

PatrickHOLFORD

100% health for life

VITAMIN C

for COVID-19

prevention and treatment

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VITAMIN C FOR COVID

Vitamin C is a safe, inexpensive and highly effective anti-viral nutrient in the right amount, both for prevention of colds, reducing duration and severity, and for the treatment of COVID-19 in the acute phase with life-saving potential. Yet it is classified as 'fake information', not recommended by governments and rarely prescribed by doctors.

This has to change. Sign our petition.

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VITAMIN C
REVIEW

CONCERNS &
BIAS

[RESEARCH RESOURCE](#)

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Review

Vitamin C—An Adjunctive Therapy for Respiratory Infection, Sepsis and COVID-19

Patrick Holford ^{1,*}, Anitra C. Carr ² , Thomas H. Jovic ^{3,4}, Stephen R. Ali ^{3,4}, Iain S. Whitaker ^{3,4}, Paul E. Marik ⁵ and A. David Smith ⁶

Received: 19 October 2020; Accepted: 3 December 2020; Published: 7 December 2020



Abstract: There are limited proven therapies for COVID-19. Vitamin C's antioxidant, anti-inflammatory and immunomodulating effects make it a potential therapeutic candidate, both for the prevention and amelioration of COVID-19 infection, and as an adjunctive therapy in the critical care of COVID-19. This literature review focuses on vitamin C deficiency in respiratory infections, including COVID-19, and the mechanisms of action in infectious disease, including support of the stress response, its role in preventing and treating colds and pneumonia, and its role in treating sepsis and COVID-19. The evidence to date indicates that oral vitamin C (2–8 g/day) may reduce the incidence and duration of respiratory infections and intravenous vitamin C (6–24 g/day) has been shown to reduce mortality, intensive care unit (ICU) and hospital stays, and time on mechanical ventilation for severe respiratory infections. Further trials are urgently warranted. Given the favourable safety profile and low cost of vitamin C, and the frequency of vitamin C deficiency in respiratory infections, it may be worthwhile testing patients' vitamin C status and treating them accordingly with intravenous administration within ICUs and oral administration in hospitalised persons with COVID-19.

VITAMIN C FOR

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SHARE



University of Otago, Christchurch

Te Whare Wānanga o Otāgo ki Ōtautahi



Vitamin C and COVID-19 Research Resource

i This online resource is an up-to-date repository of published and ongoing vitamin C and COVID-19 research studies and related resources. Contact: Associate Professor Anitra Carr (anitra.carr@otago.ac.nz) if you wish to provide relevant resources or receive further information. Page last updated: 8 April 2021

- › Observational studies
- › Intervention trials
- › Registered clinical trials
- › Use in clinical practice
- › Case reports
- › Mechanisms of action
- › Review articles
- › In the media





- ▶ Almost all animals and many insects make it. It has probably existed as a key antioxidant since oxygen-based life.
- ▶ Animals make several grams a day bodyweight equivalent to man - much more when under viral attack or stress.
- ▶ Studies in healthy volunteers support a 200mg daily dose to produce a plasma level of circa 70 to 90 $\mu\text{mol/L}$ [8,9].
- ▶ Complete plasma saturation occurs between 1 - 12g daily - 3g every four hours, being the highest tolerated oral dose, giving a predicted peak plasma concentration of circa 220 $\mu\text{mol/L}$ [10].
- ▶ Higher intakes of vitamin C are likely to be needed during viral infections with 2–3 g/day required to maintain normal plasma levels between 60 and 80 $\mu\text{mol/L}$ [11,12].

Animals that don't make vit C



- ▶ Primates – which includes tarsiers, monkeys and apes, including humans
- ▶ Guinea pig and capybara – jungle dwelling rodents
- ▶ Fruit-eating bats – many, but not all, species of bats
- ▶ Red vented bulbul bird – a jungle dwelling, fruit eating bird
- ▶ The Amazonian ornamental 'oscar' fish and teleost fish

Should we be doing what animals that make vitamin C do under viral attack?



1 lemon = 83mg

A goat makes
up to 13 g a day
(156 lemons)

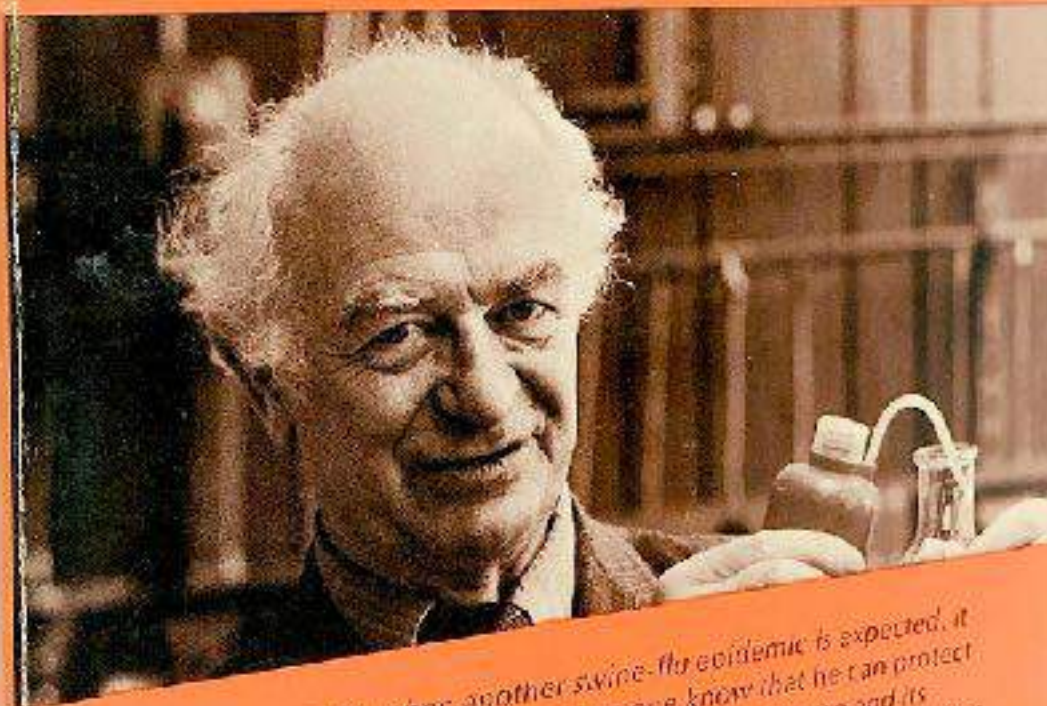
up to 100g under
stress/viral attack
(>1000 lemons)



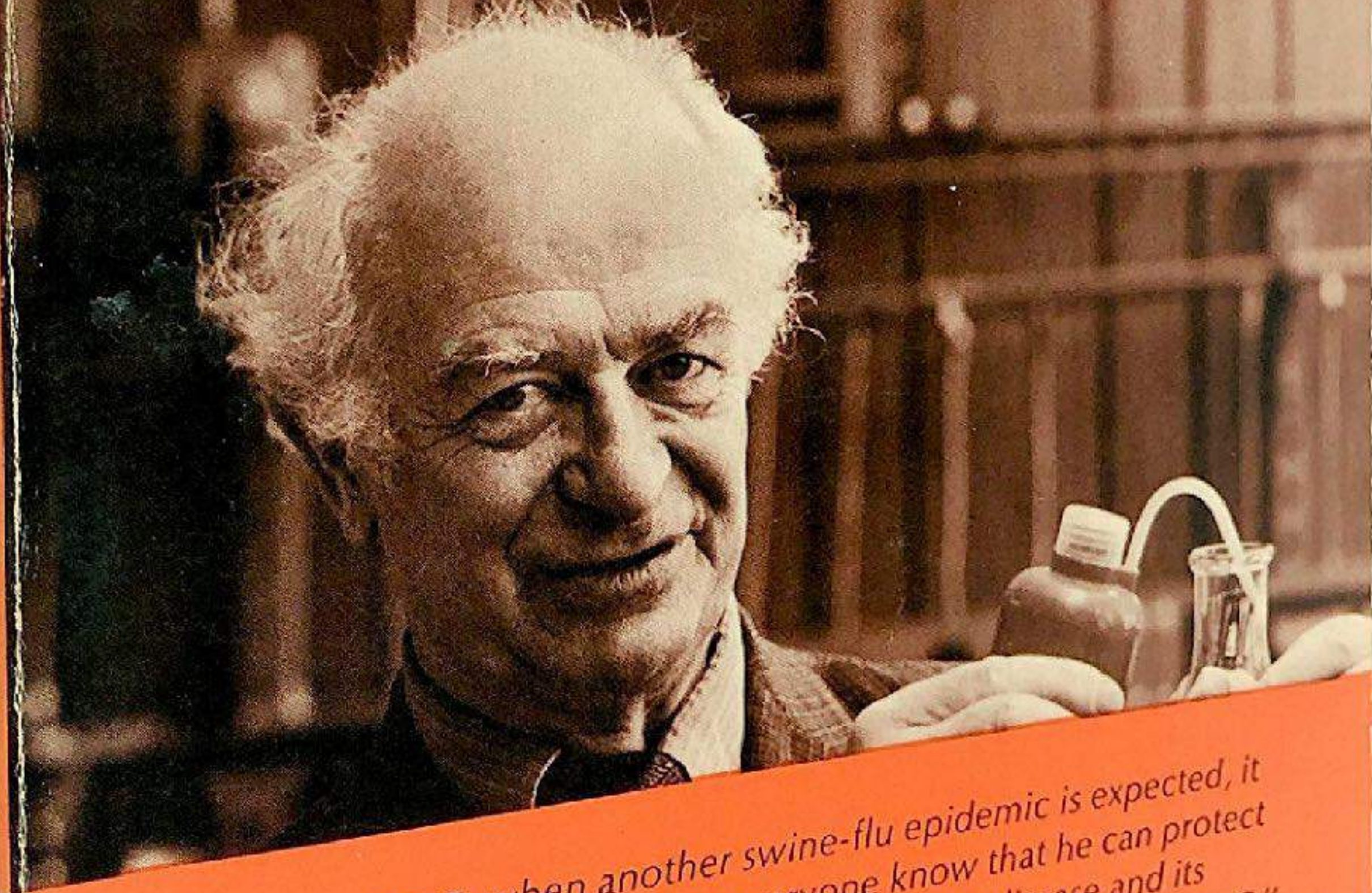
LINUS PAULING

1948 PRESIDENTIAL MEDAL FOR MERIT
1954 NOBEL PRIZE IN CHEMISTRY
1952 NOBEL PEACE PRIZE
1975 NATIONAL MEDAL OF SCIENCE

Vitamin C the Common Cold and the Flu

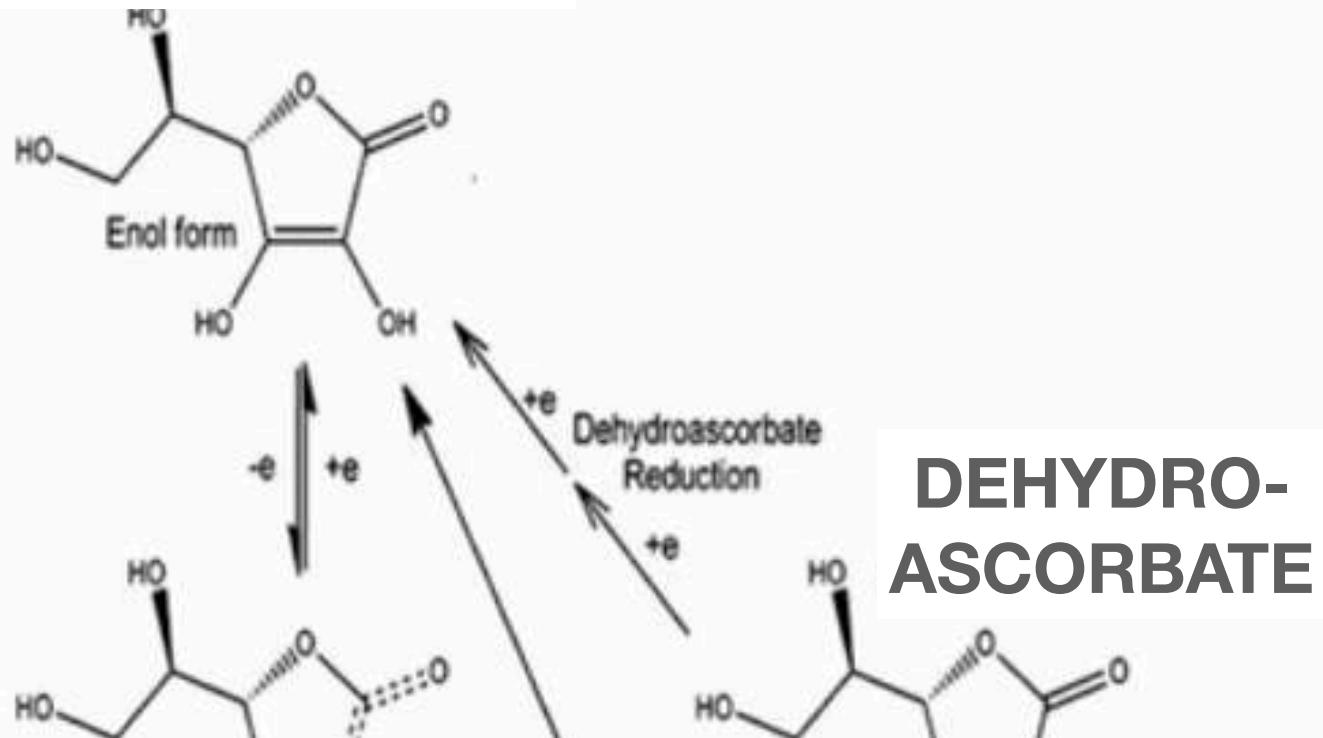


"In 1976-1977, when another swine-flu epidemic is expected, it is especially important that everyone know that he can protect himself to a considerable extent against the disease and its consequences by the use of this important nutrient, vitamin C."

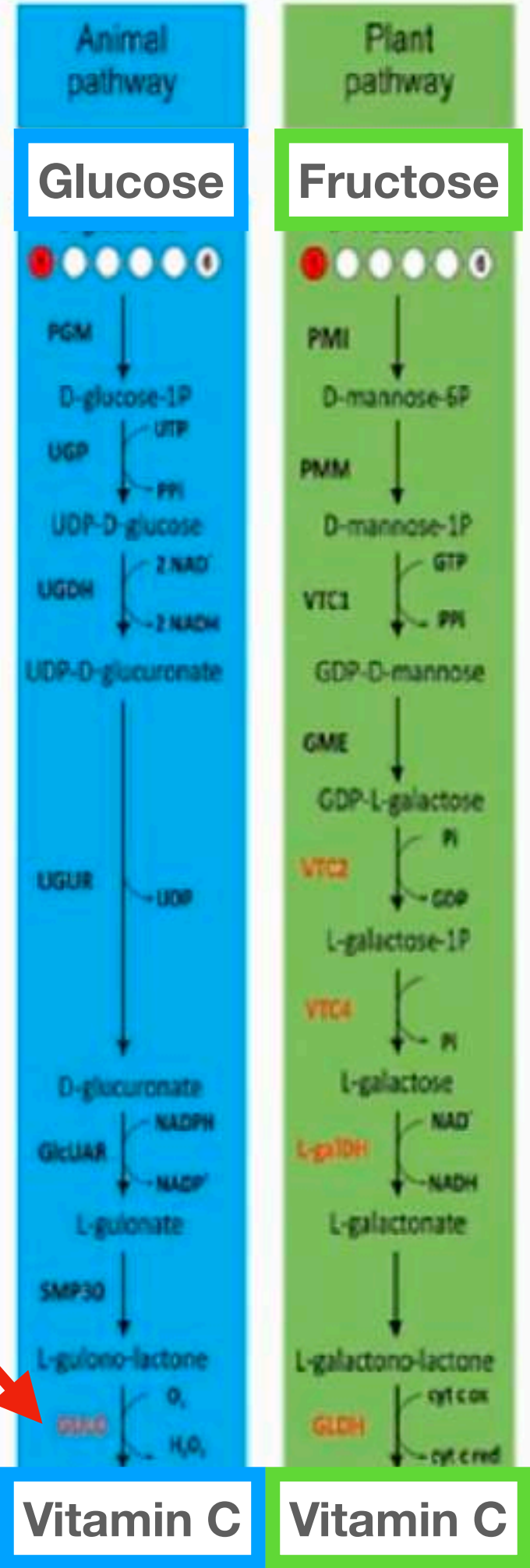
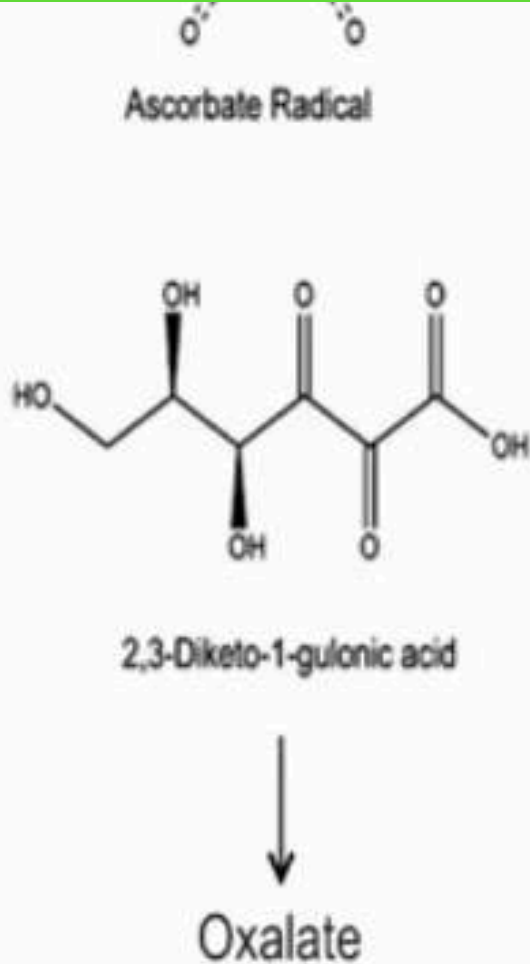


"In 1976-1977, when another swine-flu epidemic is expected, it is especially important that everyone know that he can protect himself to a considerable extent against the disease and its consequences by the use of this important nutrient, vitamin C."

