Lotte & John Hecht Memorial Foundation

CDMRP

VIT VICTORY

A phase III multi-center randomized trial: VItamin C in Thermal injuRY: The VICToRY Trial

Clinical trials.gov ID #NCT04138394

Sponsor: Dr. Daren Heyland

Principal Investigators:

- Dr. Daren Heyland, Critical Care Department, Queen's University, Kingston, ON, Canada
- Dr. Christian Stoppe, Anesthesiology Department, Wurzburg University, Wurzburg, Germany
- - Dr. Leopoldo Cancio, Director, U.S. Army Burn Center, USAISR, Fort Sam Houston, TX, U.S.A.

Project Lead: Maureen Dansereau, Critical Care Department, Queen's University, Kingston, ON, Canada

Critical Care Nutrition

Clinical Evaluation Research Unit

Queen's University

Introduction and Study Design

The Clinical Evaluation Research Unit (CERU)

Our Research group is nested in Queen's University, Kingston, Ontario, Canada

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CRITICAL CARE NUTRITION SYSTEMATIC REVIEWS | Click here to read the latest and best summaries of evidence in critical care nutrition

EFFORT

NUTRIC

PEPuP

Español

Critical Care Nutrition at the Clinical Evaluation Research Unit (CERU)

is dedicated to improving nutrition therapies in the critically ill through knowledge *generation*, *synthesis*, and *translation*. We engage in a broad range of research activities and promote a culture of best practices in critical care nutrition. Ultimately, this will result in improved clinical outcomes for critically ill patients and increased efficiencies to our health care systems.

www.criticalcarenutrition.com

VICToRY Team

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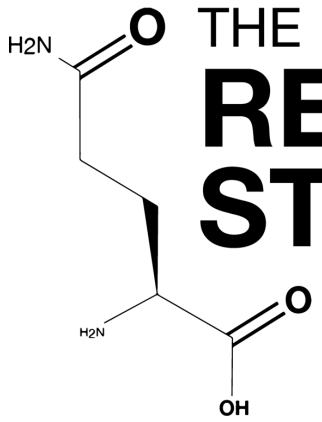
THE RE–*ENERGIZE* STUDY

Queen's University



Original Article

sb&h

Scars, Burns & Healing
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SAGE

A RandomizEd trial of ENtERal Glutamine to minimIZE thermal injury (The RE-ENERGIZE Trial): a clinical trial protocol

Daren K. Heyland[1,2,3], Paul Wischmeyer[4], Marc G. Jeschke[5], Lucy Wibbenmeyer[6], Alexis F. Turgeon[7,8], Henry T. Stelfox[9], Andrew G. Day[2] and Dominique Garrel[10]
For the RE-ENERGIZE Trial Team

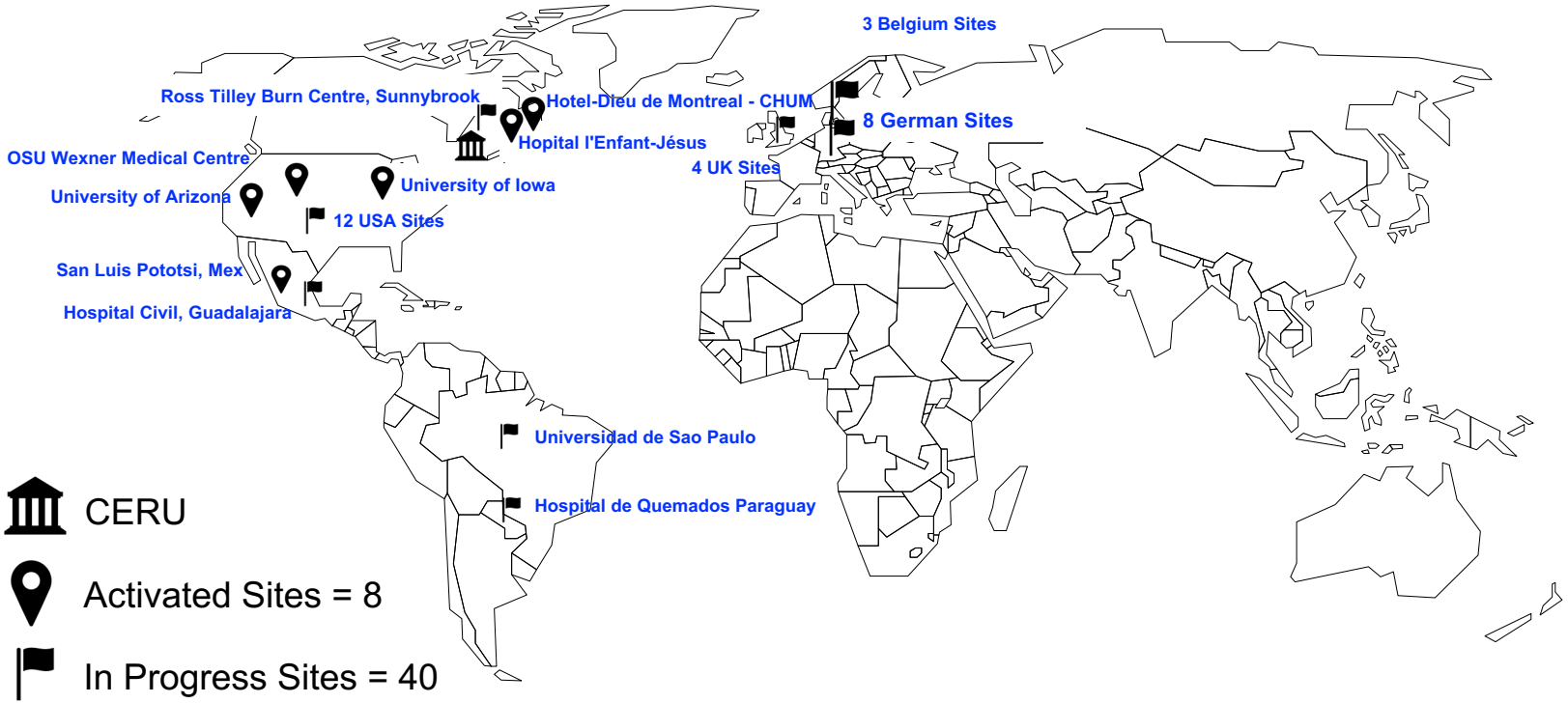
We have completed the largest trial ever of severe burn patients

