006659

Consumption of gold kiwifruit reduces severity and duration of selected upper respiratory tract infection symptoms and increases plasma vitamin C concentration in healthy older adults

RCT in crossover

Denise C. Hunter[1]*, Margot A. Skinner[1], Frances M. Wolber[2], Chris L. Booth[2], Jacelyn M. S. Loh[1]†, Mark Wohlers[1], Lesley M. Stevenson[1]‡ and Marlena C. Kruger[2]

[1]*The New Zealand Institute for Plant and Food Research Limited, 120 Mt Albert Road, Private Bag 92169,*

....

samples were collected at baseline and at the end of each treatment and washout period. Gold kiwifruit did not significantly reduce the overall incidence of URTI compared with banana, but significantly reduced the severity and duration of head congestion, and the duration of sore throat. Gold kiwifruit significantly increased plasma vitamin C, α-tocopherol and lutein/zeaxanthin concentrations, and erythrocyte folate concentrations, and significantly reduced plasma lipid peroxidation. No changes to innate immune function (natural killer cell activity, phagocytosis) or inflammation markers (high-sensitivity C-reactive protein, homocysteine) were detected. Consumption of gold kiwifruit enhanced the concentrations of several dietary plasma analytes, which may contribute to reduced duration and severity of selected URTI symptoms, offering a novel tool for reducing the burden of URTI in older individuals.

in 4 sett.
giorni di:

mal di gola
2 vs 5,5

congest . Testa
<1 vs 4,5

Effectiveness of honey for symptomatic relief in upper respiratory tract infections: a systematic review and meta-analysis

Hibatullah Abuelgasim ,[1] Charlotte Albury,[2] Joseph Lee[2]

- A Cochrane systematic review found that honey can improve cough in children; honey has not been systematically reviewed for other URTI symptoms, or in other patient groups

What are the new findings?

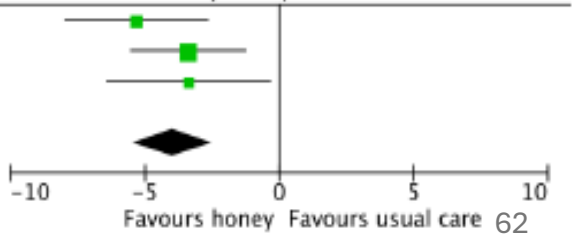
- Honey is more effective than usual care alternatives for improving URTI symptoms, particularly cough frequency and cough severity

How might it impact on clinical practice in the foreseeable future?

- Honey can be used as an alternative to antibiotics by clinicians who wish to offer treatment for URTIs, which may help to combat antimicrobial resistance

Study or Subgroup	Honey Mean	Honey SD	Honey Total	Usual care Mean	Usual care SD	Usual care Total	Weight	Mean Difference IV, Fixed, 95% CI
Ayazi 2017	-9.5104	7.3608	67	-4.2	4.5	20	30.2%	-5.31 [-7.96, -2.67]
Cohen 2017	-5.16	7.3612	75	-1.77	5.4431	66	46.9%	-3.39 [-5.51, -1.27]
Paul 2007	-10.71	7.4898	35	-7.3434	7.5016	70	22.9%	-3.37 [-6.41, -0.33]
Total (95% CI)			**177**			**156**	**100.0%**	**-3.96 [-5.42, -2.51]**

Heterogeneity: $Chi^2 = 1.42$, $df = 2$ ($P = 0.49$); $I^2 = 0\%$
Test for overall effect: $Z = 5.35$ ($P < 0.00001$)



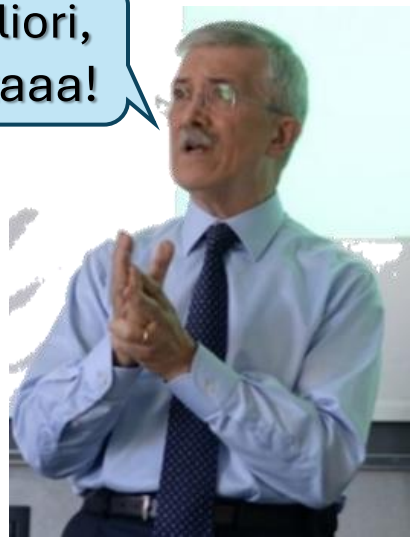
Effect of a test-and-treat approach to vitamin D supplementation on risk of all cause acute respiratory tract infection and covid-19: phase 3 randomised controlled trial (CORONAVIT)

BMJ Accept: 14 July 2022

D.A. Jolliffe, PhD1*†..., A.R. Martineau, PhD1,2*†

This **first** phase 3 **RCT**, including **6200 participants**, shows that implementation of a population-level test-and-treat approach to **oral** vitamin D replacement at a **dose of 800 IU** or **3200 IU per day** (6-month supply) did **not reduce risk of all-cause acute respiratory Infections** (ARI) **or COVID-19** among adults with a high baseline prevalence of sub-optimal vit. D status (media 15,9 ng/ml)

Fino a (improbabili) prove migliori, meglio **D**-menticarsene. Bastaaa!



	3.200 UI/die	800 UI/die	No Vit. D
Ogni ARI (OR)	1,09 (0,82-1,46)	1,26 (0,96-1,66)	1,00
COVID-19 (OR)	1,13 (0,78-1,63)	1,39 (0,98-1,97)	1,00
COVID-19 %	3%	3,6%	2,6%
Ricoveri COV (OR)	1,42 (n.s.)	1,17	1,00

Prevention of covid-19 and other acute respiratory infections with cod liver oil supplementation, a low dose vitamin D supplement: quadruple blinded, randomised placebo controlled trial

BMJ Accepted: 19 July 2022

Sonja H Brunvoll,[1] Anders B Nygaard,[1] Merete Ellingjord-Dale,[1] Petter Holland,[1] ...

RCT in quadruplo cieco, 34.600 adulti 18-75 aa. che non prendevano supplementi di Vit. D, seguiti in media 5,5 mesi freddi, con olio fegato merluzzo (400 UI Vit. D) o placebo (NB: metanalisi aveva trovato effetto vs infezioni respiratorie con basse dosi, non con boli. Poi gli autori hanno sconfessato anche quello...)

- Test SARS-CoV-2^{+}: RR 1,00 (nessuna differenza)
- COVID-19 grave: 0,70% con supplemento, 0,58% con placebo (RR 1,20, n.s.)
- ≥1 infezione respiratoria: 22,94% supplemento, 22,13% placebo (RR 1,04, n.s.)

Conclusione

Olio di fegato di merluzzo (Vit. D + A) d'inverno **non** riduce incidenza d'infezione da SARS-CoV-2, né COVID-19 grave, né altre infezioni respiratorie vs placebo.