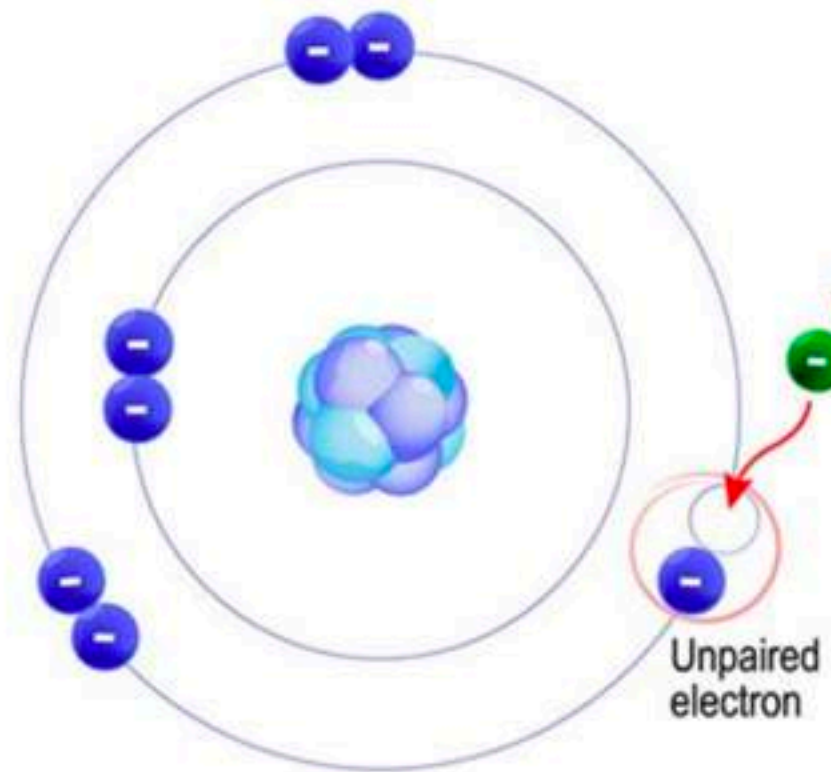
ASCORBIC ACID



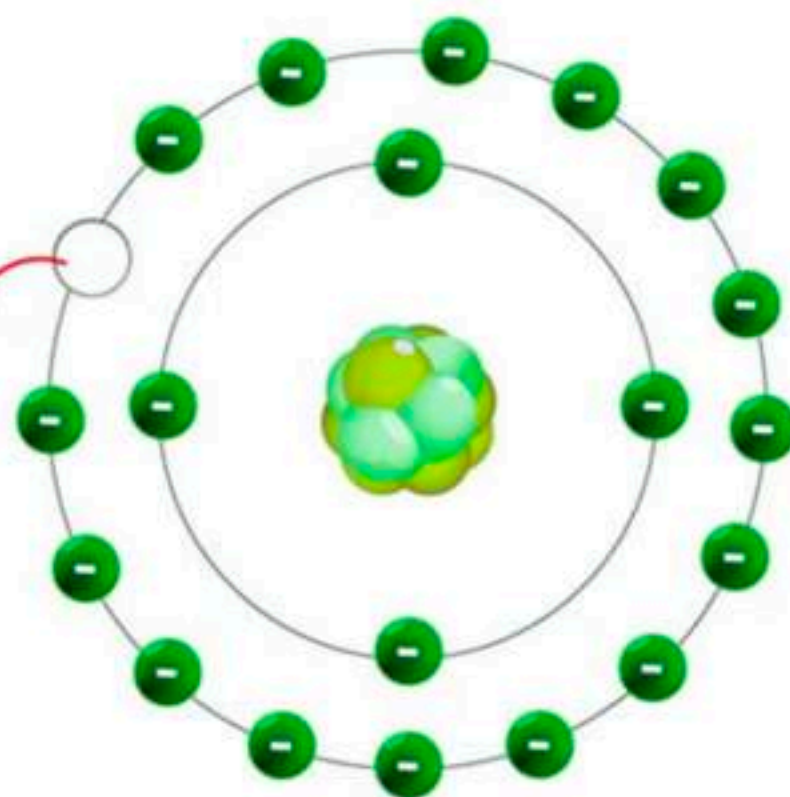
L-gulono-γ-lactone oxidase (GOLO)



Free radical



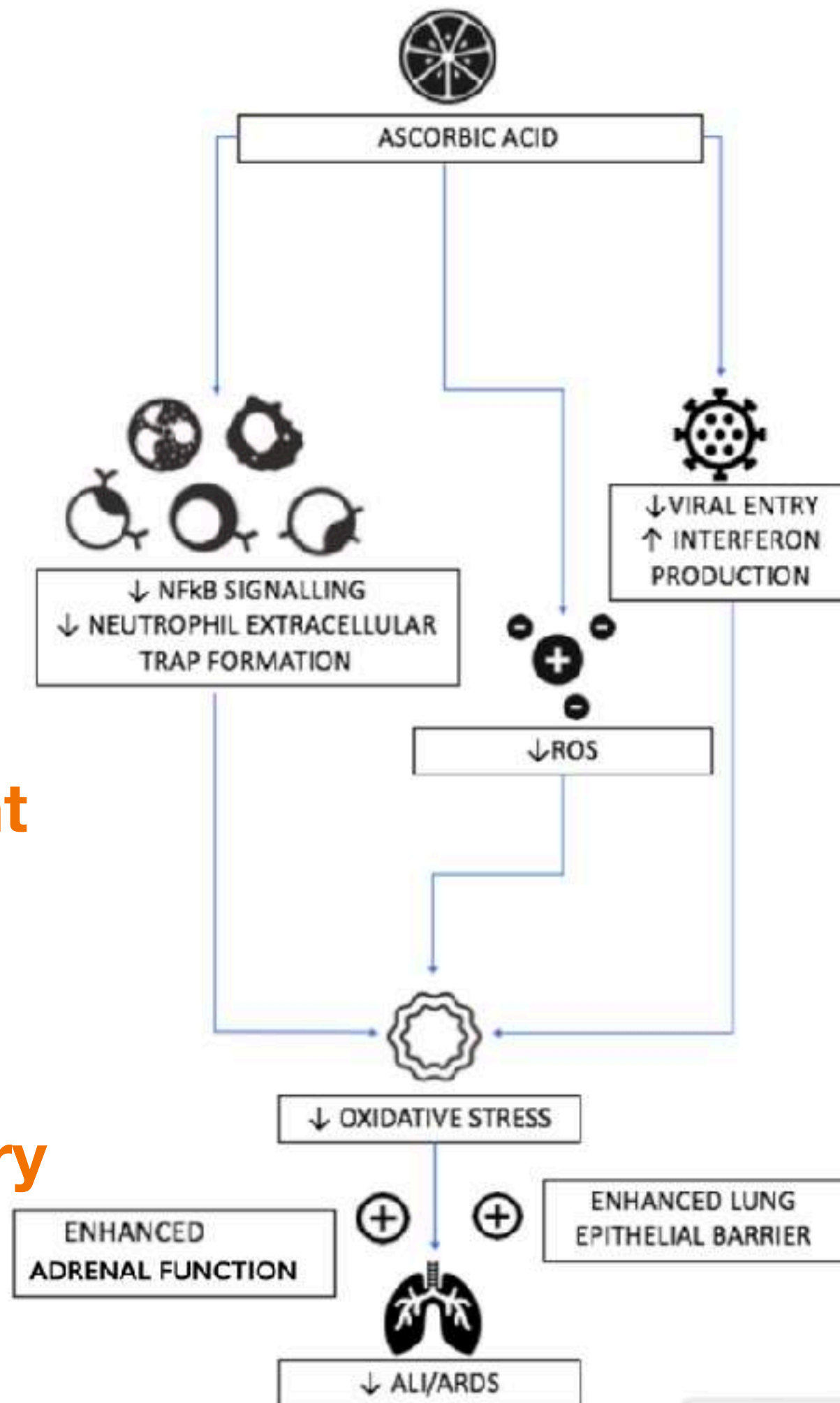
Antioxidant



anti-viral

anti-oxidant

anti-inflammatory



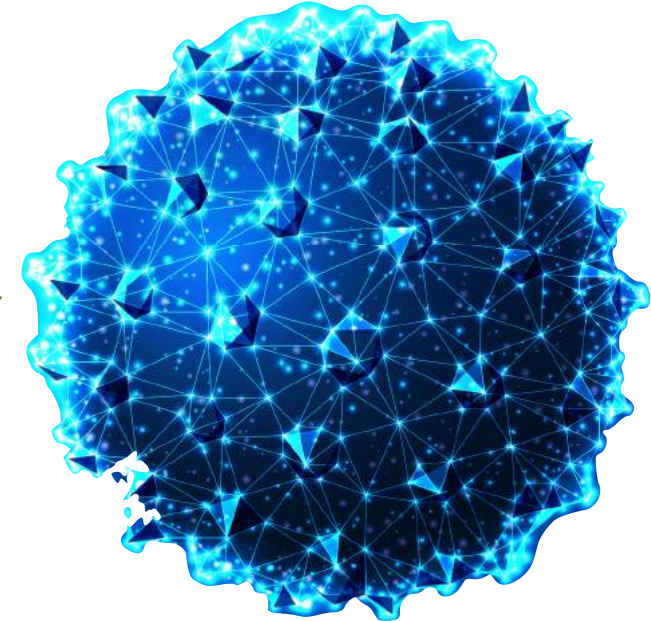
VITAMIN C

Neuraminidase spike ~~X~~ gets
virus out of cells

BLACK ELDERBERRY

Haemagglutinin spike ~~X~~ gets
virus into cells

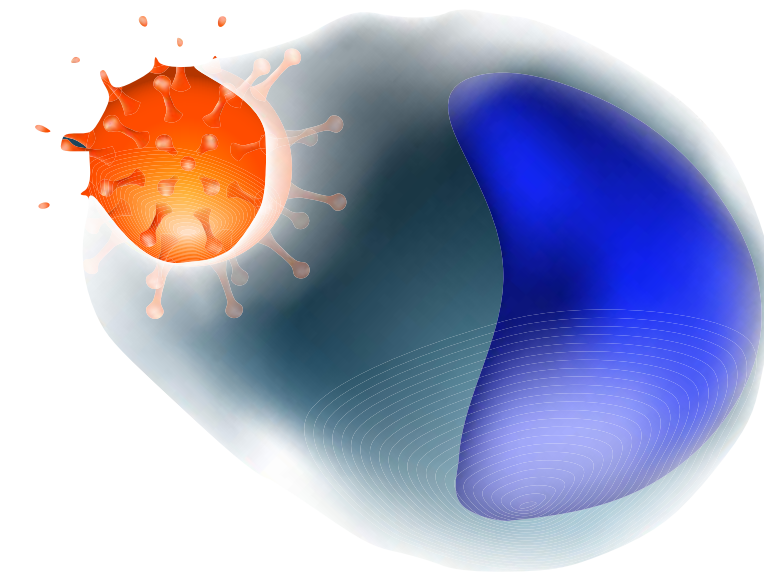
T-cells attack virus



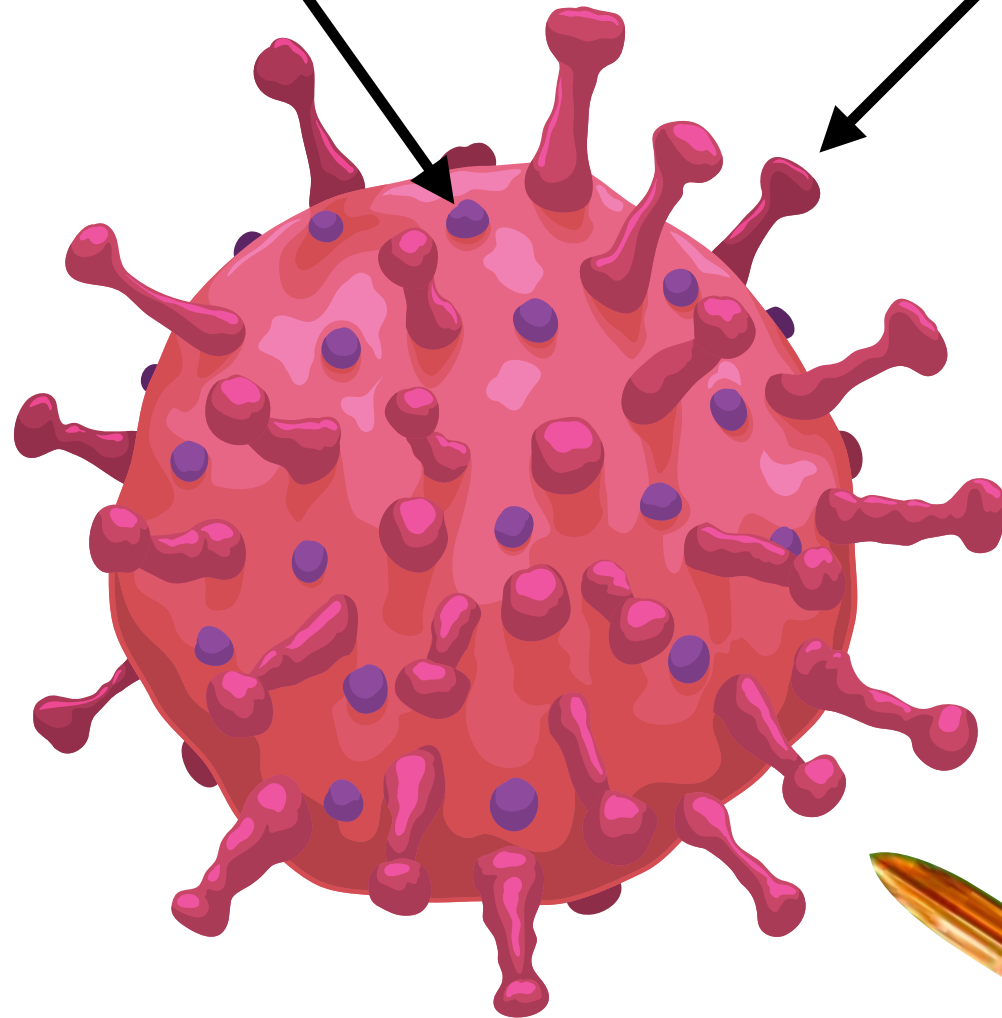
boosted by
**VITAMIN C, ZINC &
VITAMIN D**