1200 patients involving more than 60 burn units around the world

Comparing enteral glutamine compared to placebo

Manuscript under review at NEJM

Global Collaborative Research Infrastructure



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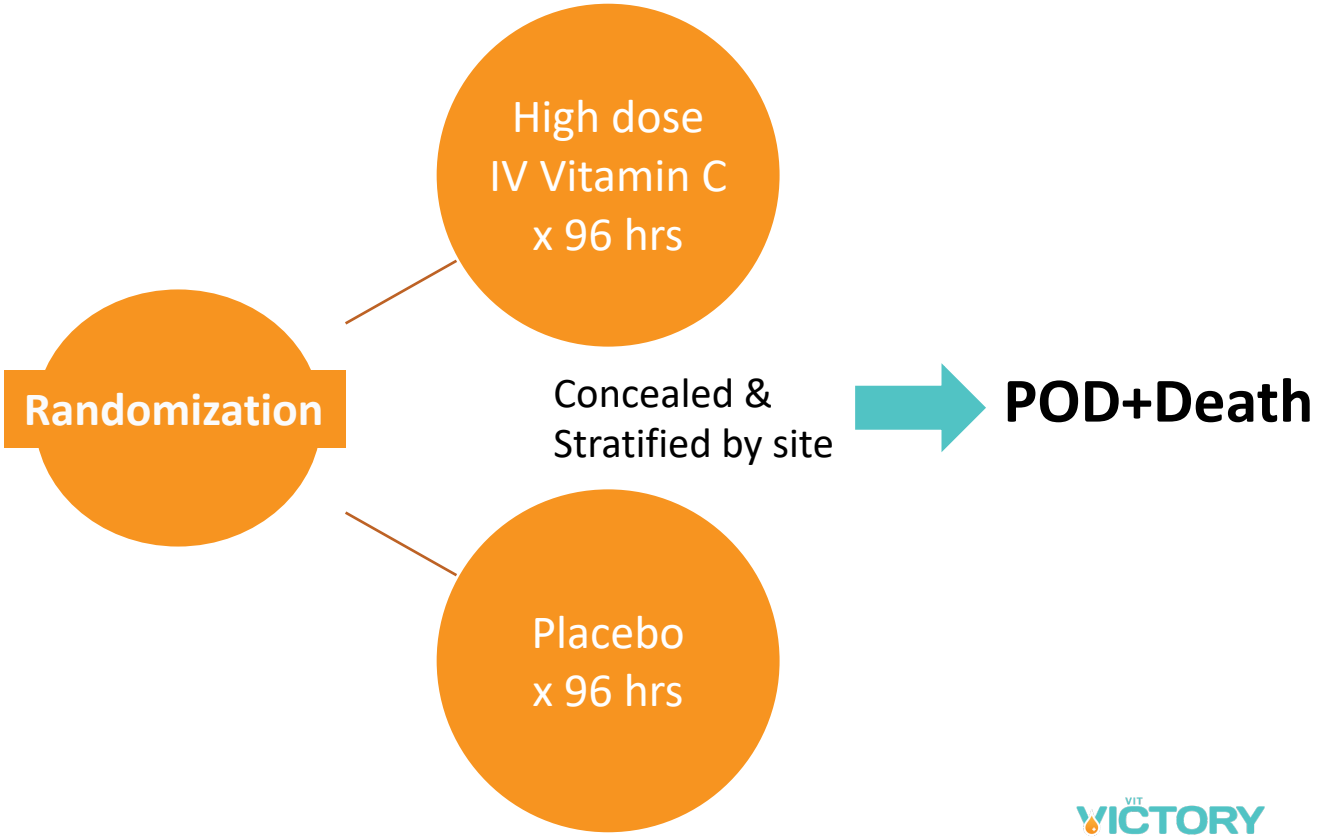
VItamin C in Thermal injury: A phase III multi-center randomized trial

Patients

666 patients
≥18 years of age
Deep 2nd and/or 3rd degree burns requiring skin grafting with TBSA ≥ 20%.



VIT VICTORY

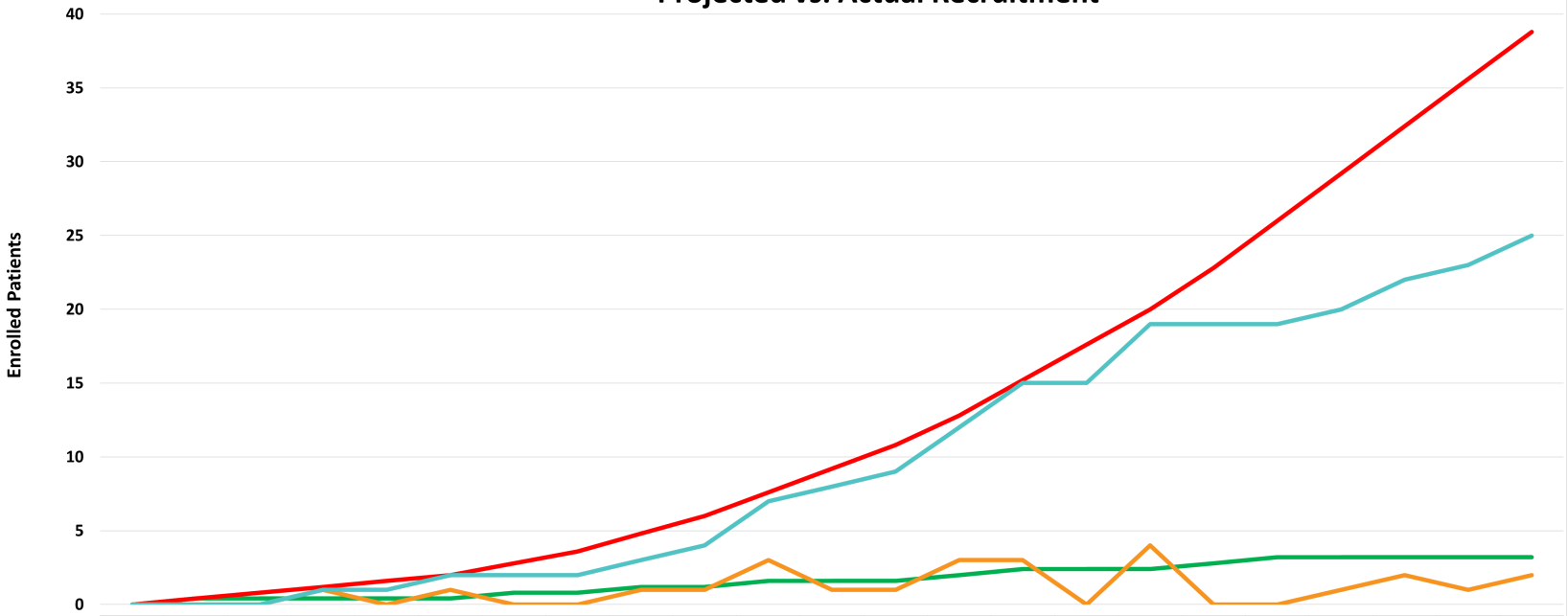
Enrollments to Date

- X6- Arizona Burn Center - University of Arizona, USA
- X5- Hotel-Dieu de Montreal – CHUM, Canada
- X2- The Ohio State University Medical Center, USA
- X9- Hopital l'Enfant-Jésus, Canada
- X4- Hospital Central Dr. Ignacio Morones Prieto, Mexico
- X3 -Harborview Medical Center, Seattle, USA
- X2 University of Iowa, Iowa City, USA

Total 31 enrollments to date (2022-05-17). First patient enrolled on October 10th, 2020.