The D-Health Trial: a randomised controlled trial of the effect of vitamin D on mortality >21.000 partecipanti, doppio cieco

V. InfoVax del 6-3-'22

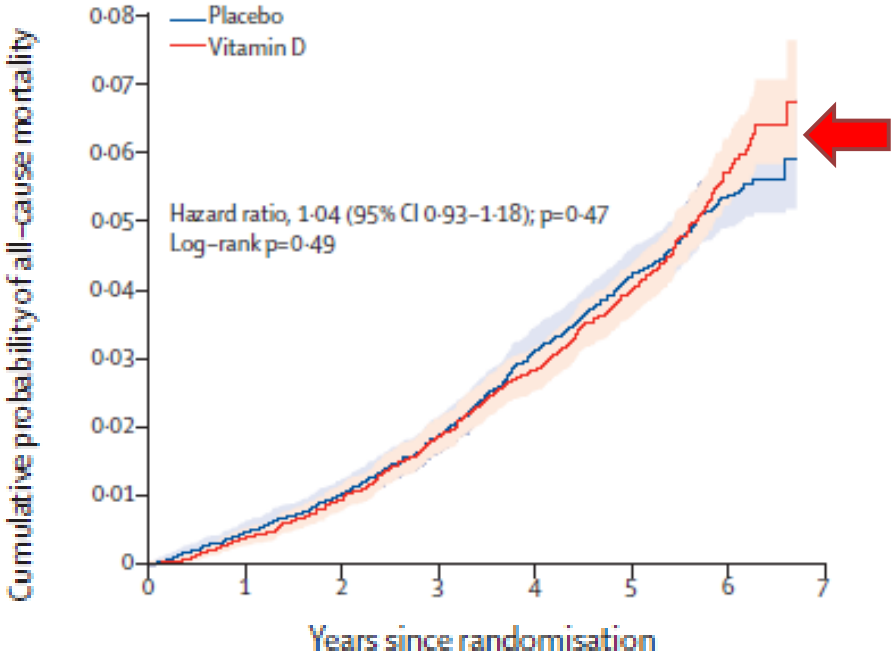
Rachel E Neale, Catherine Baxter, Briony Duarte Romero, Donald S A McLeod, Dallas R English, Bruce K Armstrong, Peter R Ebeling, Gunter Hartel, Michael G Kimlin, Rachel O'Connell, Jolieke C van der Pols, Alison J Venn, Penelope M Webb, David C Whiteman, Mary Waterhouse

Summary

Background The effect of supplementing unscreened adults with vitamin D_3 on mortality is unclear. We aimed to determine whether monthly doses of vitamin D_3 influenced mortality in older Australians.

Lancet Diabetes Endocrinol 2022
Published Online
January 10, 2022

their data to be destroyed. The HR of vitamin D_3 effect on all-cause mortality was 1.04 [95% CI 0·93 to 1·18]; p=0·47) and the HR of vitamin D_3 effect on cardiovascular disease mortality was 0·96 (95% CI 0·72 to 1·28; p=0·77). The HR for cancer mortality was 1·15 (95% CI 0·96 to 1·39; p=0·13) and for mortality from other causes it was 0·83 (95% CI 0·65 to 1·07; p=0·15). The odds ratio for the per-protocol analysis was OR 1·18 (95% CI 1·00 to 1·40; p=0·06). In exploratory analyses excluding the first 2 years of follow-up, those randomly assigned to receive vitamin D had a numerically higher hazard of cancer mortality than those in the placebo group (HR 1·24 [95% CI 1·01–1·54]; p=0·05).



Dopo i 6 anni la mortalità pare aumentare...

Quanto costano 25.000 U.I. di Vit. D?

Forma farmaceutica	25.000 UI Dibase	25.000 UI Generico
Gocce 100.000 UI (250 UI/goccia)	1,35	1,11
Flacone 25.000 UI	5,42	4,50
Flacone 50.000 UI	4,25	

Ian R Reid

51.75

Triplo **business mondiale**:

1) farmaci di enorme impiego,

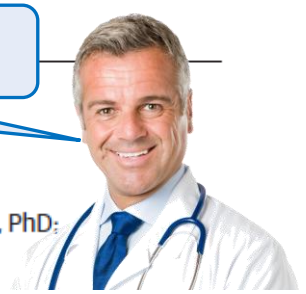
2) esami di laboratorio ripetuti,

3) integratori/cibi fortificati

JAMA Network Open

2025;8(5):e2511499. doi:10.1001/jamanetworkopen.2025.11499

Antibiotici in tutti i ricoveri COVID? **No!**



Original Investigation | Infectious Diseases

Antibiotic Treatment in Patients Hospitalized for Nonsevere COVID-19

Michael S. Pulia, MD, PhD; Meggie Griffin, MS; Rebecca Schwei, MPH, PhD; Aurora Pop-Vicas, MD, MPH; Lucas T. Schulz, PharmD; Meng-Shiou Shieh, PhD; Penelope Pekow, PhD; Valerie M. Vaughn, MD, MSc; Peter K. Lindenauer, MD, MSc

DESIGN, SETTING, AND PARTICIPANTS This retrospective cohort study used a target trial emulation design. Participants were adult, immunocompetent patients admitted to general care for COVID-19 from April 2020 to December 2023 at 1053 US-based acute-care hospitals that contribute

Antibiotici x **polmonite acquisita in comunità** (basso rischio)

RESULTS The cohort included 520 405 patients with COVID-19 (median [IQR] age, 66 [53-78] years; 266 186 [51.2%] male), including 92 708 Black patients (17.8%), 63 619 Hispanic patients (12.2%), and 304 649 White patients (58.5%); 279 656 patients (53.7%) had Medicare insurance. A total of 160 482 patients (30.8%) were treated with a CAP antibiotic regimen on day 1 of admission. The primary composite outcome was higher in the CAP group (20.8%) compared with the unexposed (no antibiotic) group (18.4%), but the difference did not meet the predefined criteria for clinical significance (ASD, 4.1%). Patients who received CAP antibiotics had higher odds of poor clinical outcomes (propensity matched-odds ratio [OR], 1.03 [95% CI, 1.01-1.05]; $P = .003$; inverse probability treatment weighted-OR, 1.03 [95% CI, 1.02-1.05]; $P < .001$; standardized mortality ratio weighted-OR, 1.10 [95% CI, 1.08-1.12]; $P < .001$).