SELENIUM & VIT C
reload

Macrophages
attack virus



infected cells
produces
interferon
boosted by
VITAMIN C



Three phases of action



- ▶ Maintaining sufficiency
- ▶ Reducing duration and severity of respiratory infection with high oral doses from onset of symptoms
- ▶ High dose oral and IV treatment of COVID-19

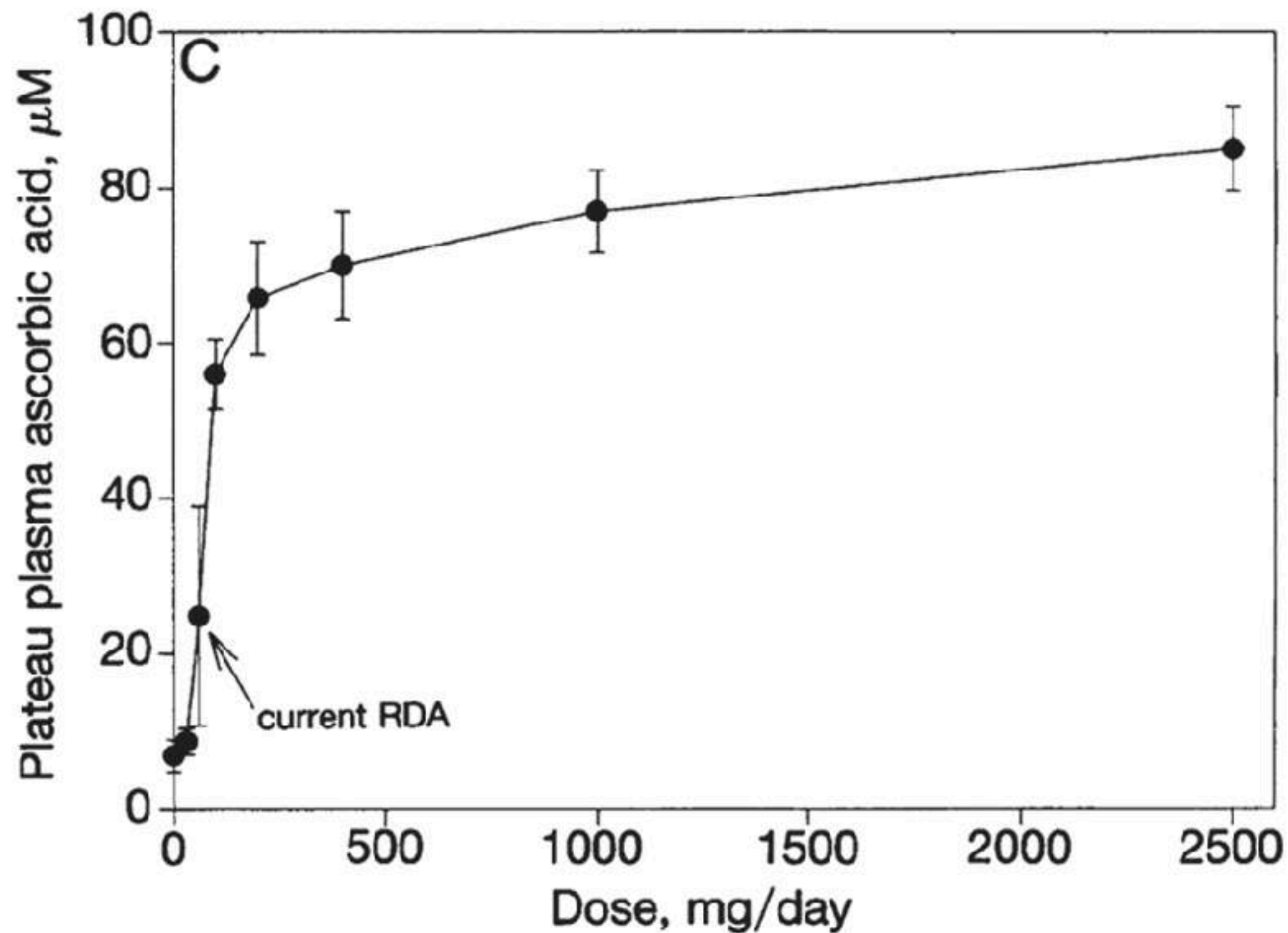


Figure 2 – Plasma vitamin C after supplementation up to 2.5g.

Data from M Levine et al, Proc Natl Acad Sci USA. 1996; 93:3704-3709. See reference 45. Reproduced with permission.

1. Vitamin C for prevention



- ▶ Supplementing up to 1g twice a day more than doubles or triples blood plasma levels compared to 'RDA' levels, even though the excess is finally excreted. This is a big advantage because it is much harder for viruses and certain pathogenic bacteria, to survive at these concentrations.
- ▶ Whether or not supplementing 500mg to 2g+ a day leads to less infection(eg PCR positive) or severity.
- ▶ An infected but asymptomatic person will infect 1 in 100 contacts and half of those infected will be asymptomatic. A symptomatic infected person will infect 4 out of 100, one of which will be asymptomatic. So 1 in 200 people exposed to an asymptotically infected person will become symptomatic compared to 1 in 33 exposed to a symptomatic infected person.

Plasma vs Urine vitamin C

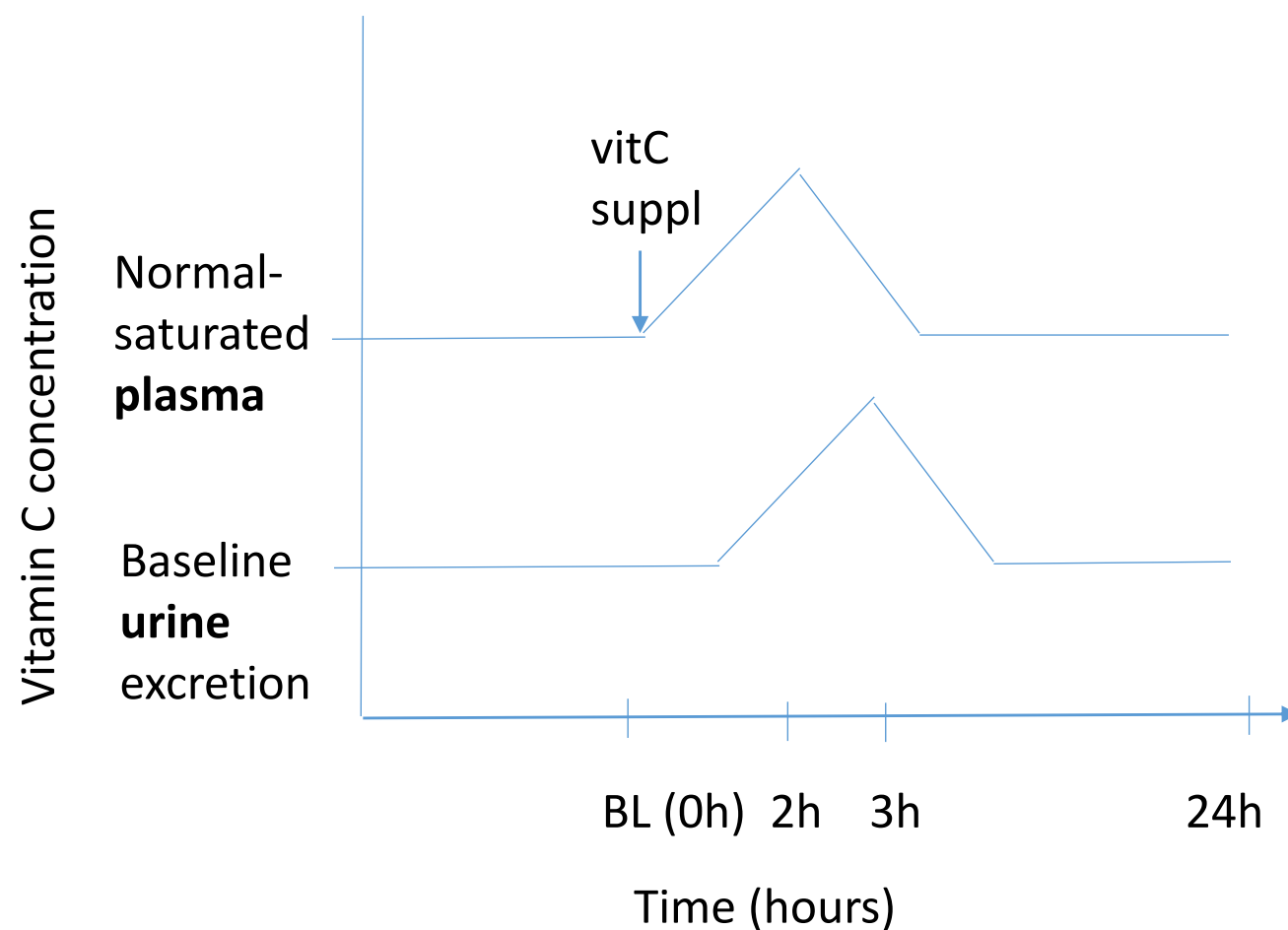


Person with normal to saturated plasma vitC:

Get peak in plasma ~2hrs post suppl

Get peak in urine ~3 hrs post suppl

Has returned to baseline by 24 hr later

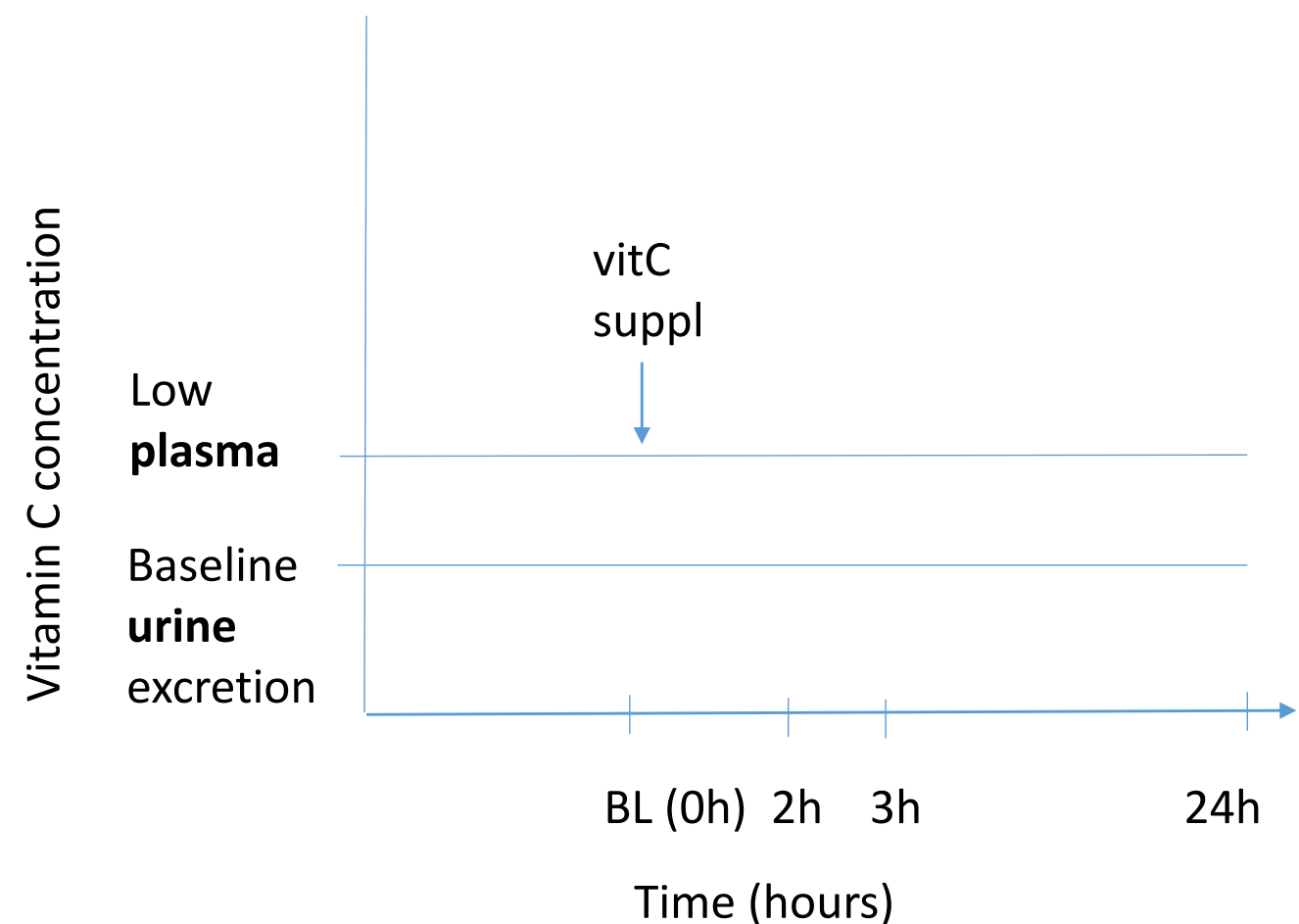


Person with low to deficient plasma vitC:

Get no peak in plasma (due to tissue uptake)

Therefore, get no peak in urine

i.e. need vitC 'challenge' to confirm status



...immediately or, alternatively, wet the
test strip by passing through the urine
cup.

When using, run the edge of the strip against
the rim of the urine collection cup to remove
excess urine.

30 seconds after removing from urine, compare
right side of test area with corresponding color
chart.

NOTE:

A normal level for urine Vitamin C is 100 mg/dl or
more. If the strip reveals a lower result, increase
your vitamin C intake and test again.
For questions regarding your results,
contact your physician.



DO NOT USE AFTER 90 DAYS OF BREAKING THE FOIL SEAL

DATE OPENED





VitaC4Care study

Prof P Myint - Aberdeen Uni
Assoc. Prof A Carr - Otago Uni
Dr K Stavoura - NHS Grampian
Dr A Sneedon - Rowett Institute

Relative blood Vitamin C increase

10 g gulp - Ascorbic Acid vs. Sodium Ascorbate

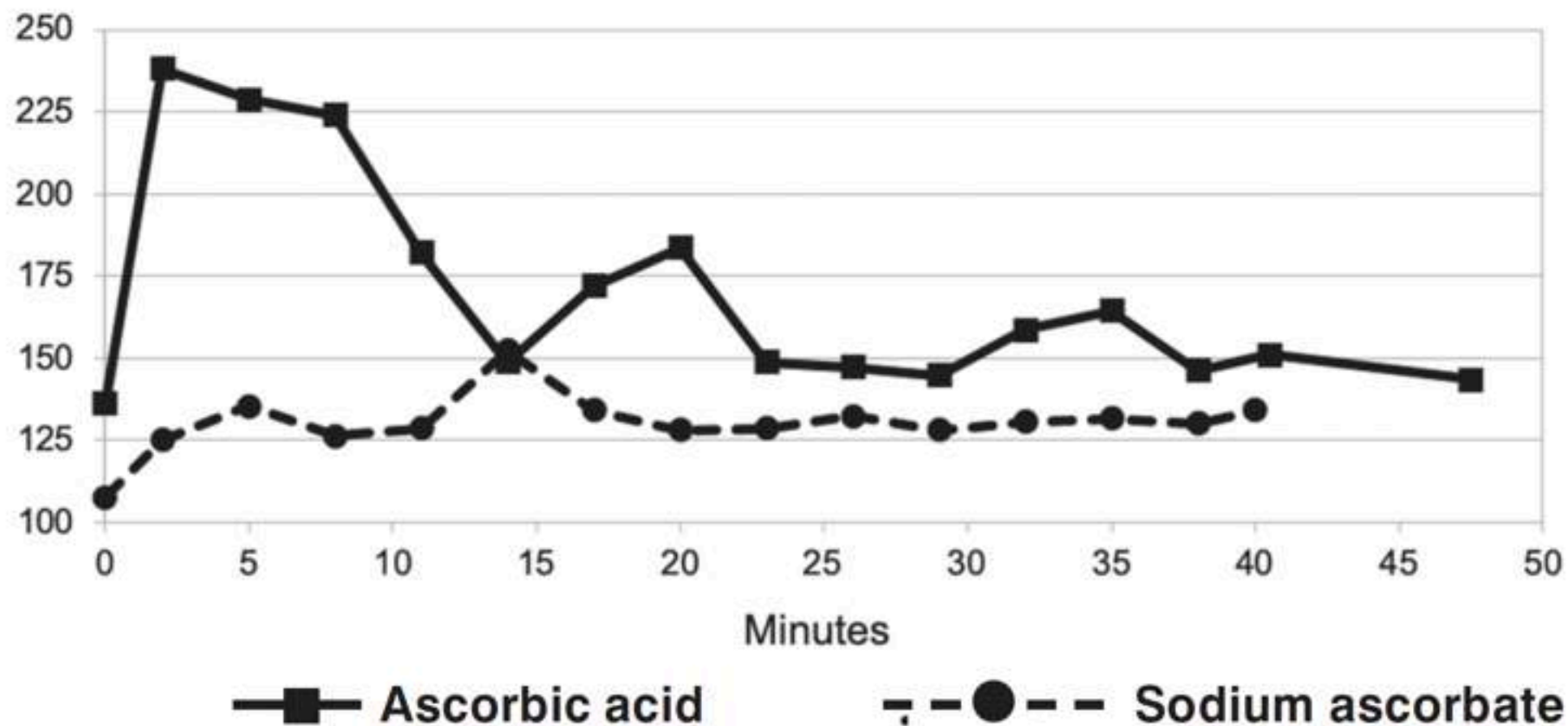


Figure 5 - Absorption of oral ascorbic acid vs oral sodium ascorbate.