Enrollment rate 0.8 (#patient/month) // 0.3 (#patient/site/month)

Current Status-Enrollment



	Jul-20	Aug-20	Sep-20	Oct-20	Nov-20	Dec-20	Jan-21	Feb-21	Mar-21	Apr-21	May-21	Jun-21	Jul-21	Aug-21	Sep-21	Oct-21	Nov-21	Dec-21	Jan-22	Feb-22	Mar-22	Apr-22	May-22
Projected Monthly	0.0	0.4	0.4	0.4	0.4	0.4	0.8	0.8	1.2	1.2	1.6	1.6	1.6	2.0	2.4	2.4	2.4	2.8	3.2	3.2	3.2	3.2	3.2
Projected Cumulative	0.0	0.4	0.8	1.2	1.6	2.0	2.8	3.6	4.8	6.0	7.6	9.2	10.8	12.8	15.2	17.6	20.0	22.8	26.0	29.2	32.4	35.6	38.8
Actual Monthly	0	0	0	1	0	1	0	0	1	1	3	1	1	3	3	0	4	0	0	1	2	1	2
Actual Cumulative	0	0	0	1	1	2	2	2	3	4	7	8	9	12	15	15	19	19	19	20	22	23	25

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Why are we doing this trial?

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Clinical Significance of Burn Injuries

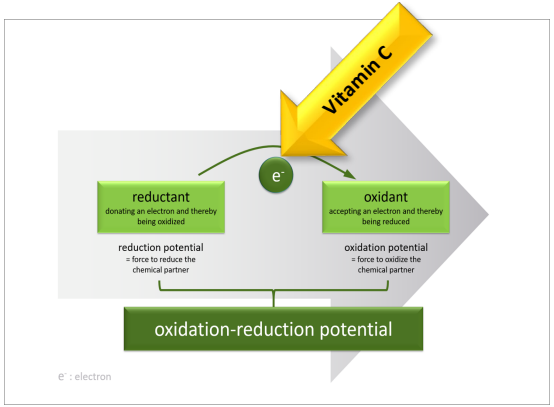
- Worldwide, burn injuries represent a significant public health problem.
- Ranked the fourth most common injury.
- Leading cause of disability adjusted life years in low and middle-income countries.
- Mortality from burn injuries has plateaued and the leading cause of death from burn injuries continues to be sepsis and multiple organ failure.
- Burn patients present with up to a 3-fold higher prevalence of sepsis than other trauma patients.

The many functions of Vitamin C

Essential & Pleiotropic

"the most powerful antioxidant"

- Counters influence of free radicals
- Protects the cells and organs from damage to macromolecules, such as cell membranes and DNA



Oudemans-van Straten, *Critical Care* 2014, doi: 10.1186/s13054-014-0460-x
Frei, *Adv. Exp. Med. Biol.,* 1990, doi: 10.1007/978-1-4684-5730-8_24

- Synthesis
  - Catecholamines
  - Collagen
  - Carnitine
- Metabolism:
  - Peptide amidation
  - Tyrosine, cholesterol & steroid metabolism
  - Cytochrome p450
- Circulation
  - Vasopressor responsiveness
  - Microcirculatory blood flow
  - Protection of endothelial barriers
- Iron absorption
- Stem cell differentiation
- Prevention of apoptosis
- Bacterial defense

Hill, *Nutrients* 2018, doi: 10.3390/nu10080974
Carr, *Nutrients* 2017, doi: 10.3390/nu9111211

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Vitamin C and Immune Function

Table 1. Role of vitamin C in immune defense.

Immune System	Function of Vitamin C	Refs.
Epithelial barriers	Enhances collagen synthesis and stabilization	[30–35]
	Protects against ROS-induced damage [1]	[36–40]
	Enhances keratinocyte differentiation and lipid synthesis	[41–45]
	Enhances fibroblast proliferation and migration	[46,47]
	Shortens time to wound healing in patients	[48,49]
Phagocytes (neutrophils, macrophages)	Acts as an antioxidant/electron donor	[50–53]
	Enhances motility/chemotaxis	[54–63]
	Enhances phagocytosis and ROS generation	[64–71]
	Enhances microbial killing	[54,55,57,58,70,72]
	Facilitates apoptosis and clearance	[71,73,74]
	Decreases necrosis/NETosis	[73,75]
B- and T-lymphocytes	Enhances differentiation and proliferation	[62,63,76–82]
	Enhances antibody levels	[78,83–85]
Inflammatory mediators	Modulates cytokine production	[75,77,86–94]
	Decreases histamine levels	[56,61,95–101]

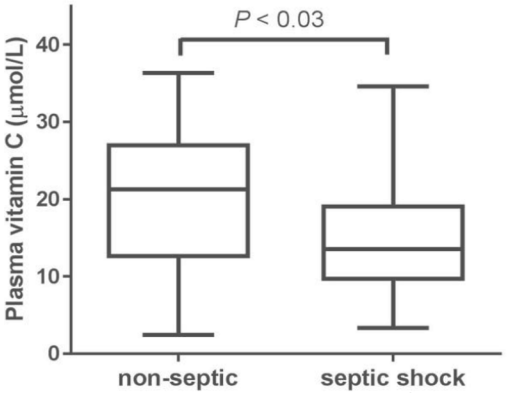
[1] ROS, reactive oxygen species; NET, neutrophil extracellular trap. Note that many of these studies comprised marginal or deficient vitamin C status at baseline. Supplementation in situations of adequate vitamin C status may not have comparable effects.

Carr, Maggini. *Nutrients* 2017; doi:10.3390/nu9111211

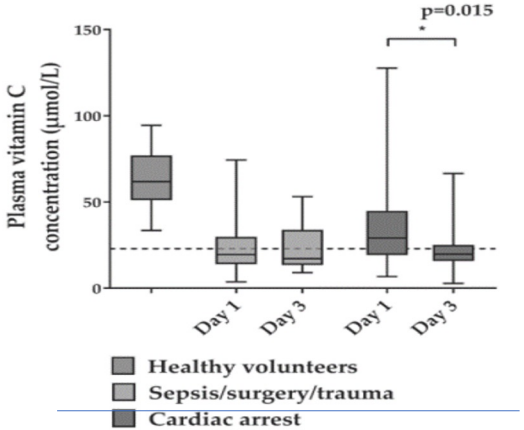
Hypovitaminosis C in Critically Ill

+ Observational studies have estimated that nearly 40% of patients with sepsis are vitamin C deficient, defined as plasma concentrations less than 23 µmol/L.