To our knowledge, this study is the largest investigation into clinical outcomes for patients with COVID-19 treated with and without antibiotics to date. Previous research has primarily focused on in-hospital mortality[49-53] and data from the first half of 2020,[16,17,49,51,52] with the most recent study including data through June 2022.[19] A study by Widere et al[19] included 322 867 admissions from March 2020 to June 2022 across 66 US health systems. Using propensity matching, Widere et al[19] found higher odds of in-hospital mortality associated with early empirical antibiotics vs no early empirical antibiotics (OR, 1.27 [95% CI, 1.23-1.33]). Important limitations of Widere et al[19] include use

Table 3. Deterioration or In-Hospital Mortality for Community-Acquired Pneumonia Antibiotic vs No Antibiotic Treatment Day 1 of Admission in Patients Hospitalized for COVID-19

Model	Odds ratio (95% CI)	*P* value
Unadjusted[a]	1.33 (1.31-1.35)	<.001
Adjusted for covariates[a]	1.07 (1.05-1.09)	<.001
Adjusted for covariates and propensity score[a]	1.64 (1.41-1.90)	<.001
Propensity score matched[b]	1.03 (1.01-1.05)	.003
SMRW[a]	1.10 (1.08-1.12)	<.001
IPTW[a]	1.03 (1.02-1.05)	<.001

Una metanalisi di RCT ha trovato + eventi avversi per ogni giorno in + di antibiotici.

Journal of Cardiothoracic and Vascular Anesthesia 35 (2021) 578–584

Contents lists available at ScienceDirect

Journal of Cardiothoracic and Vascular Anesthesia

journal homepage: www.jcvaonline.com

Cortisonici: solo se...

«Pz ricoverati sono piccola minoranza, non tutti richiedono O_2, e se no ma corticosteroidi muoiono di più»

Original Article

Corticosteroids for Patients With Coronavirus Disease 2019 (COVID-19) With Different Disease Severity: A Meta-Analysis of Randomized Clinical Trials

Laura Pasin, MD*, Paolo Navalesi, MD*,†, Alberto Zangrillo, MD‡,§, Artem Kuzovlev, MD‖, ...

Study or Subgroup	Corticosteroids Events	Total	Control Events	Total	Weight	Risk Ratio IV, Random, 95% CI
2.1.1 Mechanically ventilated patients						
CoDEX TRIAL	85	151	91	148	25.4%	0.92 [0.76, 1.11]
Prado Jeronimo CM	43	54	49	57	26.5%	0.93 [0.78, 1.10]
RECOVERY TRIAL	96	324	283	683	25.4%	0.72 [0.59, 0.86]
Subtotal (95% CI)		**529**		**888**	**77.2%**	**0.85 [0.72, 1.00]**
Total events	224		423			
Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 4.74$, df = 2 (P = 0.09); $I^2 = 58\%$						
Test for overall effect: Z = 1.97 (P = 0.05)						
2.1.2 Patients not requiring oxygen						
Prado Jeronimo CM	1	30	0	42	0.4%	4.16 [0.18, 98.78]
RECOVERY TRIAL	89	501	145	1034	22.4%	1.27 [1.00, 1.61]
Subtotal (95% CI)		**531**		**1076**		**1.28 [1.00, 1.62]**
Total events	90		145			
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.54$, df = 1 (P = 0.46); $I^2 = 0\%$						
Test for overall effect: Z = 1.98 (P = 0.05)						
Total (95% CI)		**1060**		**1964**	**100.0%**	**0.93 [0.76, 1.15]**
Total events	314		568			
Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 14.32$, df = 4 (P = 0.006); $I^2 = 72\%$						
Test for overall effect: Z = 0.66 (P = 0.51)						
Test for subgroup differences: $Chi^2 = 7.55$, df = 1 (P = 0.006), $I^2 = 86.7\%$						

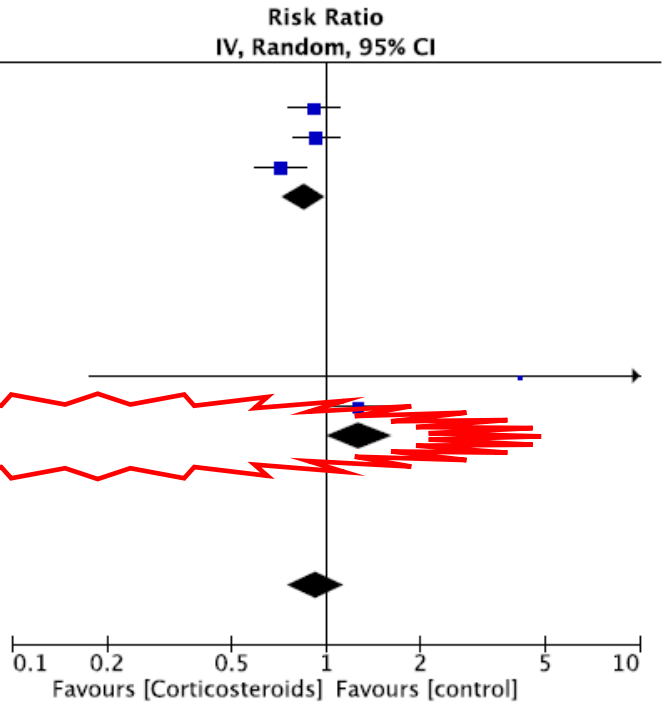


Fig 2. Tests for comparison between mechanically ventilated subgroups and those who did not require oxygen therapy based on random-effects models

Per ricorrere ai corticosteroidi devono esserci buoni motivi…

Annals of Internal Medicine

Association Between Oral Corticosteroid Bursts and Severe Adverse Events

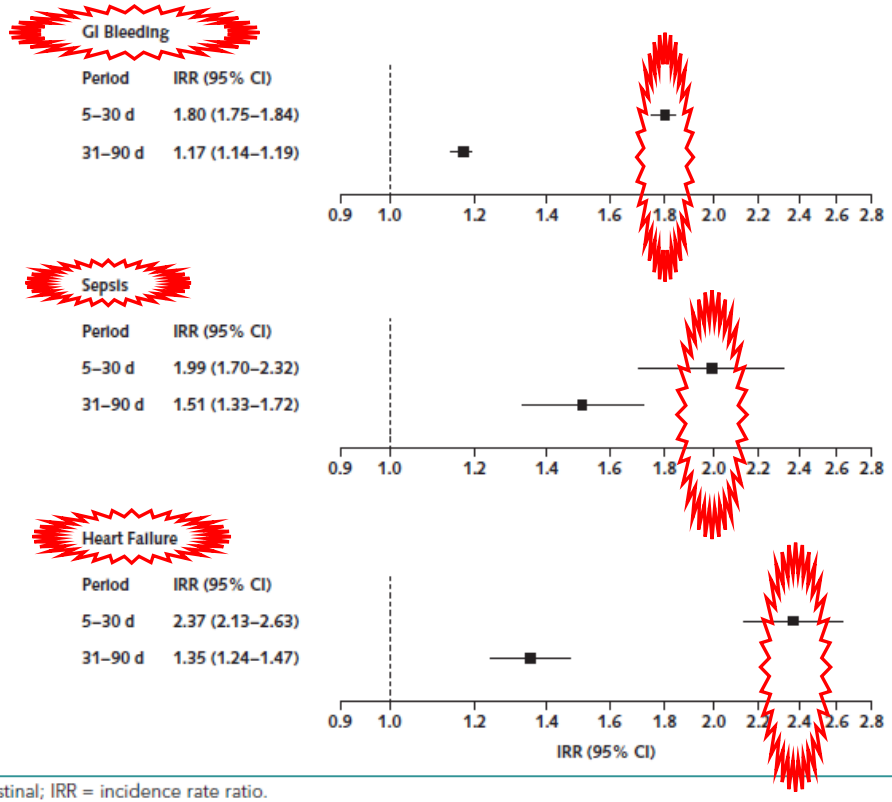
A Nationwide Population-Based Cohort Study

durata mediana: 3 giorni!

