# COVID 19 TREATMENT GUIDELINES

FROM THE NATIONAL INSTITUTES OF HEALTH
COVID19TREATMENTGUIDELINES.NIH.GOV

# Guidelines Document

- 351 Page Document
- Most up-to-date guideline (mentioned on page 1 of the document)
- Read the Table of Contents. What is being addressed first? Where does Budesonide and Vitamin C,D and Zinc fall? In the back.

# Budesonide (Pg 205)

- **NIH's recommendation**: "There is insufficient evidence for the Panel to recommend either for or against the use of inhaled budesonide for the treatment of COVID-19." pg 205
- **Rationale**: Two Trials. "Results of these trials suggest that in adult outpatients with mild COVID-19, initiation of inhaled budesonide may reduce the need for urgent care or emergency department assessment or hospitalization and reduce time to recovery."
- BUT…… "The findings from these trials should be interpreted with caution given the open-label design of the studies, incomplete data, and other limitations."

# Why is Budesonide not Recommended? (Pg 205)

**(1) Incomplete Data** – Tell me this isn't the dumbest thing you have read: "The study was halted early after an independent statistical analysis determined that having additional participants would not alter the trial outcome"

•Ok, so you are telling me they halted this study because having more people added to it would not alter the outcome? Ok, what does that have to do with anything. You clearly have an OUTCOME (complete data) but let's call it incomplete because adding more people won't affect the COMPLETE DATA?!

# Why is Budesonide not Recommended? (Pg 205)

(2) **Other Limitations**: Table 4B (page 221) tells us what "other limitations are:

- Open-Label Study
- Small Sample Size – WTF?!
- Completed in a single UK region – WTF cares?!

# Why is Budesonide not Recommended? (Pg 205)

Summary on why Budesonide is not recommended:
1.Sample size is too small. (But you said adding more participants wouldn’t change anything.)
2.The study was halted early. It was halted early because you knew adding more participants to the study wouldn't change the results (complete data) you clearly already have!

# Why is Budesonide not Recommended?

## Table 4b. Inhaled Corticosteroids: Selected Clinical Data

*Last Updated: August 4, 2021*

The clinical trials described in this table do not represent all the trials that the Panel reviewed while developing the recommendations for inhaled corticosteroids. The studies summarized below are those that have had the greatest impact on the Panel's recommendations.

| Study Design | Methods | Results | Limitations and Interpretation |
|---|---|---|---|
| **STOIC: Inhaled Budesonide for the Treatment of Early COVID-19**[1] | | | |
| Open-label, Phase 2, RCT in the United Kingdom (n = 146) | **Key Inclusion Criteria:**<br>• Outpatients aged ≥18 years<br>• Duration of symptoms ≤7 days<br>**Key Exclusion Criteria:**<br>• Use of inhaled or systemic glucocorticoids within the past 7 days<br>• Known allergy or contraindication to budesonide<br>**Interventions**<br>*1:1 Randomization:*<br>• Usual care (supportive therapy)<br>• Usual care plus budesonide 800 mcg inhaled twice daily until symptom resolution<br>**Primary Endpoint:**<br>• COVID-19-related urgent care visit, including ED visit, or hospitalization | **Number of Participants:**<br>• ITT analysis: Budesonide (n = 73) and usual care (n = 73)<br>• Per-protocol analysis: Budesonide (n = 70) and usual care (n = 69)<br>**Participant Characteristics:**<br>• Mean age: 45 years<br>• 58% women<br>• Median number of comorbidities: 1; 9% had CVD, 5% had diabetes<br>• 95% with positive SARS-CoV-2 RT-PCR<br>• Median duration of symptoms prior to randomization: 3 days<br>**Outcomes:**<br>• Median duration of budesonide use: 7 days.<br>• COVID-19-related urgent care visits or hospitalizations occurred in 1 participant (1%) in the budesonide arm and 10 participants (14%) in the usual care arm (difference in proportions 13%; 95% CI, 4–22; $P$ = 0.004). Relative risk reduction of 91% for budesonide, NNT of 8. | **Key Limitations:**<br>• Open-label study<br>• Small sample size<br>• Completed in a single UK region<br>• The study was halted early after an independent statistical analysis determined that having additional participants would not alter the trial outcome.<br>**Interpretation:**<br>• In adult outpatients with mild COVID-19, inhaled budesonide may reduce the need for urgent medical care defined by urgent care or ED assessment and/or hospitalization. These findings should be interpreted with caution given the above limitations. |

# Ok, enough of what the NIH says about their recommendation of Budesonide. Let's read the study!

Pg 208, #30 – Ramakrishnan S, Nicolau

**Findings**: …"

1.Clinical recovery was 1 day shorter in the budesonide group compared with the usual care group.
2.The mean proportion of days with a fever in the first 14 days was lower in the budesonide group
3.The proportion of participants with at least 1 day of fever was lower in the budesonide group when compared with the usual care group.
4.As-needed antipyretic medication was required for fewer proportion of days in the budesonide group compared with the usual care group
5.Fewer participants randomly assigned to budesonide had persistent symptoms at days 14 and 28 compared with participants receiving usual care.
6.The mean total score change in the CCQ and FLUPro over 14 days was significantly better in the budesonide group compared with the usual care group
7.Budesonide was safe, with only five (7%) participants reporting self-limiting adverse events. "

**Interpretation:** "Early administration of inhaled budesonide reduced the likelihood of needing urgent medical care and reduced time to recovery after early COVID-19."