- **Increased loss**
  - Consumption
  - Renal loss (hyperfiltration and decreased reabsorption)
  - Reduced recycling
  - Compartment shifts
- **Decreased intake**
  - Slow build-up of enteral nutrition
  - Degradation within parenteral nutrition
- Hemodilution



Carr. *Critical Care* 2017; doi:10.1186/s13054-017-1891-y



Rozemeijer. *Nutrients* 2019; doi:10.3390/nu11051031

+ Low levels inversely correlated with measures of multiorgan dysfunction. (Borrelli. *Crit Care Med* 1996)

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High Dose Vitamin C in Burn-Injured Patients

+ 37 burn-injured patients (pseudo) randomized to 66 mg/kg/24 hr IV infusion

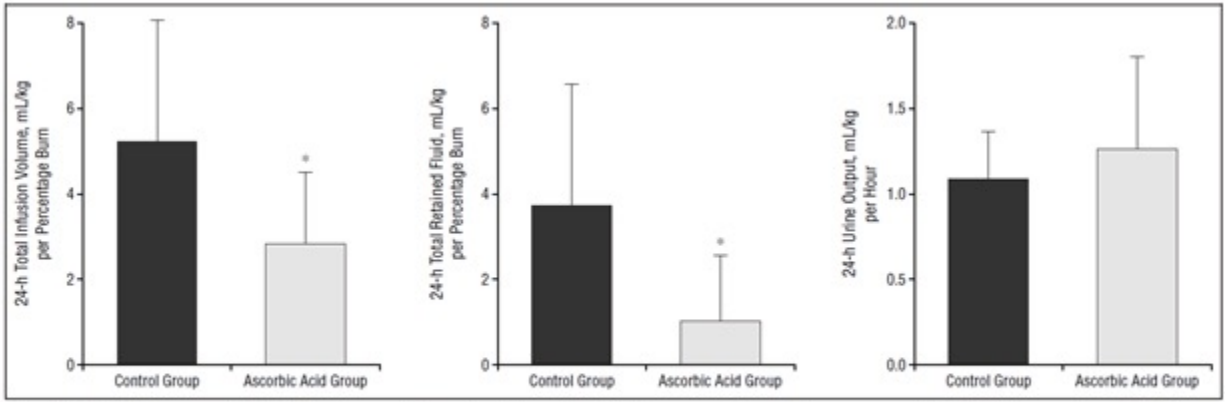
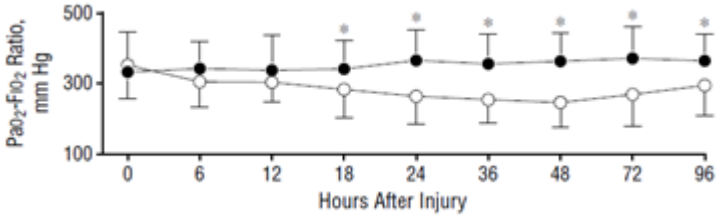


Figure 2. *The 24-hour resuscitation fluid volume requirement and urine output in both groups. Data are given as mean ± SD. Fluid volume requirement in the control group was 5.5 ± 3.1 mL/kg per percentage of total body surface area (TBSA) burn, whereas the ascorbic acid group required only 3.0 ± 1.7 mL/kg per percentage of TBSA burn, representing a 45.5% reduction. Asterisk indicates P<.05 compared with the ascorbic acid group.*



<10% of RE-EN sites use this protocol

Tanaka et al. *Arch Surg* 2000;135:326-31.

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Vitamin C in Burns

- Low utilization
- Concern that such a high dose of intravenous Vitamin C may cause renal failure and worsen clinical outcomes (retrospective study by Lin et. al. JBCR 2018)
- Need more data!

Hydrocortisone, Vitamin C and Thiamine for the Treatment of Severe Sepsis and Septic Shock: A Retrospective Before-After Single Center Study

+ Cocktail of Hydrocortisone 50 mg q 6h x 7 days, IV Ascorbic Acid 1.5 grams q 6h, and Thiamine 200 mg q 12h x 4 days

TABLE 2] Outcome and Treatment Variables

Variable	Treated (n = 47)	Control (n = 47)
Hospital mortality, No. (%)	4 (8.5)	19 (40.4)[a]
ICU LOS, median and IQR, d	4 (3-5)	4 (4-10)
Duration of vasopressors, mean ± SD, h	18.3 ± 9.8	54.9 ± 28.4 [a]
RRT for AKI, No. (%)	3 of 31 (10%)	11 of 30 (33%)[b]
ΔSOFA, 72 h	4.8 ± 2.4	0.9 ± 2.7[a]
Procalcitonin clearance, median % and IQR, 72 h	86.4 (80.1-90.8)	33.9 (−62.4 to 64.3)[a]

AKI = acute kidney injury; LOS = length of stay; RRT = renal replacement therapy; ΔSOFA = change in Sepsis-Related Organ Failure Assessment score. See Table 1 legend for expansion of other abbreviations.
[a] $P < .001$.
[b] $P = .02$.

Marik et al. *Chest* 2017;151:1229-38.

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Effect of high-dose Ascorbic acid on vasopressor's requirement in septic shock

- Single-center RCT of 28 patients
- Treated patients received 25 mg/kg intravenous ascorbic acid every 6 h for 72 h.

Table 4: Primary and secondary outcomes of the study in ascorbic and placebo groups

Characteristics	Ascorbic acid group (*n*=14)	Control group (*n*=14)	*P*
Mean dose of norepinephrine (mcg/min) during the study period (72 h)	7.44±3.65	13.79±6.48	0.004
Mean dose of norepinephrine (mcg/min) during first 24 h (mcg/min)	6.51±3.53	12.58±5.99	0.003
Total dose of norepinephrine during the first 24 h (mcg)	156.42±84.81	302.14±143.85	0.003
Duration of norepinephrine administration (h)	49.64±25.67	71.57±1.60	0.007
Length of ICU stay (days)	21.45±10.23	20.57±13.04	0.85
28-day mortality	2 (14.28)	9 (64.28)	0.009

Data presented as mean±SD or *n* (%). SD=Standard deviation, ICU=Intensive Care Unit

Zabet et al. *J Res Pharm Pract* 2016;5:94-100.