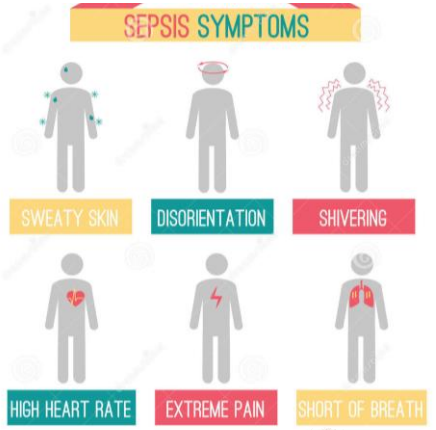
Ann Intern Med 2020; 173; 3025

Tsung-Chieh Yao, MD, PhD; Ya-Wen Huang, MS; Sheng-Mao Chang, PhD; Shun-Yu Tsai, BS; Ann Chen Wu, MD, MPH; and Hui-Ju Tsai, MPH, PhD

Figure 2. IRRs for GI bleeding, sepsis, and heart failure in 2 posttreatment periods (5-30 d and 31-90 d) associated with steroid bursts.



GI = gastrointestinal; IRR = incidence rate ratio.



Acido folico

Vitamin B9 for COVID-19

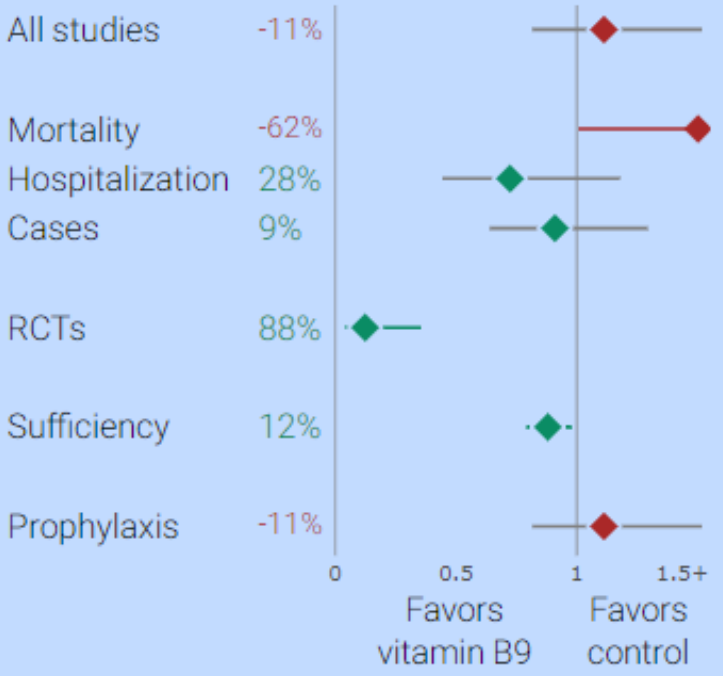
9 studies from 172 scientists

35,148 patients in 7 countries

4 sufficiency studies with 481 patients in 4 countries

Results to date are contradictory. Several studies show higher mortality, however counfounding by indication may be significant — patients prescribed folic acid may have significantly higher risk on average. Folic acid may not be the best form for supplementation.

COVID-19 VITAMIN B9 STUDIES. JUL 2023. C19EARLY.ORG/B9



Vitamin B9 COVID-19 studies. Results to date are contradictory. Several studies show higher mortality, however counfounding by indication may be significant – patients prescribed folic acid may have significantly higher risk on average. Studies independent of prescriptions based on patient condition show positive results *[Deschasaux-Tanguy, Farag]*, as do sufficiency studies. Folic acid may not be the most effective or safest form for supplementation *[Scaglione]*. Studies show that a significant fraction of people have genetic variations limiting the ability to convert folic acid to the active form. Recent: Chen Abdulrahman Scaglione Serseg Kumar Eskandari Ugurel. Submit updates/ corrections.