Credit: Data from O Fonoro^w, *Townsend Letter*. March 13, 2020, prior to print publication. See reference 142.

Ascorbic Acid (10g) vs. IV Sodium Ascorbate

Find

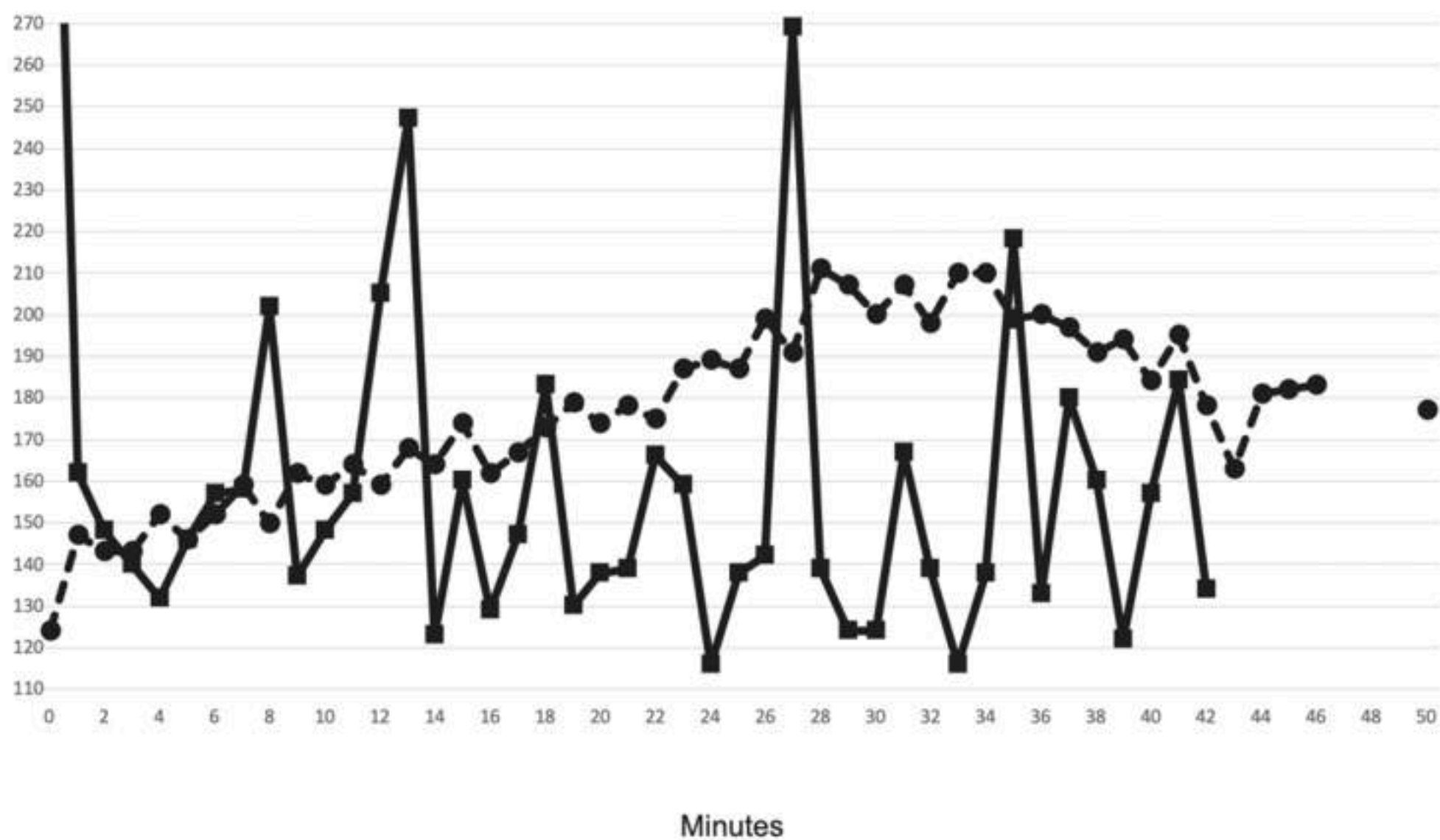
figure

Previous

Relative blood Vitamin C increase

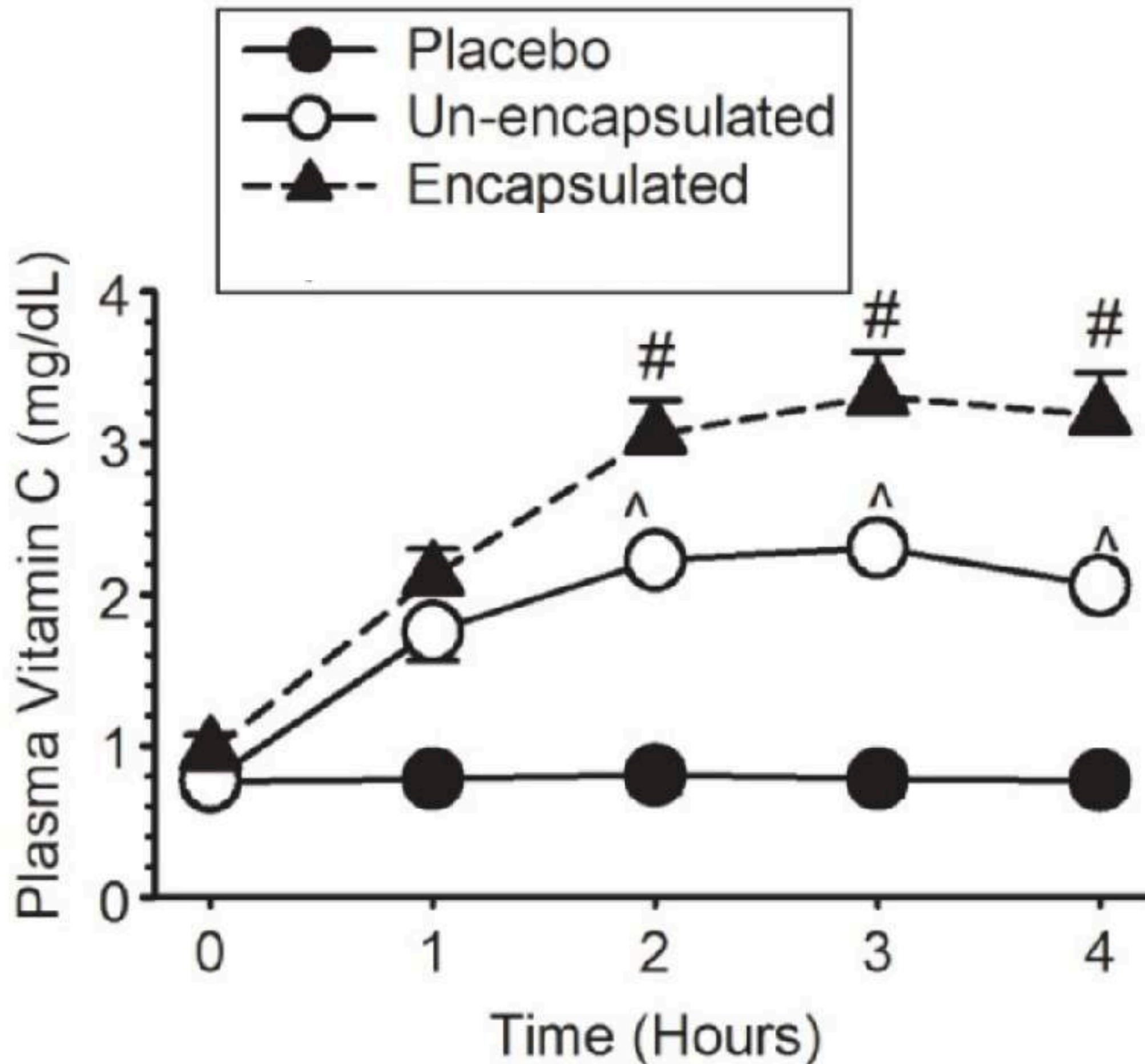
—■— Ascorbic acid

- - ● - - Sodium ascorbate



B

Ascorbic
acid



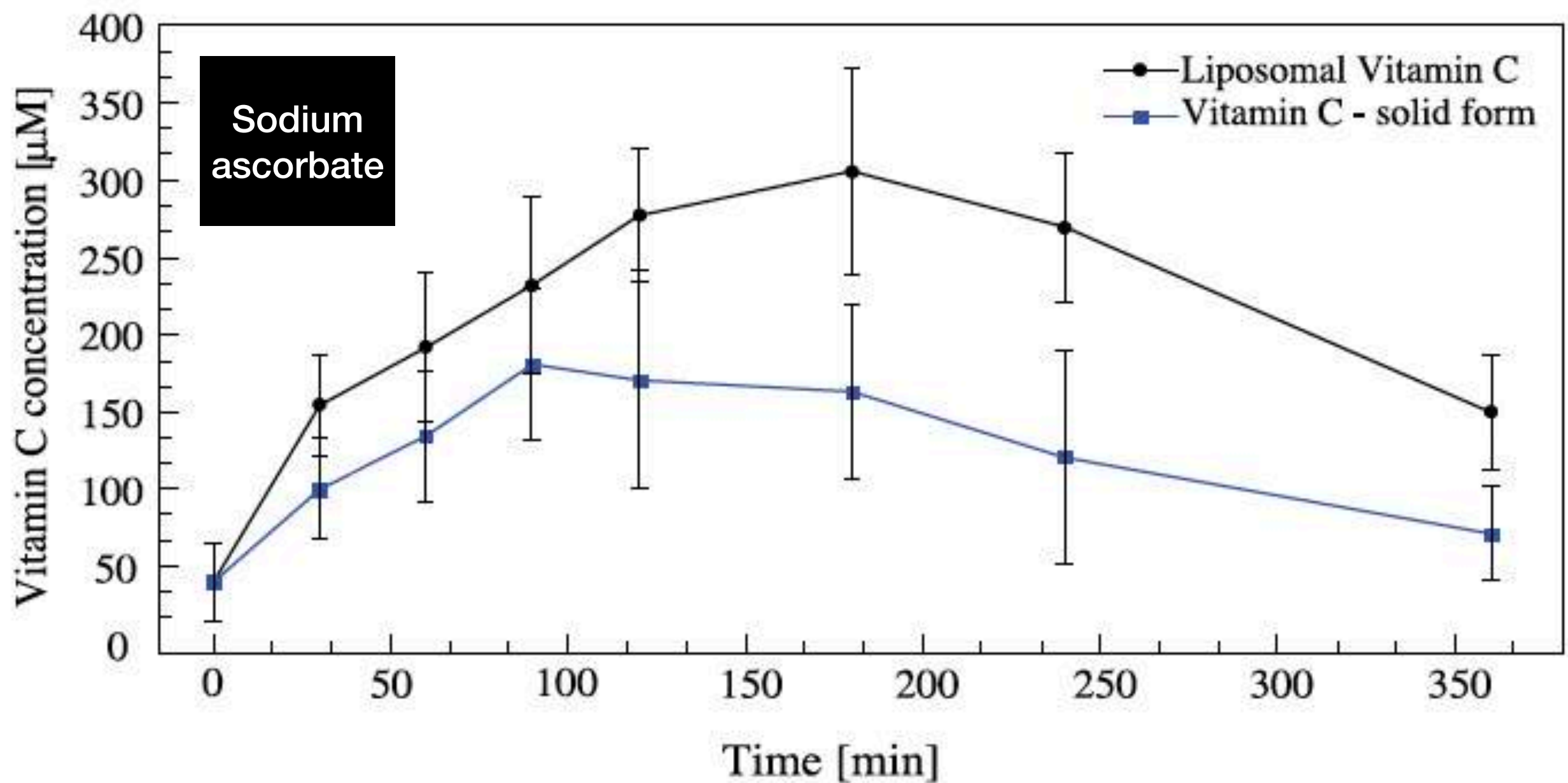


Figure 5. Averaged concentration profiles of sodium ascorbate in serum determined for two groups of persons, following the oral intake of 10 g of sodium ascorbate in the form of the aqueous solution (squares) and encapsulated in liposomes (circles). The lines between points were drawn arbitrarily to guide the eye. Values of plasma concentrations measured for specific time points for liposomal and non-liposomal dosages are significantly different ($p < 0.05$) for three last points (180, 240, and 360 min).

Vitamin C - meta-analysis



Hemilä H, Chalker E. (2013) Cochrane Database Syst Rev. 2013

- ▶ Overall, the duration of infections was reduced by 8% (approx half a day) in adults and in children by 14% (approx 1 day).
- ▶ Studies giving 3 vs 6 or 4 vs 8 g/day have shown the higher the dose the greater the effect with a 20% decrease in cold duration with 6 to 8 g/day. This equates to 1.5 to 2 days shorter colds.
- ▶ 46% of those taking 8 g/day in the first day of a cold report being symptom free after 24 hours.
- ▶ An intake of 6 g/day has been shown to restore normal vitamin C levels in leucocytes during colds. This suggests that similar daily doses may be required to have a symptom reducing effect.

Vitamin C and Infections

by  **Harri Hemilä**  

Department of Public Health, University of Helsinki, Helsinki FI-00014, Finland

Nutrients **2017**, *9*(4), 339; <https://doi.org/10.3390/nu9040339>

Received: 31 January 2017 / **Revised:** 24 February 2017 / **Accepted:** 15 March 2017

(This article belongs to the Special Issue **Vitamin C in Health and Disease**)

[View Full-Text](#)[Download PDF](#)[Browse Figures](#)

Abstract

In the early literature, vitamin C deficiency was associated with pneumonia. After its identification, a number of studies investigated the effects of vitamin C on diverse infections. A total of 148 animal studies indicated that vitamin C may alleviate or prevent infections caused by bacteria, viruses, and protozoa. The most extensively studied human infection is the common cold. Vitamin C administration does not decrease the average incidence of colds in the general population, yet it halved the number of colds in physically active people. Regularly administered vitamin C has shortened the duration of colds, indicating a biological effect. However, the role of vitamin C in common cold treatment is unclear. Two controlled trials found a statistically significant dose–response, for the duration of common cold symptoms, with up to 6–8 g/day of vitamin C. Thus, the negative findings of some therapeutic common cold studies might be explained by the low doses of 3–4 g/day of vitamin C. Three controlled trials found that vitamin C prevented pneumonia. Two controlled trials found a treatment benefit of vitamin C for pneumonia patients. One controlled trial reported treatment benefits for tetanus patients. The effects of vitamin C against infections should be investigated further. [View Full-Text](#)



Randomised controlled trial



M. Van Straten, P Josling, Advanced Therapeutics, 2012

168 people given 500mg vitamin C twice daily, or placebo for 60 days

	PLACEBO	VITAMIN C	% LESS
Number of colds	50	37	26% less
Days of infection	178	85	52% less
Duration of severe symptoms	3.1	1.8	42% less

Letter to the Lancet and BMJ



Vitamin C and the new coronavirus

Harri Hemilä - Department of Public Health, University of Helsinki, Helsinki, Finland.

Lancet Letter to the Editor - 2020-3-19

Because the disease caused by the new coronavirus is much more severe than the ordinary virus infections, the above estimates may justify a regular increased daily intake of vitamin C for the period when the prevalence of the virus is high. Furthermore, the major cause for concern about COVID-19 is the high frequency of ICU treatment that is needed. A meta-analysis of 12 trials with 1766 patients found that vitamin C had shortened ICU stay by 8% (2). Another meta-analysis of eight trials found that vitamin C shortened the duration of mechanical ventilation in patients who needed longest ventilation (3). Based on dose vs. plasma level analyses, it is unlikely that a healthy person would benefit from daily vitamin C doses over 0.5 g/day (4). However, when a patient suffers from a virus infection there may be a vitamin C dose response for up to 6-8 g/day (5). Vitamin C is a safe and inexpensive essential nutrient and therefore even small to moderate benefits may be worthwhile.