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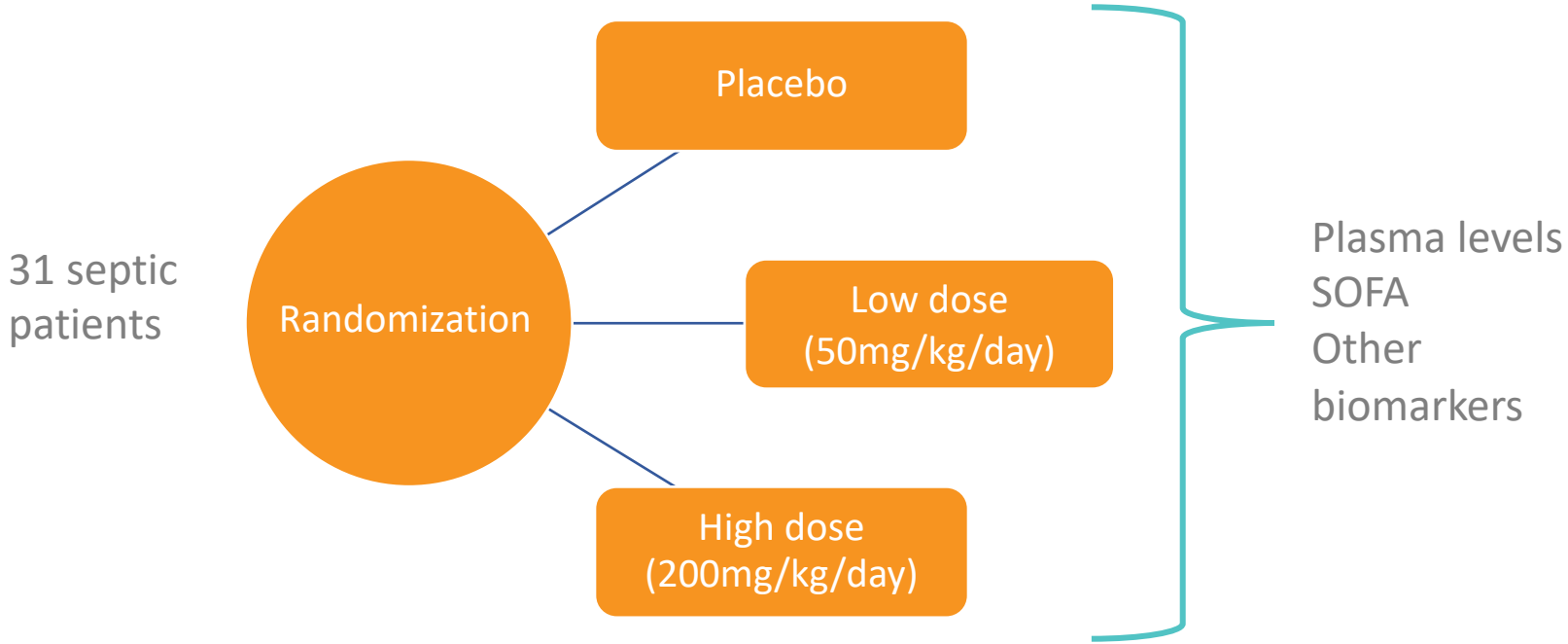
Phase I Vit C dosing study in Sepsis



Fowler et al. *J Translational Medicine* 2014;12:32

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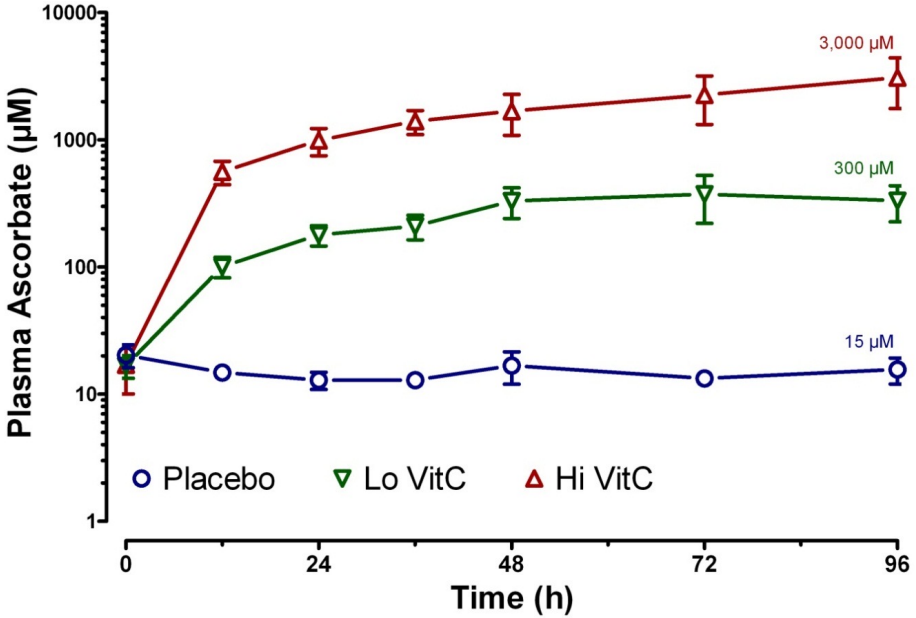
Plasma Vitamin C Levels



Fowler et al. *J Translational Medicine* 2014;12:32

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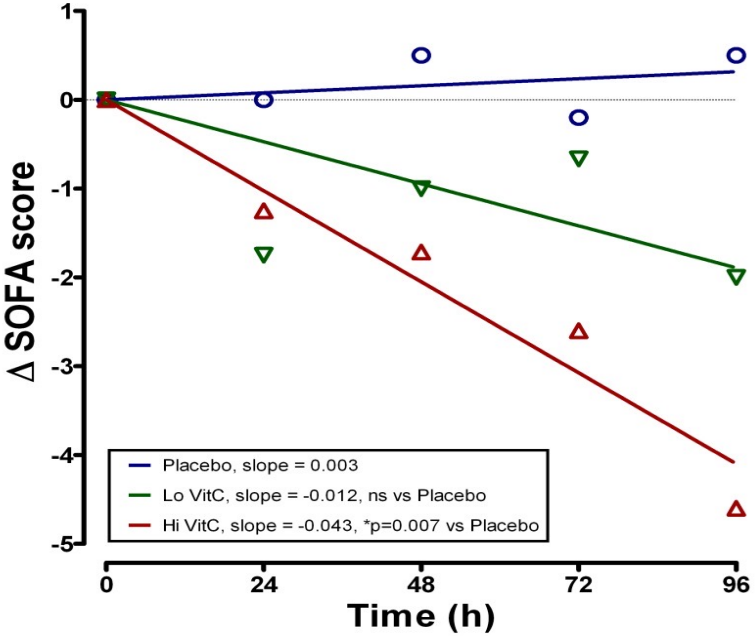
EFFECT on Organ Failure and other Mechanistic Endpoints



+ Reduced CRP and PCT (markers of inflammation)
+ Reduced Thrombomodulin (marker of vascular injury)

Moved onto a Phase II trial with the high dose!