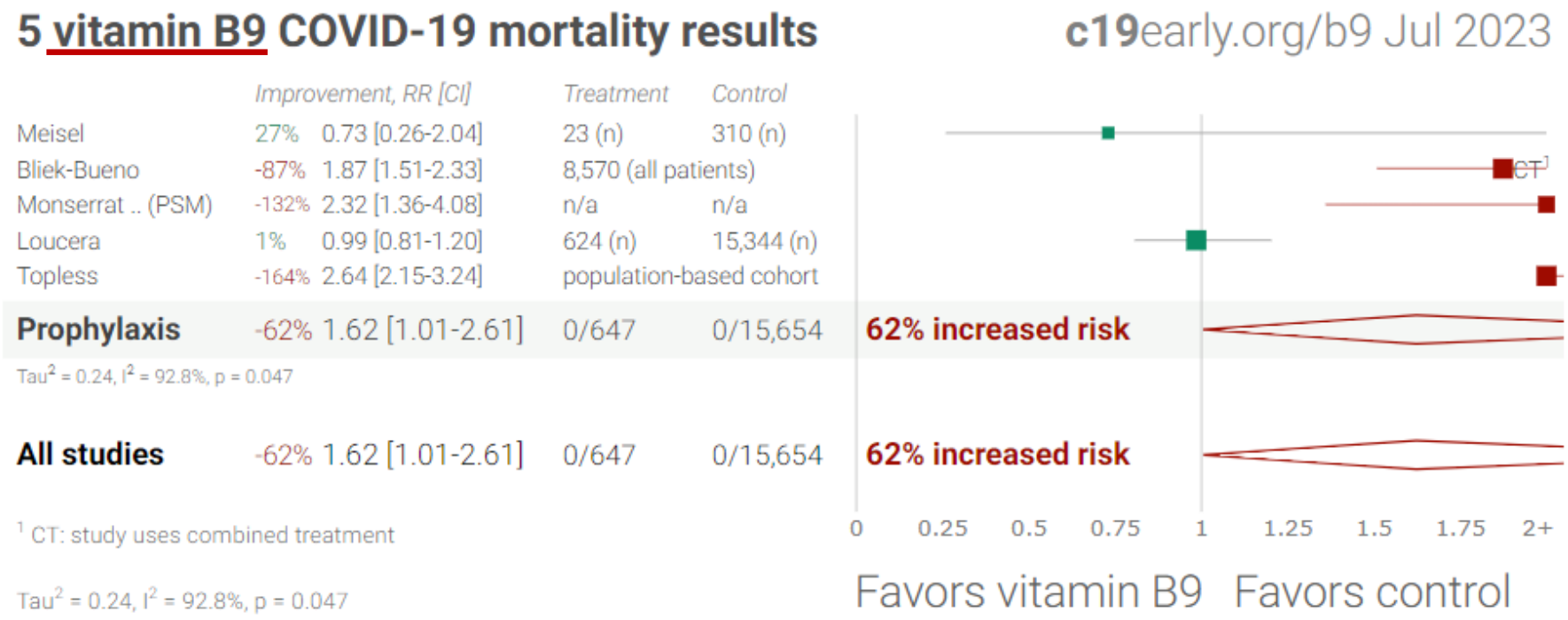
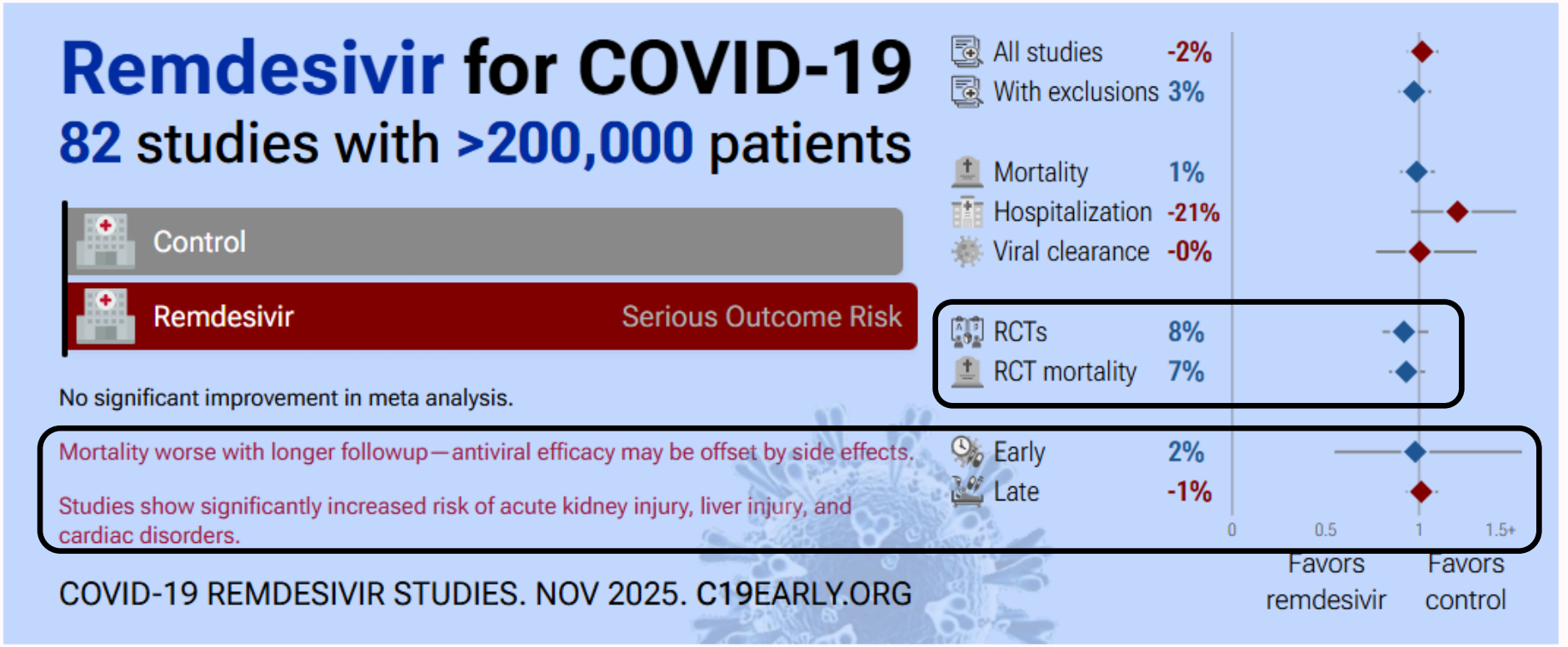


Figure 4. Random effects meta-analysis for mortality results.