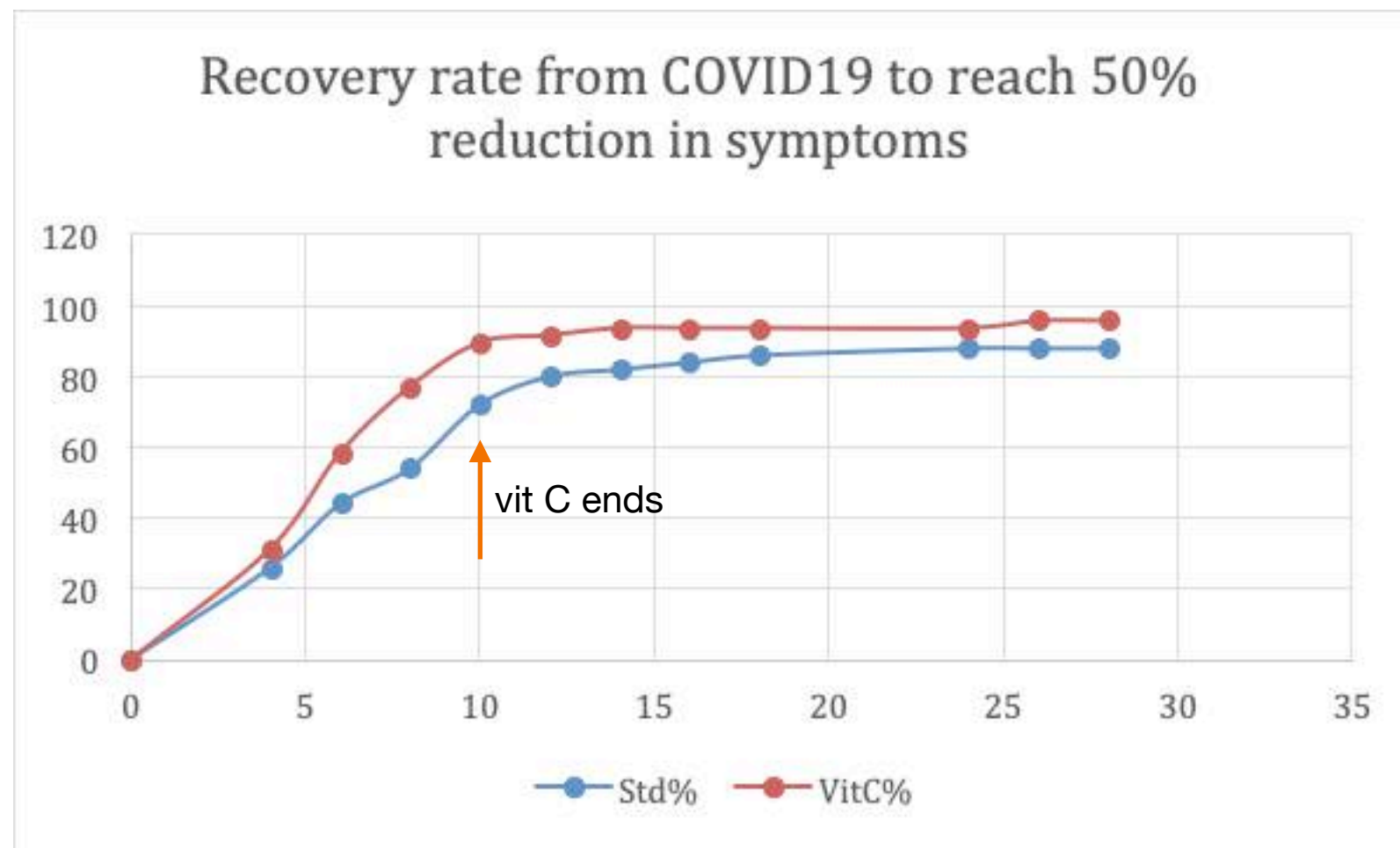
1. Hemilä H, Chalker E. Vitamin C for preventing and treating the common cold. Cochrane Database Syst Rev. 2013;(1):CD000980. <https://doi.org/10.1002/14651858.CD000980.pub4>

2. Hemilä H, Chalker E. Vitamin C can shorten the length of stay in the ICU: a meta-analysis. Nutrients. 2019;11(4):708 <https://doi.org/10.3390/nu11040708>

JAMA - 8g of vit C/7mg zinc

Thomas S et al, A to Z trial, JAMA Netw Open. 2021;4:e210369

- Study reports a decreased duration of 5.5 days vs 6.7 days on placebo in both groups (with/without zinc). Not significant.



Reanalysis of the COVID A to Z RCT

H.Hemila, A.Carr, E. Chalker Chal<https://doi.org/10.21203/rs.3.rs-289381/v1>

In this reanalysis we calculated the rate ratio of recovery between the vitamin C and usual care arms and found that vitamin C **increased the rate of recovery by 70% (95% CI 6.8% to 170%, $P = 0.025$)**. Furthermore, we calculated quantile treatment effect of vitamin C. **At the 60th percentile level of symptom distribution, duration was 9 days in the usual care arm, and 6 days in the vitamin C arm, which corresponds to reduction in symptom duration by 3 days (95% CI 3 to 4.6 days; $P < 0.001$)**. The analysis of the quantile treatment effect indicates that **there may be around 30% reduction in symptom duration in patients with the longest symptoms**.

Still
sick
100%

Rate = 85.5%/day (= 100%/1.17 days)

Rate = 50%/day (= 100%/2 days)

PH to Dr Milind Desai: “How many days were subjects symptomatic before starting vitamin C?”

Dr M Desai: “How many days they were symptomatic [prior to treatment] was recorded but obviously difficult to ascertain. This data is not available.”

PH: “When were the subjects given a PCR test?”

Dr Desai: “On or around the first day of presentation to the outpatient setting.”

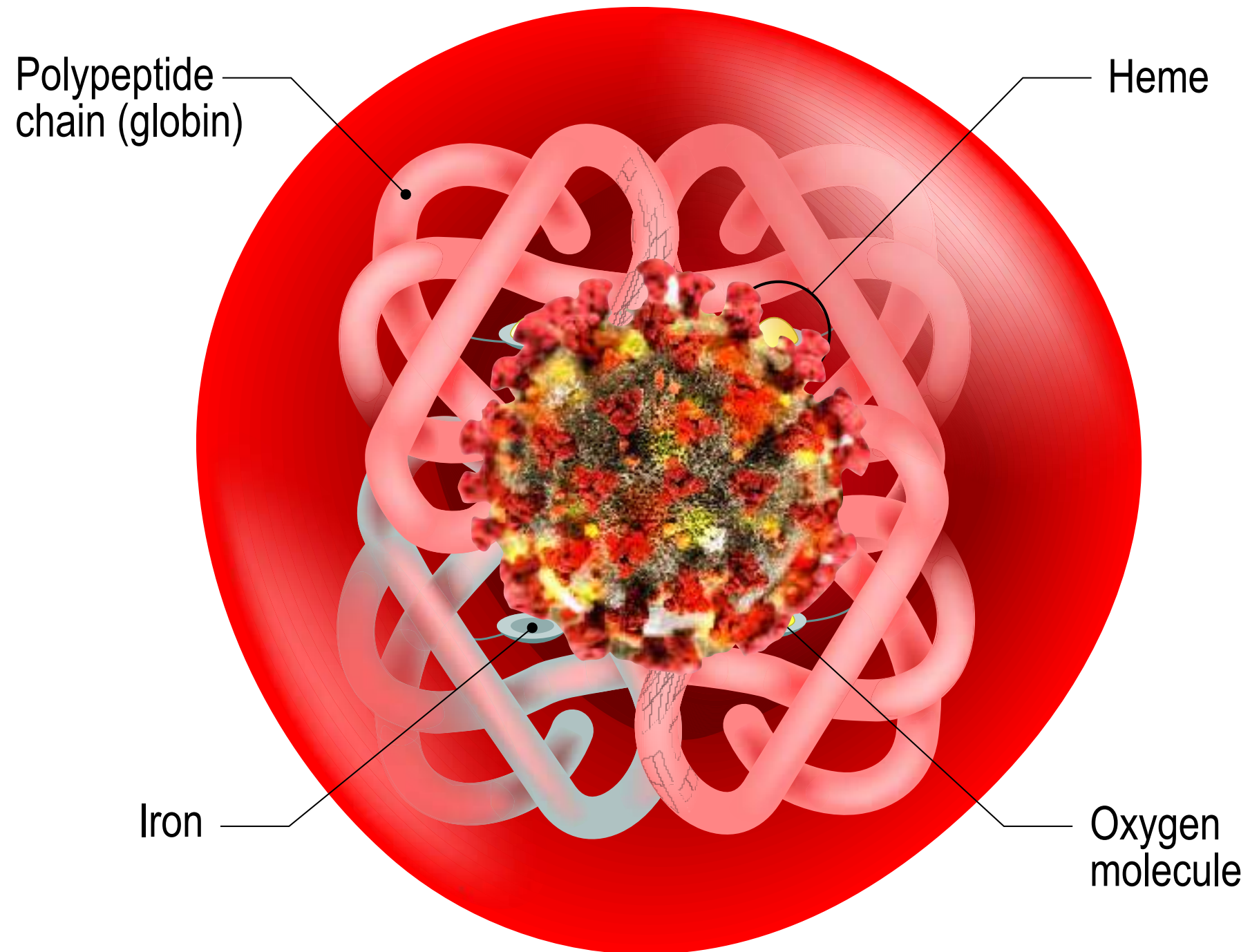
0%

4 5 days

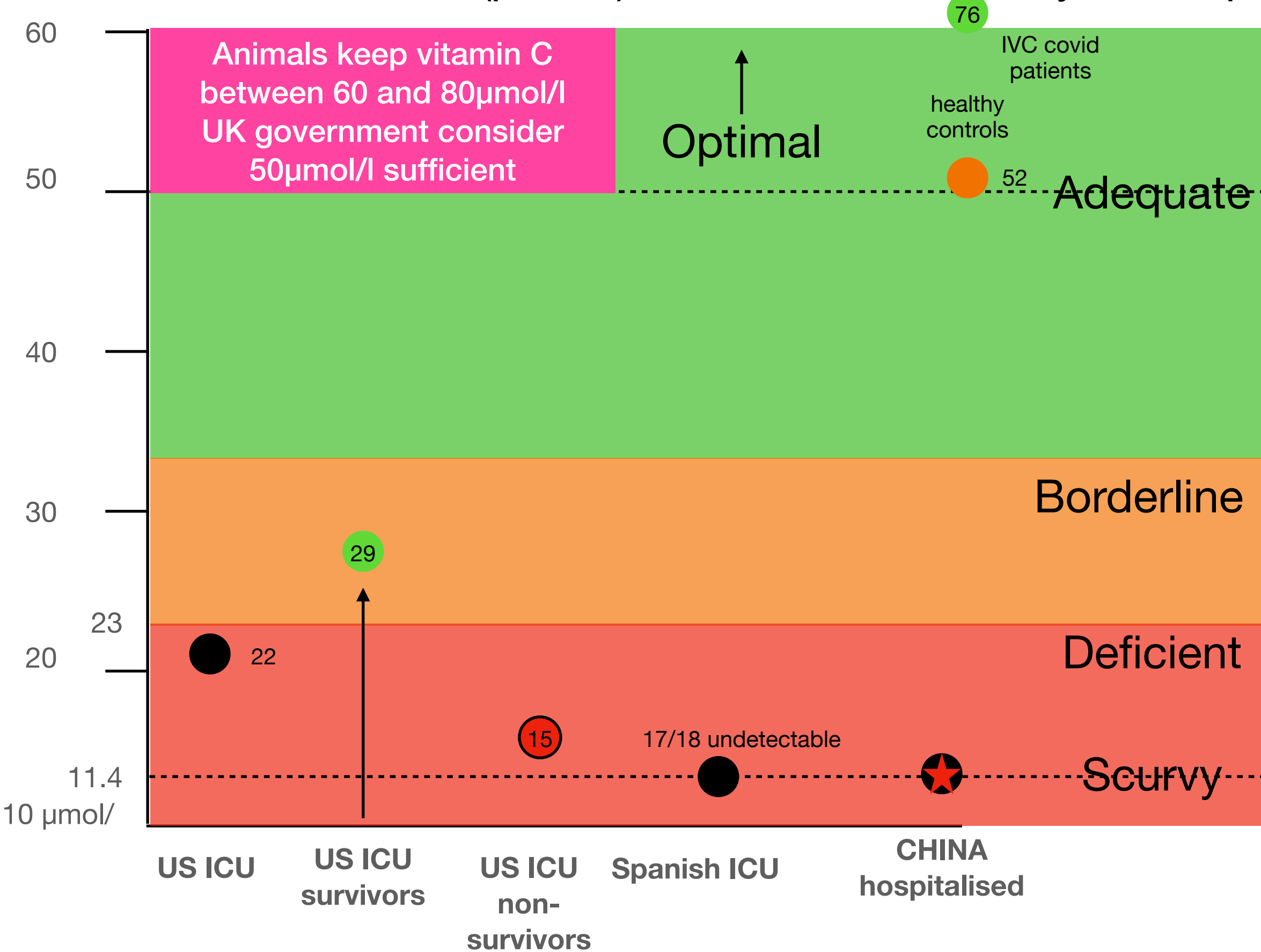
days

The COVID A to Z trial was “stopped early for futility”. In the sample size calculation, the authors assumed a 1.0 day shorter symptoms by intervention. Duration of symptoms was reduced by 1.2 days in the vitamin C arm compared with the usual care arm. Given that the observed vitamin C effect was 20% greater than the expected effect (1.2 vs. 1.0), it is illogical to have stopped the trial early because of “futility”.

HEMOGLOBIN



Serum vitamin C level (μmol/l) in COVID-19 critically ill ICU patients



Vitamin C for covid patients

Xing et al. J Pharm Biomed Anal. 2021, 196:113927. [doi: 10.1016/j.jpba.2021.113927](https://doi.org/10.1016/j.jpba.2021.113927)

- Treated 31 COVID-19 patients (+/- IV vitamin C) given 100mg/kg/day = 7.5g and 51 healthy controls
- 6 COVID-19 patients (no IV vitamin C): mean plasma vitamin C level 2 mg/dl (11 μ mol/L)
- 25 COVID-19 patients given 100 mg/kg/d IV vitamin C: mean plasma vitamin C level 13.5 mg/L (76 μ mol/L)
- 51 healthy controls: mean plasma vitamin C level 9.2 mg/L (52 μ mol/L)

COVID risk factors & vit C



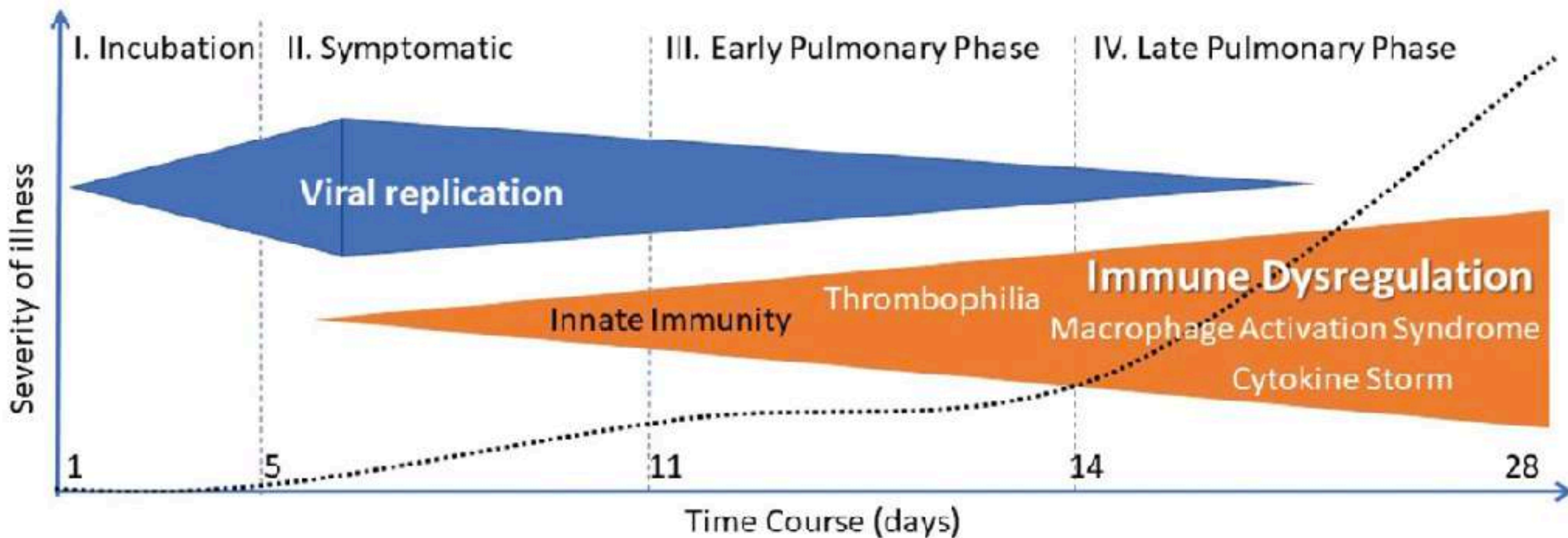
Patterson G, Isales C, Fulzele, *Aging Dis.* 2020, 12.