Fowler et al. *J Translational Medicine* 2014;12:32

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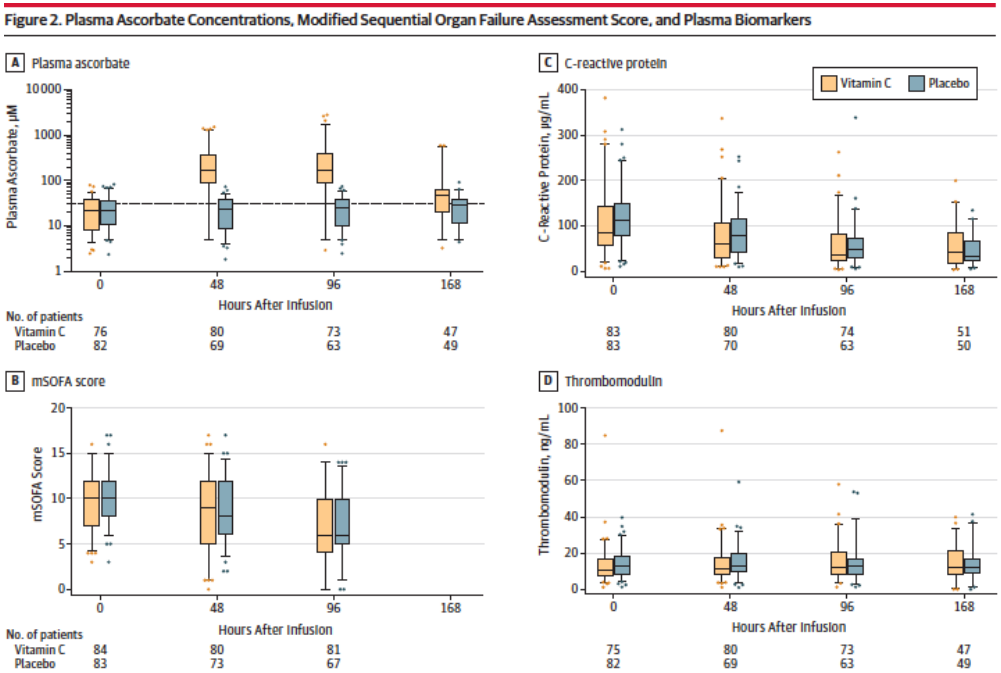
Vitamin C in Acute Lung Injury
CITRUS-ALI Trial



- 170 patients with ALI/Sepsis within 48 hrs of development of ARDS randomized to 50mg/kg q 6 hrs x 96 hrs or placebo.
- 43 of 46 prespecified outcomes NOT different between groups (including ΔSOFA and vasopressor use) except…

Fowler et al. JAMA 2019;322:1261-1270.

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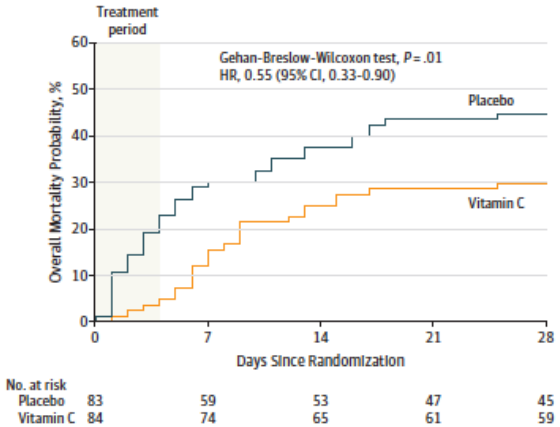
Vitamin C in Acute Lung Injury: CITRUS-ALI Trial

Variable	Hour	Vitamin C No.	Vitamin C Median or %	Vitamin C IQR	Placebo No.	Placebo Median or %	Placebo IQR	Difference, Coefficient (95% CI)	*P* Value
ICU-free days to day 28, median (IQR), d		83	11	21	82	0	18	3.2 (0.3 to 6.0)	.03
Hospital-free days, to day 60, median (IQR), d		82	22	46	80	0	39	7.0 (0.3 to 13.8)	.04

Figure 3. All-Cause Mortality From Randomization (Day 0) to Day 28 Among Patients With Sepsis-Associated Acute Respiratory Distress Syndrome



+ Significant increase in ICU- and Hospital-free days and a significant reduction in mortality except…

Fowler et al. JAMA 2019;322:1261-1270.

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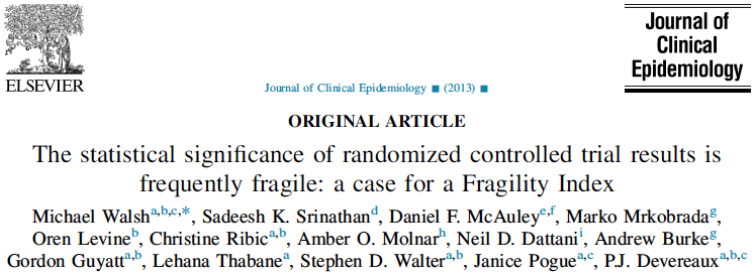
Vitamin C in Acute Lung Injury: CITRUS-ALI Trial

Observed Trial Results		
	P-value:	0.037
category names ↓→	Event	non event
Vit C	25	59
placebo	38	44

Effect of 1 more death in Vit C group		
	P-value:	0.055
category names ↓→	Event	non event
Vit C	26	58
placebo	38	44

- Results are very fragile!
- Fragility Index=1



Walsh et al. *J Clin Epidemiol* 2014 Jun;67:622-8.

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Vitamin C in Acute Lung Injury: CITRUS-ALI Trial

Conclusion

- High degree of validity and generalizability
- SAFE- no adverse events reported
- Inconclusive results
  - Primary endpoints negative
  - Positive results are ‘fragile’ and hypothesis-generating at best
  - Mechanism of action?
- Need more research

Vitamin C Systematic Reviews

ONLINE REVIEW ARTICLE

IV Vitamin C in Critically Ill Patients: A Systematic Review and Meta-Analysis

Jayshil J. Patel, MD[1]
Alfonso Ortiz-Reyes, MSc[2]
Rupinder Dhaliwal, RD[2]
John Clarke, MSc, RKin[2]
Aileen Hill, MD[3]
Christian Stoppe, MD[4]
Zheng-Yii Lee, MSc[5]
Daren K. Heyland, MD[2]

OBJECTIVES: To conduct a systematic review and meta-analysis to evaluate the impact of IV vitamin C on outcomes in critically ill patients.

DATA SOURCES: Systematic search of MEDLINE, EMBASE, CINAHL, and the Cochrane Register of Controlled Trials.

STUDY SELECTION: Randomized controlled trials testing IV vitamin C in critically ill patients.

DATA ABSTRACTION: Two independent reviewers abstracted patient characteristics, treatment details, and clinical outcomes.

DATA SYNTHESIS: Fifteen studies involving 2,490 patients were identified. Compared with placebo, IV vitamin C administration is associated with a trend toward reduced overall mortality (relative risk, 0.87; 95% CI, 0.75–1.00; $p = 0.06$; test for heterogeneity $I^2 = 6\%$). High-dose IV vitamin C was associated with a significant reduction in overall mortality (relative risk, 0.70; 95% CI, 0.52–0.96; $p = 0.03$), whereas low-dose IV vitamin C had no effect (relative risk, 0.94; 95% CI, 0.79–1.07; $p = 0.46$; test for subgroup differences, $p = 0.14$). IV vitamin C monotherapy was associated with a significant reduction in overall mortality (relative risk, 0.64; 95% CI, 0.49–0.83; $p = 0.006$), whereas there was no effect with IV vitamin C combined therapy. No trial reported an increase in adverse events related to IV vitamin C.