Accesso
28-11-’25



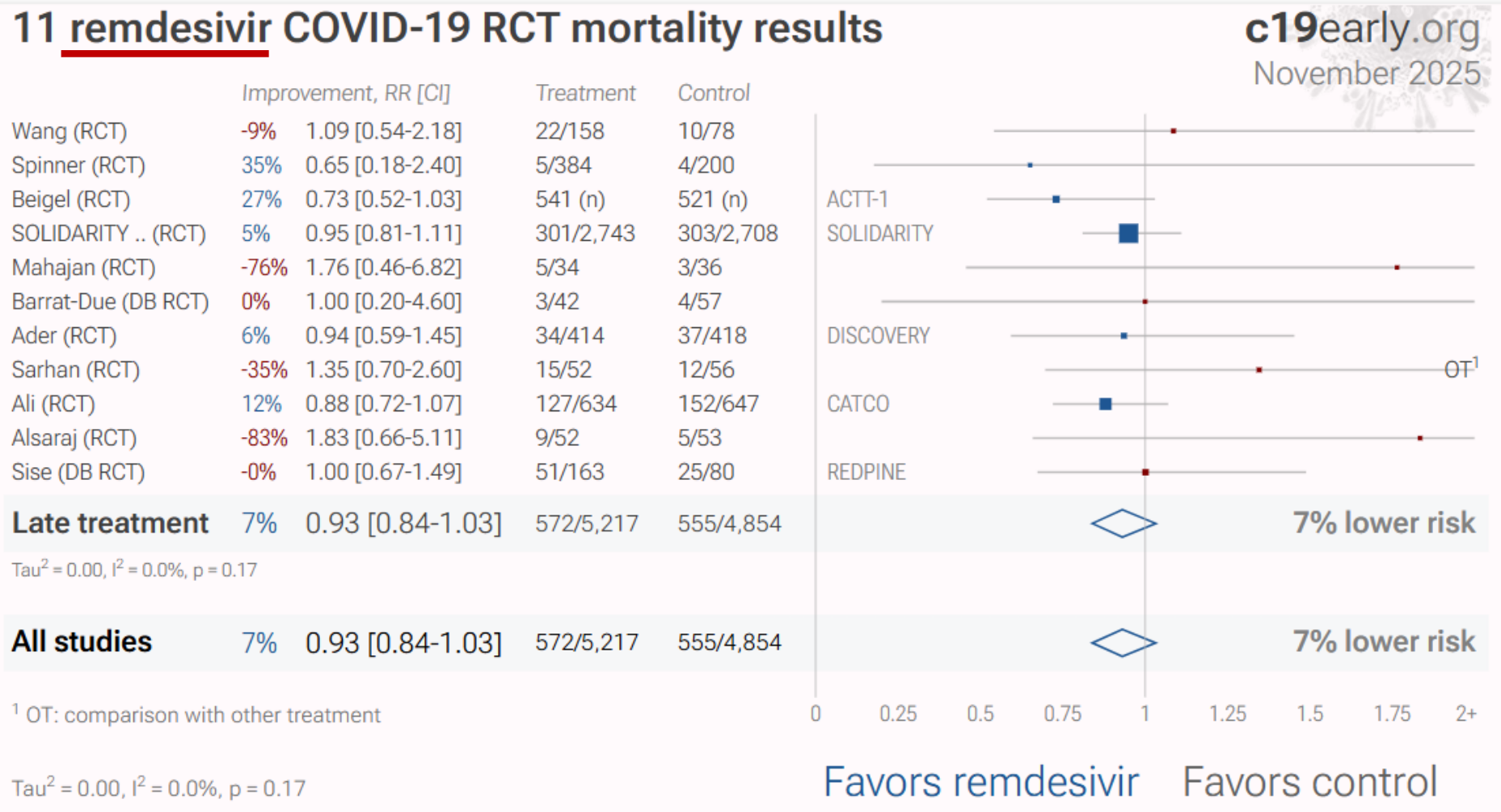


Fig. 15. **Random effects meta-analysis for RCT mortality results.**

JAMA Network Open
2021;4(7):e2114741
doi:10.1001/jamanetworkopen.2021.14741

Original Investigation | Infectious Diseases

Association of Remdesivir Treatment With Survival and Length of Hospital Stay Among US Veterans Hospitalized With COVID-19

Michael E. Ohl, MD, MSPH; Donald R. Miller, ScD; Brian C. Lund, PharmD; Takaaki Kobayashi, MD; Kelly Richardson Miell, PhD; Brice F. Beck, MA; Bruce Alexander, Pha
Kristina Crothers, MD; Mary S. Vaughan Sarrazin, PhD

Abstract

IMPORTANCE Randomized clinical trials have yielded conflicting results about the effects of remdesivir therapy on survival and length of hospital stay among people with COVID-19.

OBJECTIVE To examine associations between remdesivir treatment and survival and length of hospital stay among people hospitalized with COVID-19 in routine care settings.

Key Points

Question Is remdesivir treatment associated with improved survival or shortened hospitalizations among people with COVID-19 in routine care settings?

Età media 67 anni, soprattutto maschi, ricoverati COVID$^+$ in reparti con cure di routine della Veteran Administration, appaiamento con *propensity score*.

Remdesivir non è risultato associato con mortalità a 30 giorni (12,2% vs 10,6%), simile nei pz che hanno ricevuto desametazone all'inizio di remdesivir (aHR 1,19, n.s.);

ed associato con tempi mediani di dimissione più lunghi (6 giorni vs 3 nei controlli)

Conclusione

Possibile maggior uso dei letti ospedalieri senza miglioramenti nella sopravvivenza.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 12, 2019 VOL. 381 NO. 24

A Randomized, Controlled Trial of Ebola Virus Disease Therapeutics

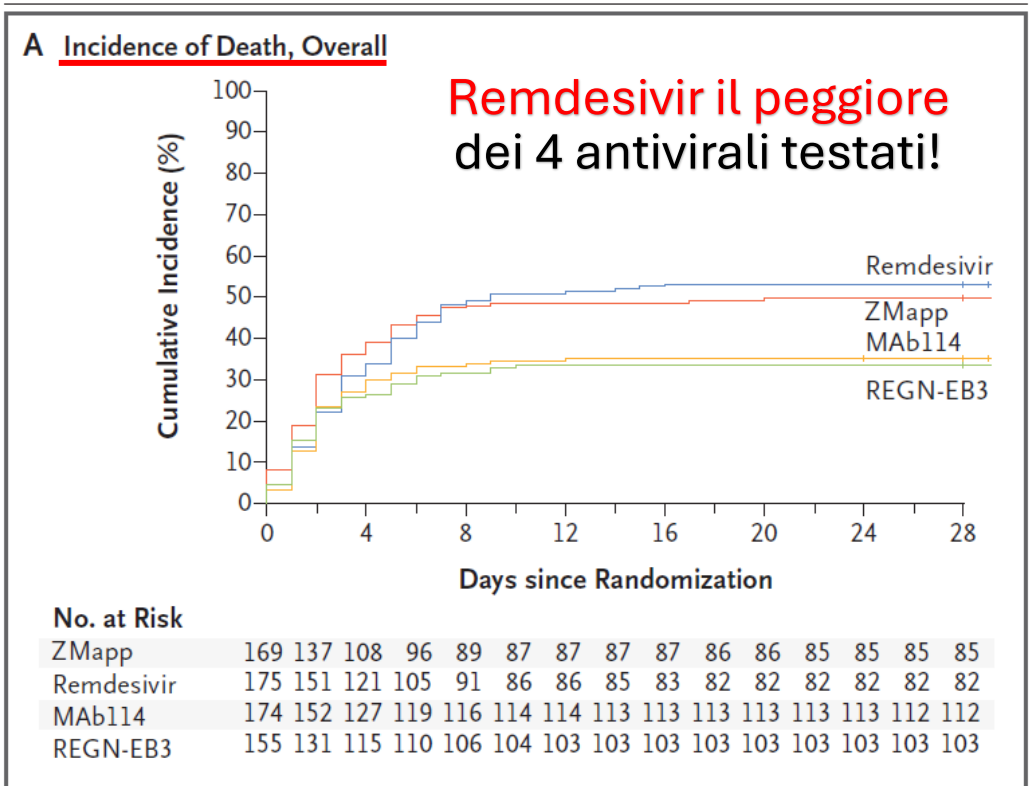
Sabue Mulangu, M.D., Lori E. Dodd, Ph.D., Richard T. Davey, Jr., M.D., Olivier Tshiani Mbaya, M.D., ...

Figure 1. Cumulative Incidence of Death.