# Summarize Budesonide

Based on study, “budesonide reduced the likelihood of needing urgent medical care and reduced time to recovery.” But, the panel will not recommend it because the sample size of these amazing results were too small and we could have added more but it wouldn’t have changed the amazing results.

# Supplements (pg 289)

**So nice of the NIH to summarize their recommendations of ALL 3 VITAMINS in one little box. What do they have to say?**

## Supplements

*Last Updated: February 11, 2021*

| Summary Recommendations |
| --- |
| **Vitamin C**<br>• There is insufficient evidence for the COVID-19 Treatment Guidelines Panel (the Panel) to recommend either for or against the use of vitamin C for the treatment of COVID-19. |
| **Vitamin D**<br>• There is insufficient evidence for the Panel to recommend either for or against the use of vitamin D for the treatment of COVID-19. |
| **Zinc**<br>• There is insufficient evidence for the Panel to recommend either for or against the use of zinc for the treatment of COVID-19.<br>• The Panel **recommends against** using zinc supplementation above the recommended dietary allowance for the prevention of COVID-19, except in a clinical trial **(BIII)**. |
| **Rating of Recommendations:** A = Strong; B = Moderate; C = Optional<br>**Rating of Evidence:** I = One or more randomized trials without major limitations; IIa = Other randomized trials or subgroup analyses of randomized trials; IIb = Nonrandomized trials or observational cohort studies; III = Expert opinion |

**Let's see how the studies a line with your recommendations…**

# Vitamin C Studies (pg 291)

***Intravenous Vitamin C Alone in Patients With COVID-19***

A pilot clinical trial in China randomized 56 adults with COVID-19 in the intensive care unit to receive intravenous (IV) vitamin C 24 g per day or placebo for 7 days. The study was terminated early due to a reduction in the number of cases of COVID-19 in China. Overall, the study found no differences between the arms in mortality, the duration of mechanical ventilation, or the change in median sequential organ failure assessment (SOFA) scores. The study reported improvements in oxygenation (as measured by the ratio of arterial partial pressure of oxygen to fraction of inspired oxygen [$PaO_2/FiO_2$]) from baseline to Day 7 in the treatment arm that were statistically greater than those observed in the placebo arm (+20.0 vs. -51.9; $P = 0.04$).[4]

**Ok, so 24g (or 2,400mg) of vitamin C is not bad. Let's see how it plays out.**

**They terminated the study early due a reduction in the number of cases of covid in China? How does that affect the 56 adults you were in the middle of testing? That's no reason to end the trial Was the results so great you didn't want to share them?**

**Hey, at least we found out it improves oxygenation!**

# Vitamin C Studies (pg 291)

***Intravenous Vitamin C Alone in Patients Without COVID-19***

A small, three-arm pilot study compared two regimens of IV vitamin C to placebo in 24 critically ill patients with sepsis. Over the 4-day study period, patients who received vitamin C 200 mg/kg per day and those who received vitamin C 50 mg/kg per day had lower SOFA scores and lower levels of proinflammatory markers than patients who received placebo.[5]

In a randomized controlled trial in critically ill patients with sepsis-induced ARDS (n = 167), patients who received IV vitamin C 200 mg/kg per day for 4 days had SOFA scores and levels of inflammatory markers that were similar to those observed in patients who received placebo. However, 28-day mortality was lower in the treatment group (29.8% vs. 46.3%; $P = 0.03$), coinciding with more days alive and free of the hospital and the intensive care unit.[6] A post hoc analysis of the study data reported a difference in median SOFA scores between the treatment group and placebo group at 96 hours; however, this difference was not present at baseline or 48 hours.[7]

**What the hell?! What was the point of this study? You gave some 200 mg of vitamin C (half of what you can get in a single vitamin c pill from Walmart) .**

**AND THEN 50 MG OF VITAMIN C? A glass of Minute Maid orange juice has more vitamin c than that!!!**

**And both groups still had lower levels of proinflammatory markers…**

# Vitamin D Study (Only one Study - pg 291)

***Randomized Clinical Trial of Vitamin D Versus Placebo in Patients With Moderate to Severe COVID-19***

In a double-blind, placebo-controlled randomized trial that was conducted at two sites in Brazil, 240 hospitalized patients with moderate to severe COVID-19 received either a single dose of 200,000 international units of vitamin $D_3$ or placebo.[10] Moderate to severe COVID-19 was defined as patients with a positive result on a SARS-CoV-2 polymerase chain reaction test (or compatible computed tomography scan findings) and a respiratory rate >24 breaths/min, oxygen saturation <93% on room air, or risk factors for complications. The primary outcome in this study was the length of the hospital stay.

**They wanted to see if the length of stay in the hospital would be shortened with vitamin D. There was no significant difference between the same group. Wonder why? Maybe it's because you gave a SINGLE DOSE.**

# Supplements Summarized

**Well, supplements seem to work just fine. Sucks that they only gave 50-200 mg in one study and the other that had more vitamin c was “cut short.”**
**They also have not conducted a study on Vitamin C, Vitamin D & Zinc working together at the same time.**

**LET'S SEE A STUDY WHERE THEY USE ALL THREE VITAMINS AND BUDESONIDE! THESE STUDIES ONLY USED ONE AT A TIME.**