CONCLUSIONS: IV vitamin C administration appears safe and may be associated with a trend toward reduction in overall mortality. High-dose IV vitamin C monotherapy may be associated with improved overall mortality, and further randomized controlled trials are warranted.

Intensive Care Med (2022) 48:16–24
https://doi.org/10.1007/s00134-021-06558-0

SYSTEMATIC REVIEW

Effect of adjunctive vitamin C, glucocorticoids, and vitamin B1 on longer-term mortality in adults with sepsis or septic shock: a systematic review and a component network meta-analysis

Tomoko Fujii[1,2,3*], Georgia Salanti[4], Alessandro Belletti[5], Rinaldo Bellomo[2,6,7], Anitra Carr[8], Toshi A. Furukawa[3], Nora Luethi[2,9], Yan Luo[3], Alessandro Putzu[10], Chiara Sartini[5], Yasushi Tsujimoto[3,14], Andrew A. Udy[2,11], Fumitaka Yanase[2,6] and Paul J. Young[2,7,12,13]

nutrients

MDPI

Systematic Review

Vitamin C in Critically Ill Patients: An Updated Systematic Review and Meta-Analysis

Dhan Bahadur Shrestha [1,*], Pravash Budhathoki [2], Yub Raj Sedhai [3,*], Sujit Kumar Mandal [4], Shreeja Shikhrakar [5], Saurab Karki [6], Ram Kaji Baniya [7], Markos G. Kashiouris [8,*], Xian Qiao [9] and Alpha A. Fowler [8]

CLINICAL INVESTIGATION

Effect of IV High-Dose Vitamin C on Mortality in Patients With Sepsis: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Ryota Sato, MD[1]
Daisuke Hasegawa, MD, PhD[2]
Narut Prasitlumkum, MD[3]
Miki Ueoka, MD[4]
Kazuki Nishida, MD[5,6]
Kunihiko Takahashi, PhD[7]
Michitaka Nasu, MD[8]
Siddharth Dugar, MD[1,9]

OBJECTIVES: The aim of this study was to conduct a systematic review and meta-analysis of randomized controlled trials to investigate whether IV high-dose vitamin C improves the short-term mortality of patients with sepsis.

DESIGN: This study is a systematic review and meta-analysis of randomized controlled trials. We searched EMBASE, the Cochrane Central Register of Controlled Trials, and MEDLINE for randomized controlled trials that met inclusion criteria. The protocol was registered at the University hospital Medical Information Network Clinical Trials Registry (UMIN000040528). All analyses were presented with the use of random-effects models. The primary outcome was short-term mortality defined as 28-day, 30-day, or in-hospital mortality.

PATIENTS: Two authors independently evaluated the following eligibility criteria: 1) randomized controlled trial, 2) patients with sepsis aged ≥18 years, and 3) received intravenous high-dose vitamin C in addition to standard of care, or standard of care alone. Then, two authors independently extracted the selected patient and study characteristics and outcomes from studies that met above eligibility criteria.

MEASUREMENTS AND MAIN RESULTS: Eleven randomized controlled trials ($n = 1,737$ patients) were included in this meta-analysis. High-dose IV vitamin C was not associated with a significantly lower short-term mortality (risk ratio, 0.88; 95% CI, 0.73–1.06; $p = 0.18$; $I^2 = 29\%$) but was associated with a significantly shorter duration of vasopressor use (standardized mean difference, −0.35; 95% CI, −0.63 to −0.07; $p < 0.01$; $I^2 = 80\%$) and a significantly greater decline in the Sequential Organ Failure Assessment score at 72–96 hours (standardized mean difference, −0.20; 95% CI, −0.32 to −0.08; $p < 0.01$; $I^2 = 16\%$). One study reported significant association with hypernatremia, but adverse effects were rare, and high-dose vitamin C is deemed relatively safe.

CONCLUSIONS: In this meta-analysis, the use of IV high-dose vitamin C in patients with sepsis was not associated with lower short-term mortality although it

REVIEW ARTICLES

Thiamine, Ascorbic Acid, and Hydrocortisone As a Metabolic Resuscitation Cocktail in Sepsis: A Meta-Analysis of Randomized Controlled Trials With Trial Sequential Analysis*

Assouline, Benjamin MD[1]; Faivre, Anna MD[2,3]; Verissimo, Thomas PhD[2]; Sangla, Frédéric MD[1]; Berchtold, Lena MD[3]; Giraud, Raphaël MD, PhD[1,4]; Bendjelid, Karim MD, PhD[1,4]; Sgardello, Sebastian MD[5]; Elia, Nadia MD, MSc[4,6]; Pugin, Jérôme MD[1,4]; de Seigneux, Sophie MD, PhD[2–4]; Legouis, David MD, PhD[1,2]

Author Information

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Consistent signal of benefit for vit C
Higher dose better
No benefit for HAT
No safety issues

Critical Care Nutrition

Evaluating Vitamin C in Septic Shock: A Randomized Controlled Trial of Vitamin C Monotherapy

124 patients in septic shock
1,000 mg bolus followed by 250 mg/hr for 96 hours

Primary and Secondary Outcomes

Outcome	Vitamin C Group	Placebo Group	*p*
Primary outcome			
28-d mortality, *n* (%)	16 (26.7) (*n* = 60)	26 (40.6) (*n* = 64)	0.10
Secondary outcomes			
ICU mortality, *n* (%)	14 (23.3) (*n* = 60)	20 (31.1) (*n* = 64)	0.32
Renal function outcomes			
Paired improvement in creatinine (mg/dL),[a] median (IQR)	0.4 (0–0.7) (*n* = 49[b–d])	0.3 (–0.1 to 0.7) (*n* = 56[b–d])	0.55
Renal replacement therapy required during 96-hr study period, *n* (%)	10 (16.7) (*n* = 60[d])	2 (3.3) (*n* = 60[d])	0.02

Wacker CCM 2022

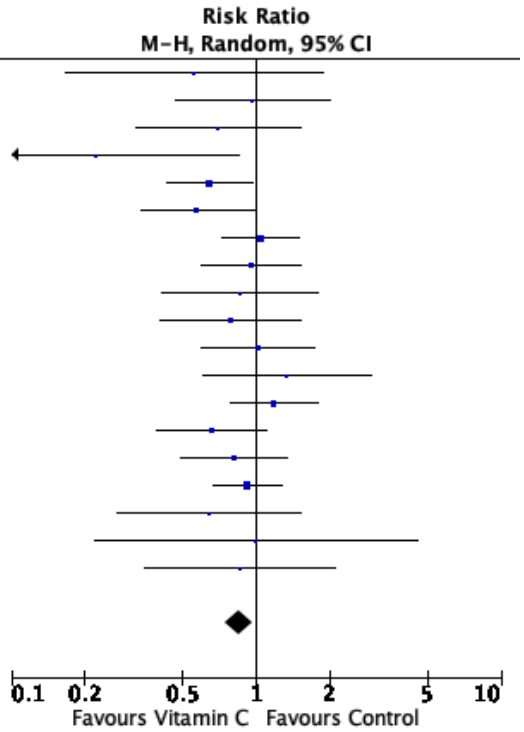
Most Current Systematic Review and Meta-analysis of Parenteral Vitamin C Trials in ICU Setting