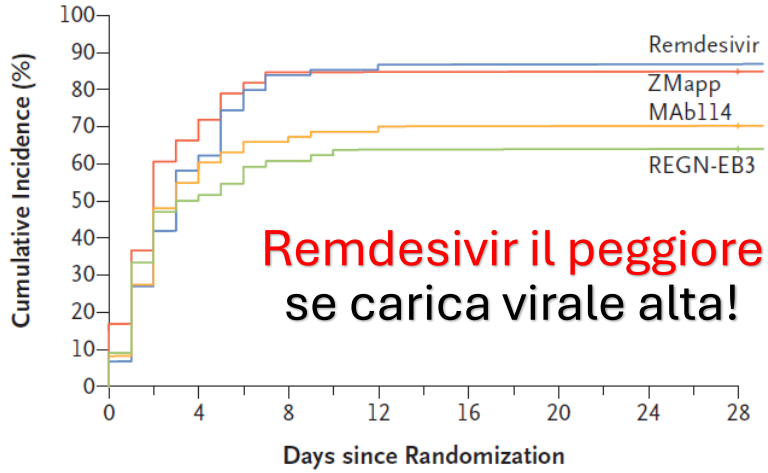
Shown are Kaplan–Meier estimates of the cumulative incidence of death. Panel A shows the estimates in the overall population, Panel B the estimates in patients who had a nucleoprotein cycle-threshold (Ct) value of 22 or less at baseline (corresponding to a high viral load), and Panel C the estimates in patients who had a Ct value of more than 22 at baseline (corresponding to a low viral load).

the duration of symptoms at enrollment, baseline nucleoprotein Ct value, and serum creatinine level all remained significant prognostic indicators of death (Table 4). Across all models, the effect estimates of treatment with MAb114 and REGN-EB3 remained significant (Table 3 and 4).

The percentage of patients who died was

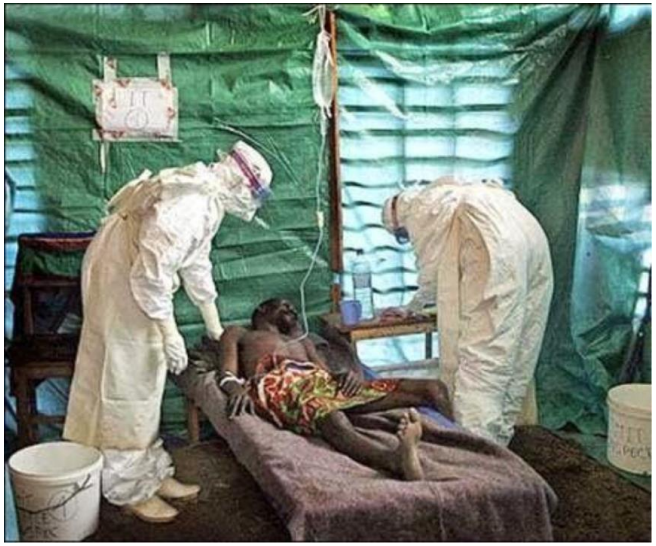


B Incidence of Death, Patients with a High Viral Load

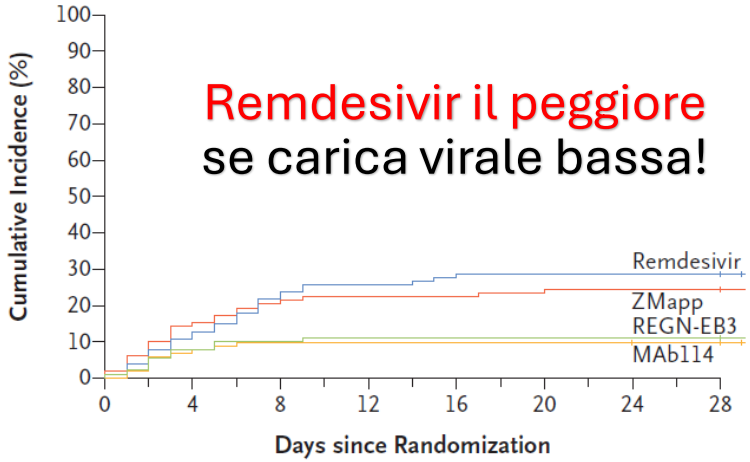


Remdesivir il peggiore
se carica virale alta!

No. at Risk															
ZMapp	71	45	24	15	11	11	11	11	11	11	11	11	11	11	11
Remdesivir	75	55	32	20	13	12	12	11	11	11	11	11	11	11	11
MAb114	73	53	33	27	25	23	23	22	22	22	22	22	22	22	22
REGN-EB3	66	44	33	30	26	25	24	24	24	24	24	24	24	24	24



C Incidence of Death, Patients with a Low Viral Load



Remdesivir il peggiore
se carica virale bassa!

No. at Risk															
ZMapp	98	92	84	81	78	76	76	76	76	75	75	74	74	74	74
Remdesivir	100	96	89	85	78	74	74	74	72	71	71	71	71	71	71
MAb114	101	99	94	92	91	91	91	91	91	91	91	91	91	90	90
REGN-EB3	89	87	82	80	80	79	79	79	79	79	79	79	79	79	79

Quotidiano Sanità 30 aprile 2020

Coronavirus. “Risultati altamente significativi” di remdesivir: i pazienti si rimettono più velocemente

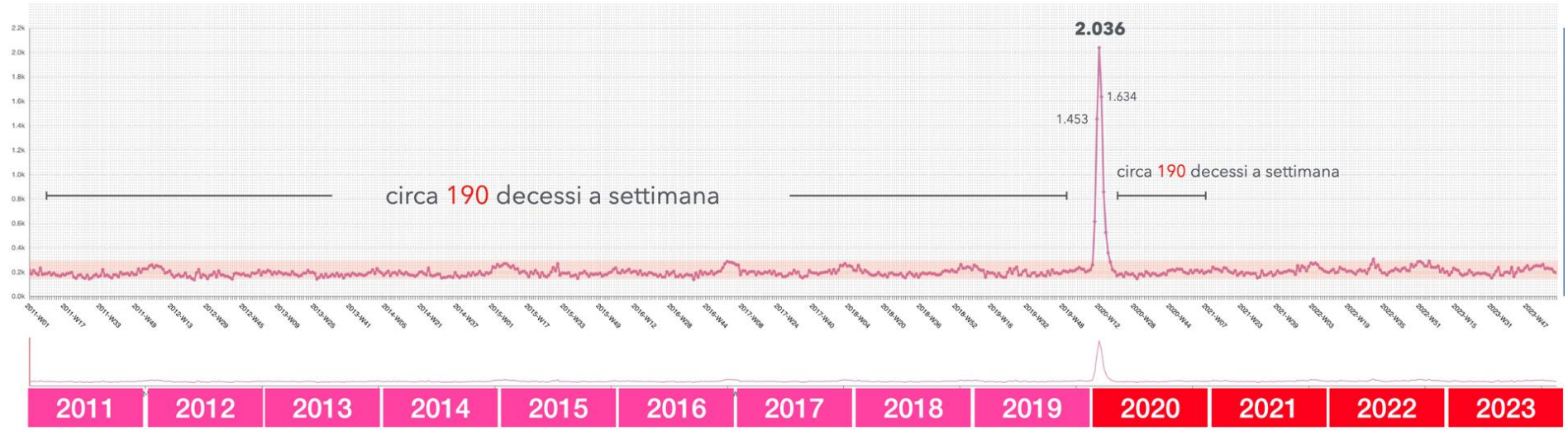
Il Dr. Anthony Fauci, punto di riferimento in America per quanto riguarda le malattie infettive, ha dichiarato che il remdesivir, farmaco antivirale sperimentale di Gilead Sciences, diventerà lo standard di cura per Covid-19, dopo che sono stati resi noti, mercoledì, i primi risultati degli studi clinici che dimostrano come il farmaco permetta una remissione più rapida dei pazienti. Si tratta però di dati preliminari, che vanno confrontati con altri studi che hanno fornito risultati contrastanti sull’efficacia del farmaco.