- Many of the risk factors for COVID-19 overlap with those for vitamin C deficiency [94]. Certain sub-groups (**male, African American, older**, those suffering with co-morbidities of **diabetes, hypertension, COPD**), all at higher risk of severe COVID-19, have also been shown to have lower serum vitamin C levels [95] as has level of **deprivation** [103].
- Average plasma vitamin C levels are generally lower in men than women, even with comparative intakes of vitamin C, which has been attributed to their higher body weight [94].
- A hypothesis of altered sodium-dependent vitamin C transporter (SVCT1 and 2) expression in these sub-groups has also been proposed [95].
- In old versus young rat hepatocytes, the vitamin C level declines by 66%, largely attributed to reduced absorption due to a 45% decline in SVCT1 with age [96].
- Inflammatory cytokines, also present in co-morbidities, downregulate SVCT2, resulting in the depletion of intracellular vitamin C [97,98].
- In the UK, an estimated 25% of men and 16% of women in the low-income/materially deprived population are deficient in vitamin C $>11 \mu\text{mol/L}$ [103].

The COVID cascade



- ▶ Iron changes from stable to unstable(Fe^{+3}) and set up chain reaction of oxidation - think rust.
- ▶ The liver works hard to make FERRITIN which rises.
- ▶ Cells can't make nitric oxide putting cardiovascular system into stress.
- ▶ OXYGENATION INDEX plummets, hence need for ventilators.
- ▶ All this triggers a CYTOKINE STORM. Immune cells over-react, so WHITE CELL COUNT SHOOTs UP. As immune cells run out of ascorbic acid, can't recycle it fast enough, can't make nitric oxide and T-CELL COUNT plummets. Inflammation rockets (eg CRP SHOOTs UP. Liver, heart and lungs under major stress.
- ▶ Adrenal function and cortisol crashes. The body stops fighting.
- ▶ Everything described here is REVERSED by ASCORBIC ACID, plus CORTISOL, ZINC, HYDROXYCHLOROQUINE/QUERCITIN



No-one dies from the virus. They die from 'cytokine' storm as the immune system over-reacts against dead virus particles. This is the same as sepsis.

EDITORIAL

Open Access



Doctor—your septic patients have scurvy!

Paul E. Marik* and Michael H. Hooper

See related research by Carr et al., <https://ccforum.biomedcentral.com/articles/10.1186/s13054-017-1891-y>.

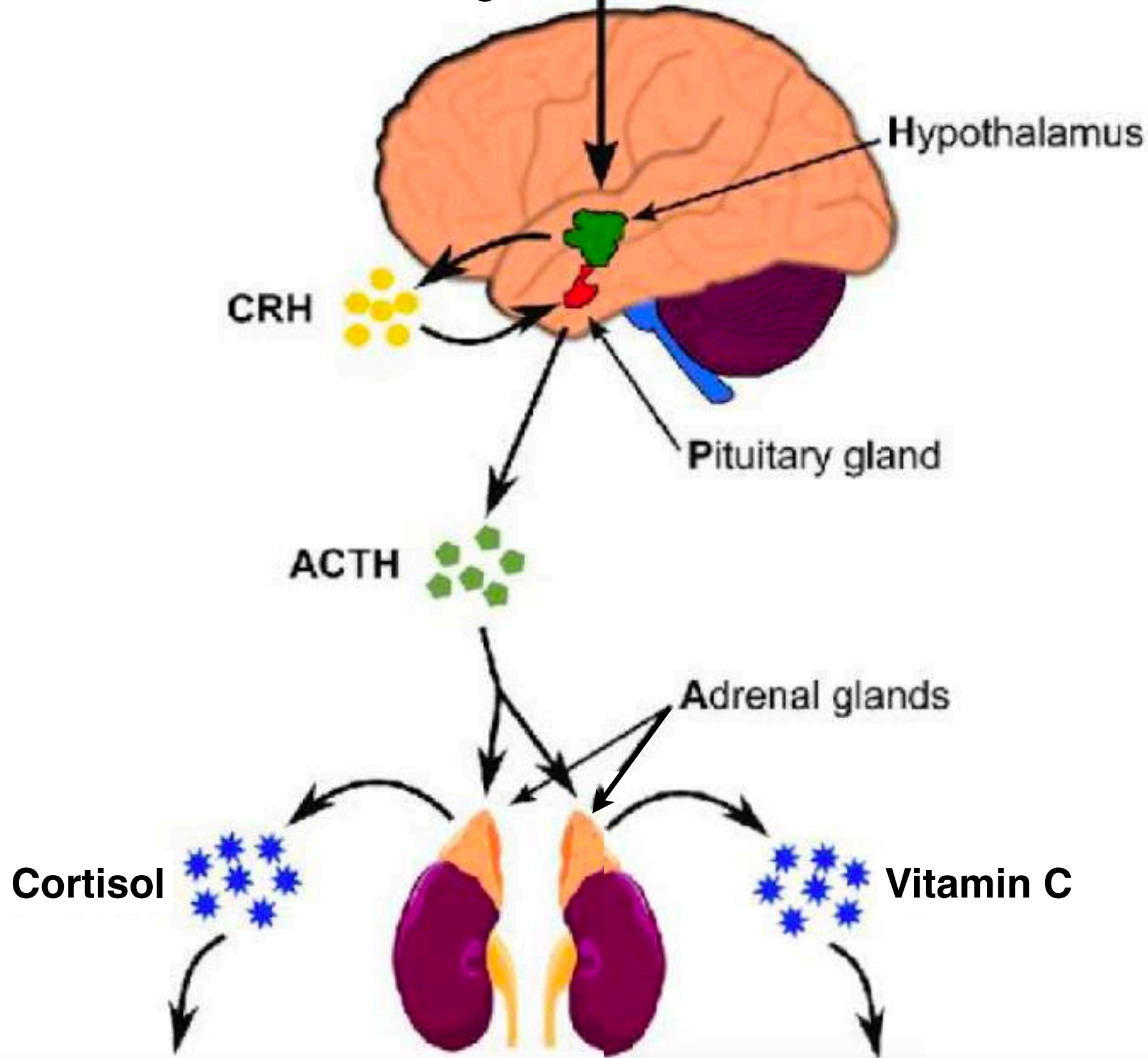
Scurvy is a disease of antiquity described in Egyptian Hieroglyphics and responsible for the deaths of thousands of sailors during the Renaissance. Today, clinicians consider scurvy a very rare disease seen only in patients with extreme dietary deficiencies. These clinicians should not be shocked to learn that almost all patients in their ICU with sepsis have undetectable vitamin C supporting a diagnosis of acute scurvy. The remainder of the patients in the ICU have hypovitaminosis C. These are the findings of a recent study [1]. Surprisingly, this is not new. It has been known that acute illness results in an acute deficiency of vitamin C with low serum and intracellular levels [2–4]. Low plasma concentrations of vitamin C are associated with more severe organ failure and increased risk of mortality [5]. The most likely explanation for the acute vitamin C deficiency (acute scurvy) in patients with sepsis (and other critical illnesses) is a consequence of metabolic consumption [1]. The fall in serum and cellular levels occurs too rapidly to be explained by decreased gastrointestinal absorption or increased urinary losses. Indeed, in a guinea pig model myocardial ascorbate was

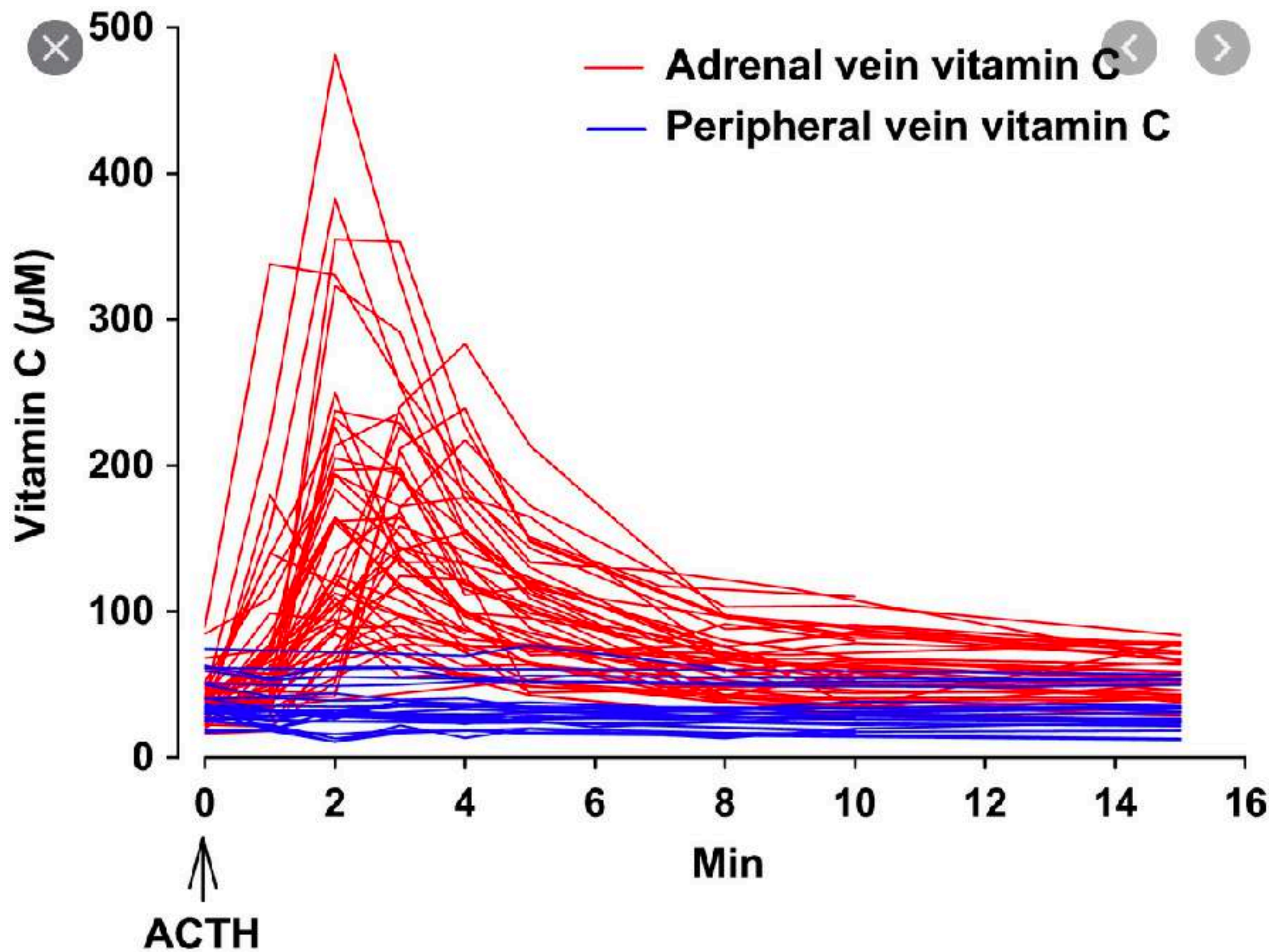
The inability to generate vitamin C makes humans very susceptible to dysfunction in a variety of biochemical pathways that are vital for surviving a critical illness such as sepsis. In experimental models of sepsis, treatment with vitamin C limited the deleterious consequences of sepsis including attenuation of the dysfunction of the endothelium and prevention of organ failures [9, 10]. Sepsis is characterized by production of reactive oxygen species (ROS) and enzymes such as nitric oxide synthase, xanthine oxidase, and phospholipase A₂. Vitamin C is a key cellular antioxidant which counteracts these ROS. In addition, vitamin C recycles other antioxidants including α -tocopherol (vitamin E) and tetrahydrobiopterin (BH₄). BH₄ plays a critical role in the function of endothelial nitric oxide synthase (eNOS). Vitamin C deficiency results in the incomplete regeneration of BH₄ resulting in the uncoupling of eNOS and the generation of superoxide and peroxynitrite [11]. Vitamin C inhibits activation of nuclear factor kappa-B (NF- κ B), a major nuclear transcription factor involved in release of numerous proinflammatory mediators [12]. Vitamin C is an essential

Almost all Covid-19 ICU patients tested have scurvy often with undetectable vitamin C levels.

Environmental stressor

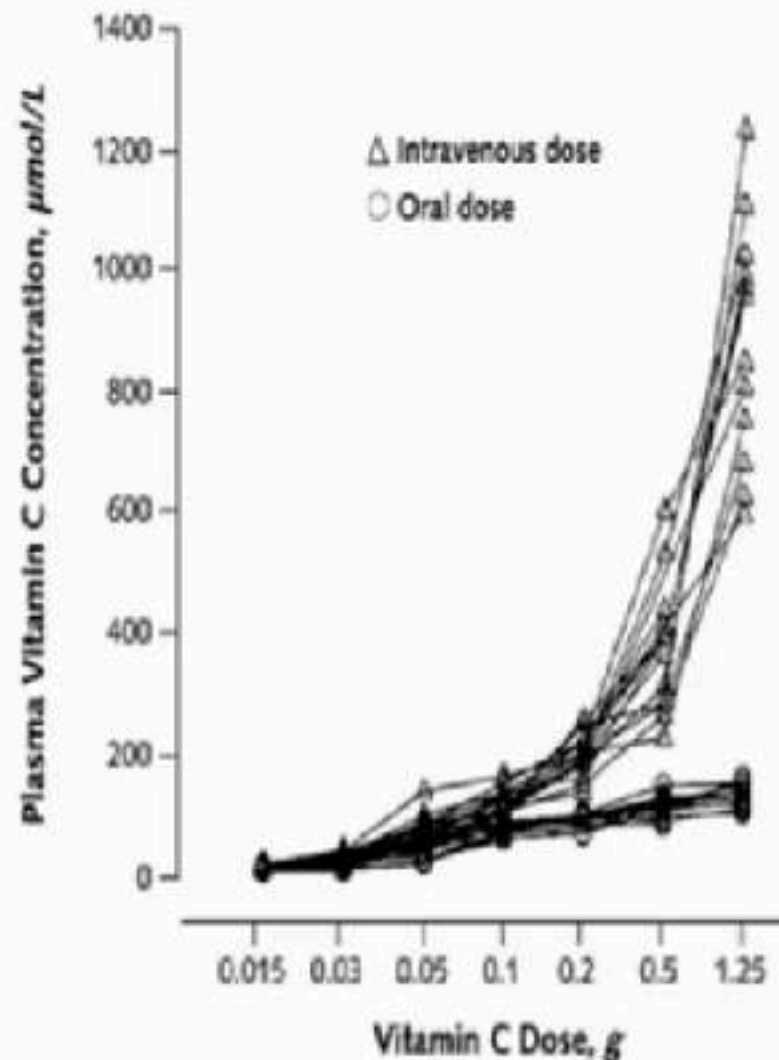
eg viral attack





Vitamin C Pharmacokinetics: Implications for Oral and Intravenous Use

Sebastian J. Padayatty, MRCP, PhD; He Sun, PhD, CBS; Yaohui Wang, MD; Hugh D. Riordan, MD; Stephen M. Hewitt, MD, PhD; Arie Katz, MD; Robert A. Wesley, PhD; and Mark Levine, MD



Intravenous vitamin C can raise plasma levels ten fold higher than the same oral dose.

Ascorbic Acid Injection

Dosage Form: injection, solution

500 mg/mL

**FOR INTRAVENOUS, INTRAMUSCULAR OR SUBCUTANEOUS USE.
CONTAINS NO PRESERVATIVES.**

There are no contraindications to the administration of ascorbic acid. Its parenteral administration is desirable for patients with an acute deficiency or for those whose absorption of orally ingested ascorbic acid is uncertain. 1 gram daily are recommended. However, as much as 6 grams have been administered parenterally to normal adults without evidence of toxicity.



(H) 中南医院

(H) 武汉大学中南医院
Hôpital Zhongnan de l'Université de Wuhan

门诊部

中国

1. Prelim results of the Zhongnan trial

- ▶ 56 patients on ventilators - 27 get IV vitamin C 12g twice a day for 7 days; 29 get placebo (sterile water)
- ▶ Overall, 5 out of 26 people (19%) died in the vitamin C group, while 10 out of 29 (35%) receiving the placebo died.
- ▶ Of those most critically ill 4 people (18%) in the vitamin C group died compared to 10 (50%) in the placebo group. That's two thirds less deaths (68% less mortality).
- ▶ In those with Pulmonary Function (PF) below 150 significant reduction in mortality
- ▶ Significant decrease in IL-6 inflammatory marker -19 v 158 pg/ml
- ▶ Signification improvement in oxygenation
- ▶ Significant reduction in time needing mechanical ventilation

Table 2 Outcomes in a trial of HDIVC in patients with COVID-19

Variable	Day	Vitamin C (n = 27)	Placebo (n = 29)	Difference, coefficient (95% CI)	P value
IMVFD28, days		26.0[9.0–28.0]	22.0[8.5–28.0]	1.3(– 4.7 to 7.2)	0.57
IMV days to day 28, days		1.5[0.0–19.0]	6.0[0.0–16.0]	– 0.8(– 6.4 to 4.9)	0.60
HFNC days to day 28, days		0.5[0.0–8.3]	2.0[0.0–7.0]	0.2(– 2.9 to 3.3)	0.85
NIV days to day 28, days		0.0[0.0–3.3]	0.0[0.0–1.8]	1.2(– 1.2 to 3.7)	0.68
Patients' condition deterioration, n, %		3(11.5)	6(24.0)	0.4(0.1 to 1.7)	0.19
Patients' condition improvement, n, %		5(19.2)	3(10.3)		0.84
ICU mortality, n, %		6(22.2)	11(37.9)	HR 0.5(0.2 to 1.5)	0.20
ICU mortality of patients with SOFA \geq 3, n, %		5(21.7)	11(52.4)	HR 0.2(0.1 to 0.9)	0.04
ICU stay, days		22.9 \pm 14.8	29.9 \pm 12.7		0.20
Hospital mortality, n, %		6(22.2)	11(37.9)	HR 0.5(0.2 to 1.5)	0.20
Hospital mortality of patients with SOFA \geq 3, n, %		5(21.7)	11(52.4)	HR 0.2(0.1 to 0.9)	0.04
Hospital stay, days		35.0 \pm 17.0	39.0 \pm 16.0		0.65
28-day mortality, n, %		6(22.2)	10(34.5)	HR 0.5(0.2 to 1.0)	0.31
28 days mortality of patients with SOFA \geq 3, n, %		5(21.7)	10(47.6)	HR 0.3(0.1 to 1.1)	0.07

50% less risk of death in ICU

80% less risk of death in ICU

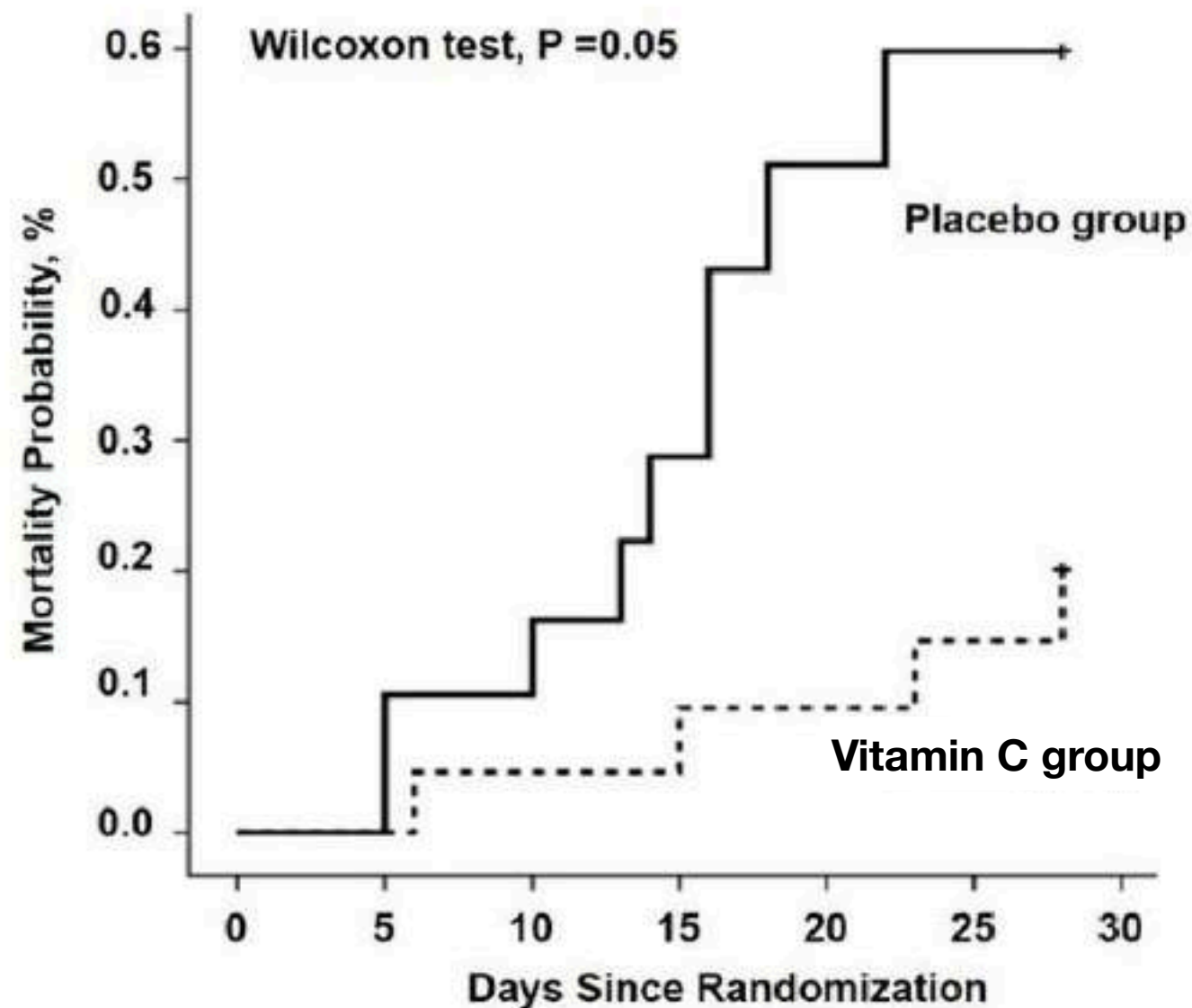
80% less risk of death in hospital

70% less risk of deaths 28 days

MECHANICALLY VENTILATED

‘68% less risk of death with vitamin C’

compared to 30% less risk (29% v 41%) in the dexamethasone steroid study



No. at Risk							
Placebo	20	19	17	15	12	11	11
HDIVC	22	22	21	20	20	19	18

B Kaplan-Meier analysis was used to estimate the 28-day mortality and survival were compared with the Wilcoxon test ($P=0.05$) among severe COVID-19 patients (baseline SOFA score ≥ 3). Cox regression was used as multiple comparisons ($P=$ HR, 0.32[95%CI, 0.10-1.06]). Abbreviations: HDIVC: high dose intravenous vitamin C; COVID-19, coronavirus disease 2019; sequential organ failure assessment.

Used with permission of Z.Peng et al.

2. High dose vit C: retrospective cohort

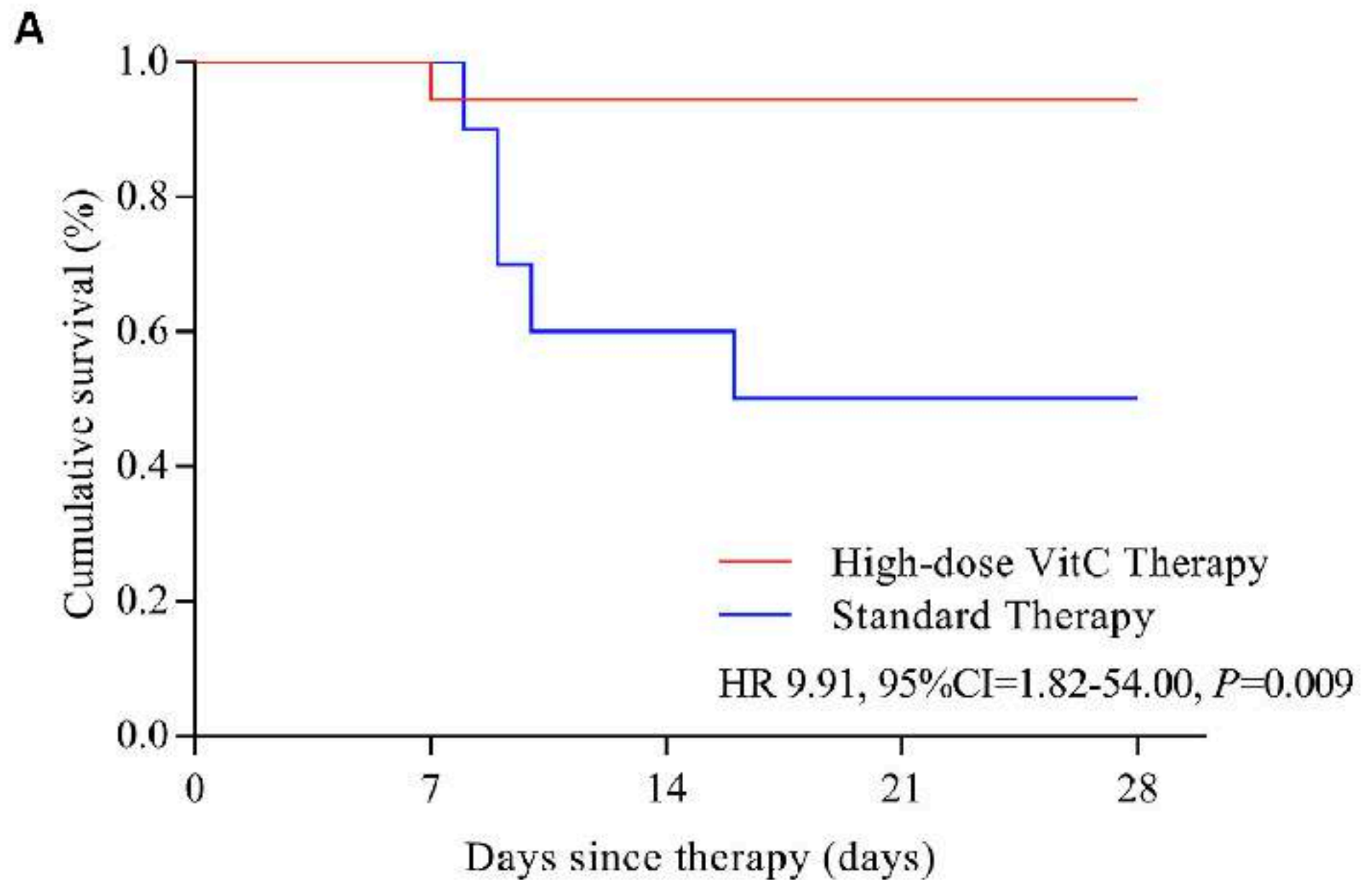


Gao et al. Aging. 2021:13. [doi: 10.18632/aging.202557](https://doi.org/10.18632/aging.202557)

- ▶ 76 covid patients were given 6g every 12 hours (24g pd) for day 1, then 6g pd for 4 days and compared to 30 given standard treatment.
- ▶ Results: The risk of 28-day mortality was reduced by 86% for the high-dose vitamin C versus the standard therapy group (HR=0.14, 95% CI, 0.03-0.72). Oxygen support status was improved more with high-dose vitamin C than standard therapy (63.9% vs 36.1%). No safety events were associated with high-dose vitamin C therapy.
- ▶ Conclusion: High-dose vitamin C may reduce the mortality and improve oxygen support status in patients with Coronavirus disease 2019 without adverse events.

9.9 times less risk of death in severe covid

Gao et al. Aging. 2021:13. [doi: 10.18632/aging.202557](https://doi.org/10.18632/aging.202557)