Remdesivir potrebbe essere il nuovo standard di cura contro Covid-19,
secondo Fauci
(*AboutPharma 30-2020*)

18 marzo 2020

Settimana 12 - 2020

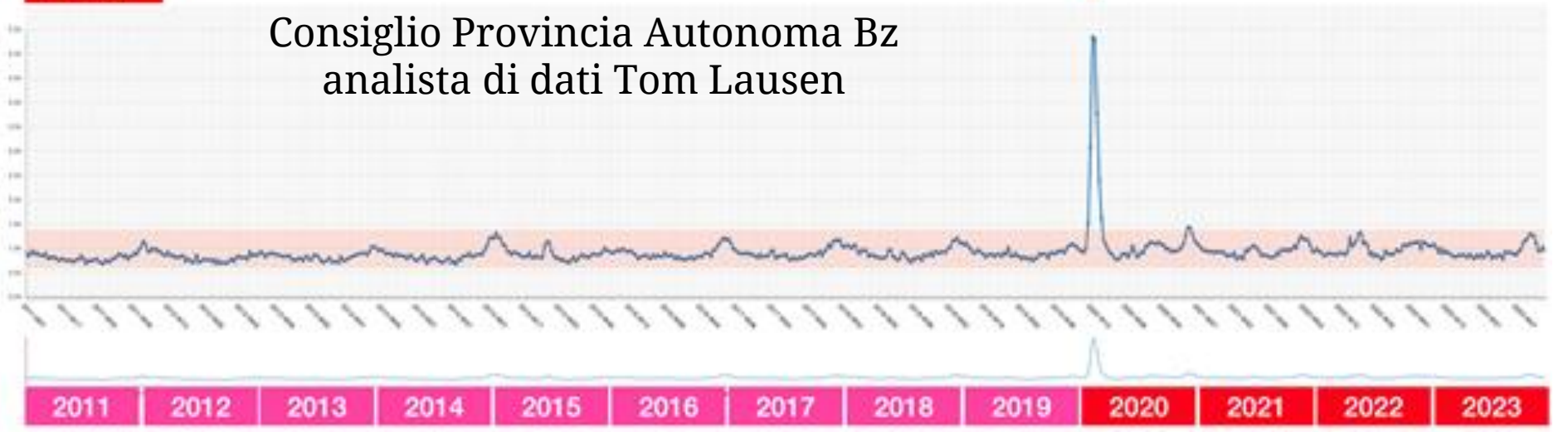
Bergamo



WEEK 12 - 2020

Madrid

Consiglio Provincia Autonoma Bz
analista di dati Tom Lausen



Overview | COVID-19 rapid guideline: managing symptoms (including at the end of life) in the community | Guidance | NICE (archive.org)

COVID-19 rapid guideline: managing symptoms (including at the end of life) in the community

NICE guideline [NG163]Published date: **03 April 2020** Guidance Tools and resources

4. Managing cough

Table 1 Treatments for managing cough in adults aged 18 years and over

Treatment	Dosage
Initial management: use simple non-drug measures, for example taking honey	A teaspoon of honey (dose insufficiente) 
First choice, only if cough is distressing: codeine linctus (15 mg/5 ml) or codeine phosphate tablets (15 mg, 30 mg)	15 mg to 30 mg every 4 hours as required, up to 4 doses in 24 hours If necessary, increase dose to a maximum of 30 mg to 60 mg 4 times a day (maximum 240 mg in 24 hours)
Second choice, only if cough is distressing: morphine sulfate oral solution (10 mg/5 ml)	2.5 mg to 5 mg when required every 4 hours Increase up to 5 mg to 10 mg every 4 hours as required If the patient is already taking regular morphine increase the regular dose by a third

5 Managing fever

5.1 - Be aware that, on average, fever is most common 5 days after exposure to the infection.

5.3 - Do not use antipyretics with the sole aim of reducing body temperature

5.4 - Advise patients to take **paracetamol** if they have fever and other symptoms that antipyretics would help treat. Tell them to **continue only while the symptoms of fever and the other symptoms are present**.
Until there is more evidence, paracetamol is preferred to non-steroidal anti-inflammatory drugs (NSAIDs) for patients with COVID-19

Table 2 Antipyretics for managing fever in adults and children

Treatment	Dosage
Adults (18 years and over): paracetamol (istruzioni del tutto inadeguate)	0.5 g to 1 g every 4 to 6 hours, maximum 4 g per day (dosi a rischio di eccesso)
Children and young people over 1 month and under 18 years: paracetamol	See the dosing information on the pack or the BNF for children

6 Managing breathlessness

6.5 - Consider an opioid and benzodiazepine combination (see tables 4 and 5) for patients with COVID-19 who:

- are at the end of life and
- have moderate to severe breathlessness and
- are distressed

Table 4 End-of-life treatments for managing breathlessness for patients aged 18 years and over

Clinical scenario	Treatment
Opioid naive (not currently taking opioids) and able to swallow	**Oral treatment** Morphine sulfate immediate-release 2.5 mg to 5 mg every 2 to 4 hours as required or morphine sulfate modified-release 5 mg twice a day, increased as necessary (maximum 30 mg daily)
Already taking regular opioids for other reasons (for example, pain relief)	**Oral treatment** Morphine sulfate immediate-release 5 mg to 10 mg every 2 to 4 hours as required or one twelfth of the 24-hour dose for pain, whichever is greater
Unable to swallow	**Parenteral treatment** Morphine sulfate 1 mg to 2 mg subcutaneously every 2 to 4 hours as required, increasing the dose as necessary

NB: Linee guida poi ritirate...

Copiate da pz tumorali in fin di vita, ma questi erano pz con problemi respiratori...

Add a benzodiazepine if required

For breathlessness and anxiety: lorazepam 0.5 mg sublingually when required (maximum 4 mg daily)

Reduce the dose to 0.25 mg to 0.5 mg in elderly or debilitated patients (maximum 2 mg in 24 hours)

For associated agitation or distress: midazolam 2.5 mg to 5 mg subcutaneou[illegible] when required (see BNF for more details on dosages)

Sedation and opioid use should not be withheld because of a fear of causi[illegible] respiratory depression

Sedation and opioid use should not be withheld because of an inappropriate fear of causing respiratory depression.

NON HAI CAPITO?