Number at risk

High-dose VitC Therapy	18	18	18	12	6
Standard Therapy	10	10	10	10	2

3. High dose vit C: RCT (open label)



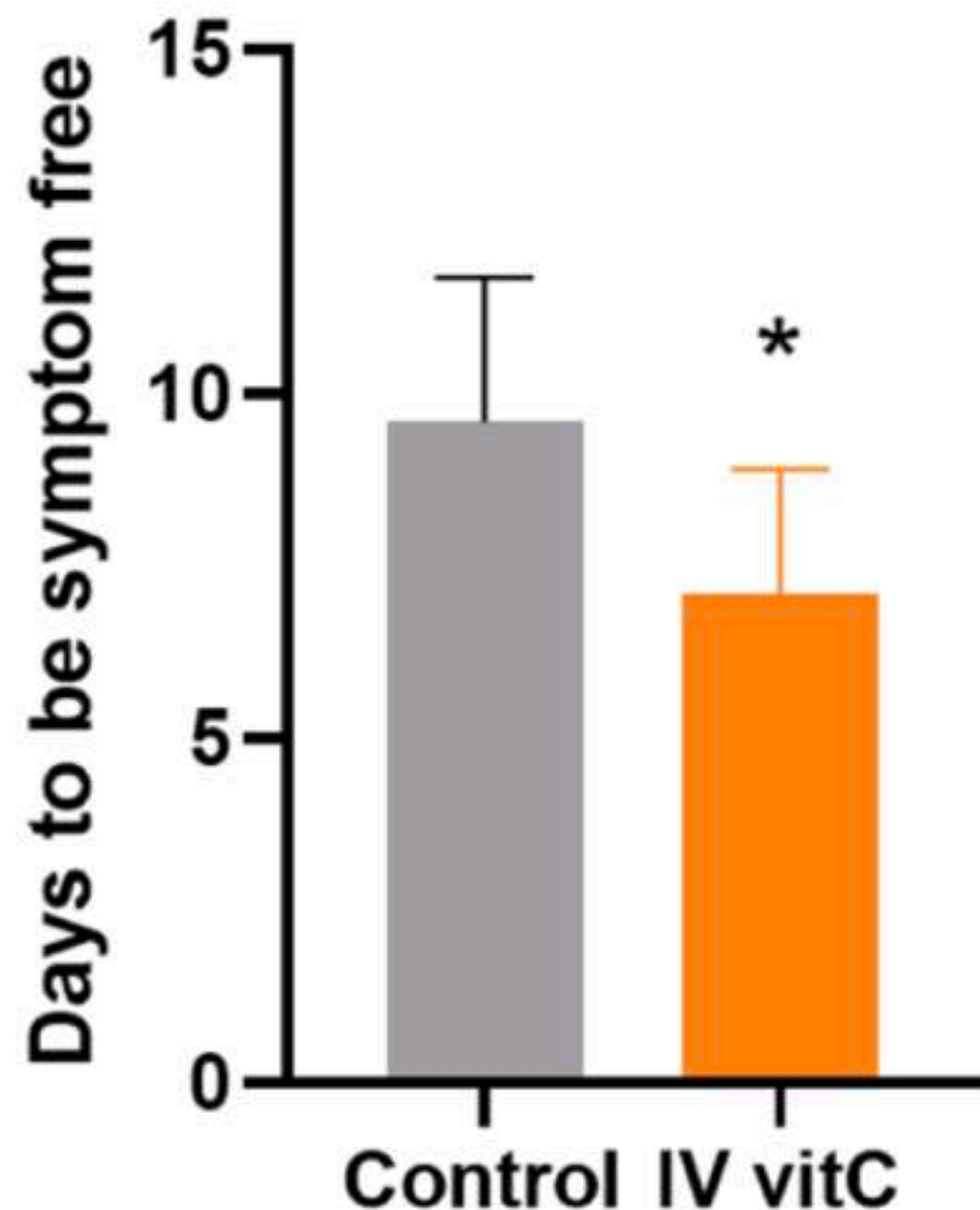
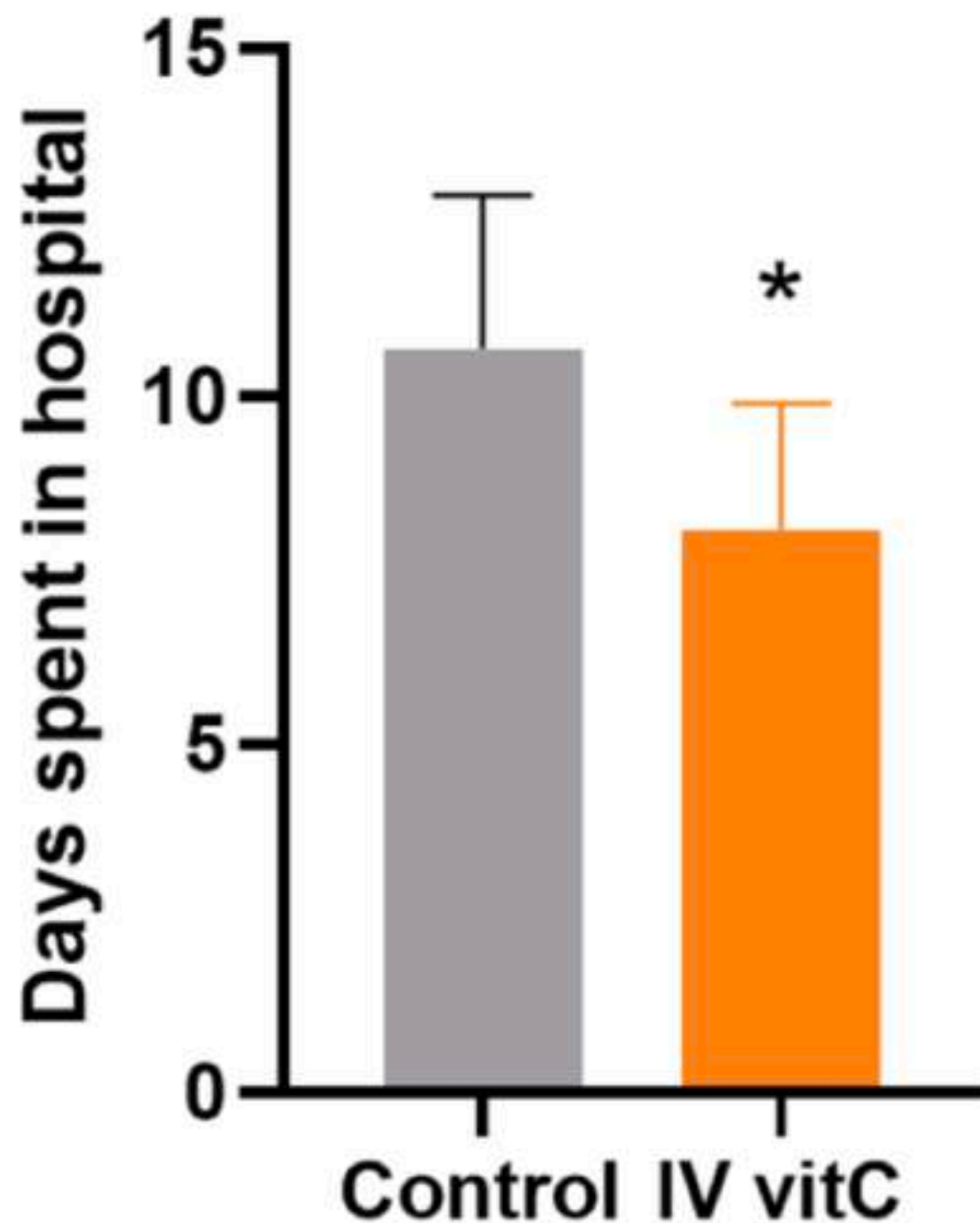
Kumari et al. Cureus 2020 12(11): e11779. [doi:10.7759/cureus.11779](https://doi.org/10.7759/cureus.11779)

- 150 severe COVID-19 patients, half given IV vitamin C 50mg/kg = 3.75g a day, half standard treatment
- Became symptom-free earlier (7.1 vs 9.6 days, $p < 0.0001$)
- Spent fewer days in the hospital (8.1 vs 10.7 days, $p < 0.0001$)
- No statistically sig. difference regarding need for mechanical ventilation (16% vs 20%, $p = 0.4$)
- No statistically sig. difference regarding mortality (9.3% vs 14.6%, $p = 0.3$)

3. High dose vit C: RCT (open label)



Kumari et al. Cureus 2020 12(11): e11779. [doi:10.7759/cureus.11779](https://doi.org/10.7759/cureus.11779)



4. High dose vit C: RCT open label



JamaliMoghadamSiahkali et al. Eur J Med Res. 2021, 26(1):20. doi: 10.1186/s40001-021-00490-1

- 60 covid patients - half given IV vitamin C 6g a day for 5 days, half standard care.
- Results: The mean body temperature was significantly lower in the case group on the 3rd day of hospitalization ($p = 0.001$). Peripheral capillary oxygen saturations (SpO_2) measured at the 3rd day of hospitalization was also higher in the case group receiving HDIVC ($p = 0.014$). The median length of hospitalization in the case group was significantly longer than the control group (8.5 days vs. 6.5 days) ($p = 0.028$). There was no difference in mortality (3 - 10% in each group.)
- There were no adverse events reported.
-

REMAP-CAP vitamin C arm



- ▶ In this domain of the REMAP-CAP trial, participants meeting the platform-entry criteria for REMAP-CAP admitted to participating intensive care units (ICU) will be randomized to receive one of two interventions:
 - ▶ 1. No vitamin C (no placebo)
 - ▶ 2. Vitamin C (50 mg/kg IV every 6 hours for 16 doses - eg $3.75\text{g} \times 4 = 15\text{g}$ a day for four days)
- ▶ As laudable as the aim of the REMAP-CAP vitamin C trial is it was apparently ready to recruit patients last summer, but for a lack of vitamin C supplies.
- ▶ The other problem with REMAP-CAP is its four day vitamin C duration. Trials already show the best results with seven or more days treatment with 12g or more.

Current mortality vz Vit C dose



- ▶ UK average ICU mortality - 41%-37% (1st-2nd wave ICNARC)
- ▶ C&W ICU using 2g (1st wave) - 29% (plus anticoagulants)
- ▶ East Virginia ICU using 12g - 6.5% (plus steroids & anticoagulants)
- ▶ Houston ICU using 12g - 3.5% (plus steroids & anticoagulants)
- ▶ **MATH+** PROTOCOL has ended mortality in those without end stage disease and >85..
- ▶ M for methylprednisolone; A for ascorbic acid; T for thiamine; H for heparin (anti-coagulant); + for vitamin D, zinc, quercitin

Current mortality vz Vit C dose

- ▶ UK average ICU mortality - 41% first wave, now 34% (Source: ICNARC)
- ▶ C&W ICU using 2g - 29% first wave (plus anticoagulants) (wanted to give 4g); now giving 6g to some, not all patients
- ▶ East Virginia ICU using 12g - 6.5% (plus steroids & anticoagulants)
- ▶ Houston ICU using 12g - 3.5% (plus steroids & anticoagulants)
- ▶ **MATH+** PROTOCOL has ended mortality.
- ▶ M for methylprednisolone; A for ascorbic acid; T for thiamine; H for heparin (anti-coagulant); + for vitamin D, zinc, quercitin

<https://www.youtube.com/watch?v=VQTfbRM1BJk>

Methylation nutrients - B6, folate, B12, TMG, zinc

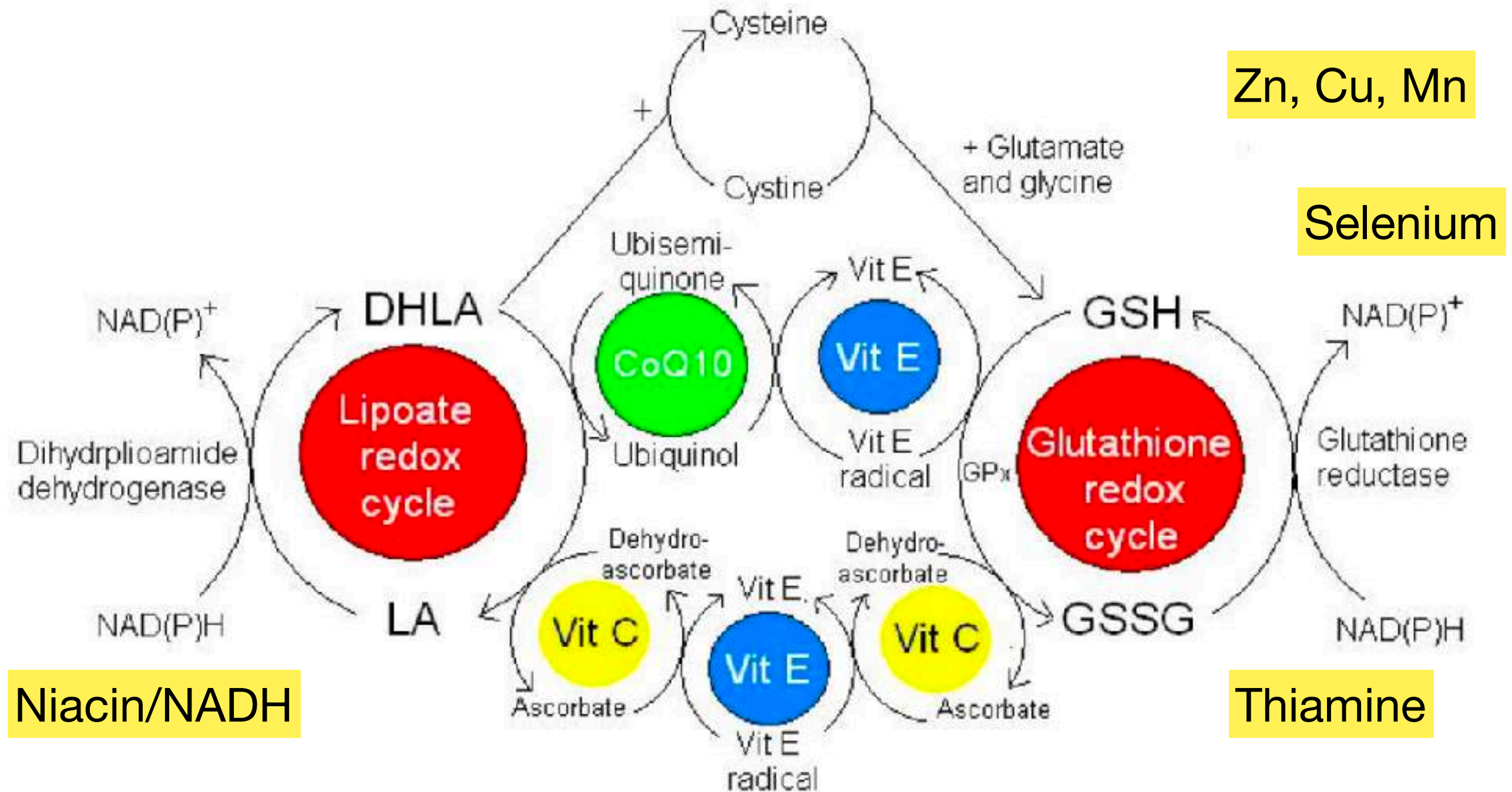


Figure 1. Cellular antioxidant recycling. GPx = glutathione peroxidase which requires selenium. Adapted from Sen, C. K. and Packer, L. 2000. Thiol Homeostasis and supplements in physical exercise. American Journal of Clinical Nutrition. 72: 653S-669S

Safety of vitamin C - kidney stones



- ▶ The Kidney Stone Research Laboratory of the University of Cape Town conducted a controlled trial in which ten volunteers were required to ingest 4 g of vitamin C per day for five days. Unlike the earlier studies, they put a preservative in the urine collection bottles to prevent the conversion of ascorbate to oxalic acid. The samples were analysed for numerous physicochemical risk factors of kidney stone formation. These risk factors were not significantly altered and the authors concluded that ingestion of large doses of vitamin C does not increase the risk of forming kidney stones - earlier trials had faulty study designs involving unpreserved urine samples .
- ▶ A prospective cohort study of 85,557 women with no history of kidney stones, with 1078 incidences of kidney stones over 14 years of follow-up, reported that vitamin C intake was not

G6PD, haemochromatosis, thalassaemia



- ▶ The latter relates to those with due to enhanced iron absorption with vitamin C. G6PD deficiency is not considered an exclusion criterion in the use of up to 6 g/day oral or intravenous vitamin C for short-term use in critical infection. The FLCCC report that 3 g every 6 h appears to be safe in patients with G6PD. It may be wise for those with haemochromatosis or thalassaemia to avoid high-dose vitamin C taken with iron-rich foods or supplements and short-term high-dose vitamin C to be medically monitored.
- ▶ High dose vitamin C gives you diarrhoea and are dangerous.
- ▶ The US DRI, having thoroughly considered the wide literature on vitamin C and many kinds of speculated harms, stated that the safe range is up to 2 g/day . The European Food Safety Authority stated that the lowest observable adverse effect level is 3–4 g/day (in relation to gastrointestinal effects) .
- ▶ Looser bowel movements and diarrhoea rarely occur below 3 g/

Vitamin C and loose bowels



- ▶ The US DRI, having thoroughly considered the wide literature on vitamin C and many kinds of speculated harms, stated that the safe range is up to 2 g/day . The European Food Safety Authority stated that the lowest observable adverse effect level is 3–4 g/day (in relation to gastrointestinal effects) .
- ▶ Looser bowel movements and diarrhoea rarely occur below 3 g/day and tolerance is increased considerably when fighting a viral infection.
- ▶ Consider low gastric acid levels (eg PPI use) in those with gastrointestinal sensitivity, helped by consuming with citrus juice or diluted vinegar (or ascorbate form).

Safety of IV vitamin C



- ▶ Diarrhea does not occur with intravenous vitamin C administration.
- ▶ A survey of 9328 patients given an average intravenous dose of 24 g of vitamin C every 4 days, primarily for cancer, infection or fatigue, reported that 101 (1%) had side effects, mostly minor, including lethargy/fatigue, a change in mental status and vein irritation/phlebitis .

[Sign the petition](#)

VITAMIN C FOR COVID

Vitamin C is a safe, inexpensive and highly effective anti-viral nutrient in the right amount, both for prevention of colds, reducing duration and severity, and for the treatment of COVID-19 in the acute phase with life-saving potential. Yet it is classified as 'fake information', not recommended by governments and rarely prescribed by doctors.

This has to change. Sign our petition.

Watch the Campaign Film [here](#) and please **SHARE!**

[Read the petition](#)

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SURVIVING RESPIRATORY DISTRESS 79

Chapter 9

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Surviving Respiratory Distress

Every year in the UK there are over 17,000 flu-related deaths, with 84% being people over 65. The winter of 2017/18 was particularly bad – 26,408 died. Of course, our focus now is on the increasing death toll of COVID-19. But what is going on at the sharp end of flu, including COVID-19 and other ‘killer’ flus that have emerged in the last two decades? How can the survival rate be increased?

In most cases fatality is due to *Acute Respiratory Distress Syndrome (ARDS)*, which is apparently occurring at varying degrees in about four in ten patients suffering from COVID-19. This figure, however, may be skewed by focussing on hospitalised cases and not considering those ‘at home’ who have had minor symptoms, and got over a likely COVID-19 infection without severe symptoms. The primary cause of ARDS is the body’s immune system overreacts producing a *cytokine storm* where our immune system overreacts producing a massive state of inflammation. This inflammation in the lungs, causing difficulty breathing, is the basis of a diagnosis of pneumonia. All this is what makes flu potentially fatal and why COVID-19 patients in ICU need ventilators to keep them breathing. The important point is that it is not the virus that is killing people, it is this state of inflammation.

How Vitamin C Reverses ARDS

During ARDS there is extreme inflammation and swelling in the *alveoli*, the balloon-like air pockets in the lungs, *haemolysis*, which is the rupturing of red blood cells and blood vessels, and

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