Mortality

Study or Subgroup	Vitamin C Events	Vitamin C Total	Control (placebo or none) Events	Control (placebo or none) Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Nathens 2002	4	301	7	294	1.1%	0.56 [0.17, 1.89]	2002
Razmkon 2011	14	49	8	27	3.0%	0.96 [0.46, 2.00]	2011
Fowler 2014	7	16	5	8	2.7%	0.70 [0.32, 1.52]	2014
Zabet 2016	2	14	9	14	0.9%	0.22 [0.06, 0.85]	2016
Fowler 2019	25	84	38	82	9.8%	0.64 [0.43, 0.96]	2019
Lv 2020	15	61	24	56	5.6%	0.57 [0.34, 0.98]	2020
Mohamed 2020	26	45	25	45	12.2%	1.04 [0.72, 1.49]	2020
Wani 2020	20	50	21	50	7.2%	0.95 [0.59, 1.52]	2020
Iglesias 2020	11	68	13	69	3.0%	0.86 [0.41, 1.78]	2020
Chang 2020	11	40	14	40	3.7%	0.79 [0.41, 1.52]	2020
Fujii 2020	22	106	21	103	5.6%	1.02 [0.60, 1.73]	2020
Hwang 2020	11	53	9	58	2.5%	1.34 [0.60, 2.97]	2020
Moskowitz 2020	35	101	29	99	9.7%	1.18 [0.79, 1.78]	2020
Wacker 2021	16	60	26	64	6.1%	0.66 [0.39, 1.10]	2021
Hussein 2021	17	47	21	47	6.5%	0.81 [0.49, 1.33]	2021
Sevransky 2021	56	252	60	249	15.7%	0.92 [0.67, 1.27]	2021
Zhang 2021	6	27	10	29	2.1%	0.64 [0.27, 1.53]	2021
Jamali Moghadam Siahkali 2021	3	30	3	30	0.7%	1.00 [0.22, 4.56]	2021
Rosengrave 2022	6	20	7	20	2.0%	0.86 [0.35, 2.10]	2022
Total (95% CI)		1424		1384	100.0%	0.85 [0.75, 0.97]	
Total events	307		350				

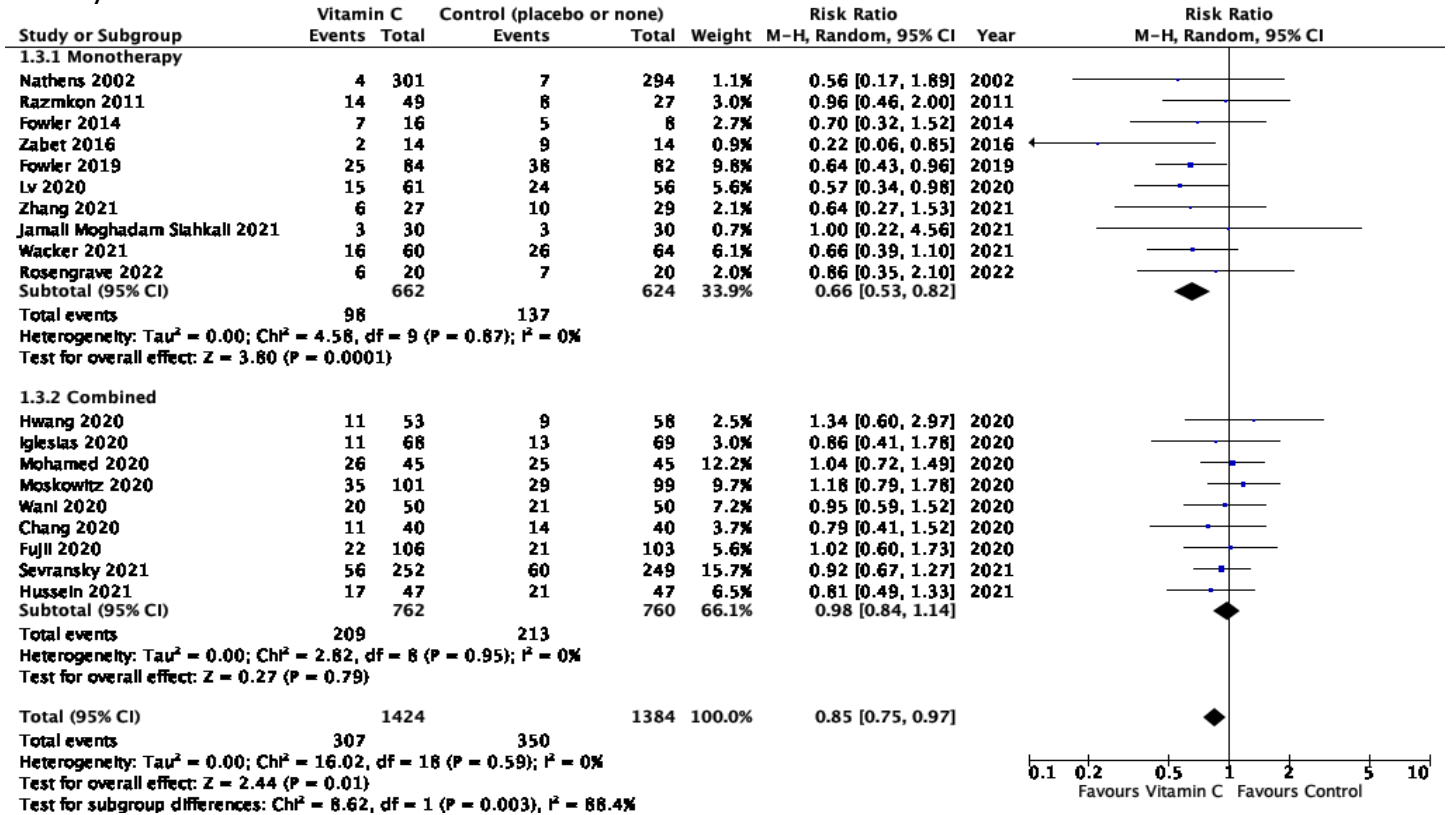
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 16.02$, $df = 18$ ($P = 0.59$); $I^2 = 0\%$

Test for overall effect: $Z = 2.44$ ($P = 0.01$)



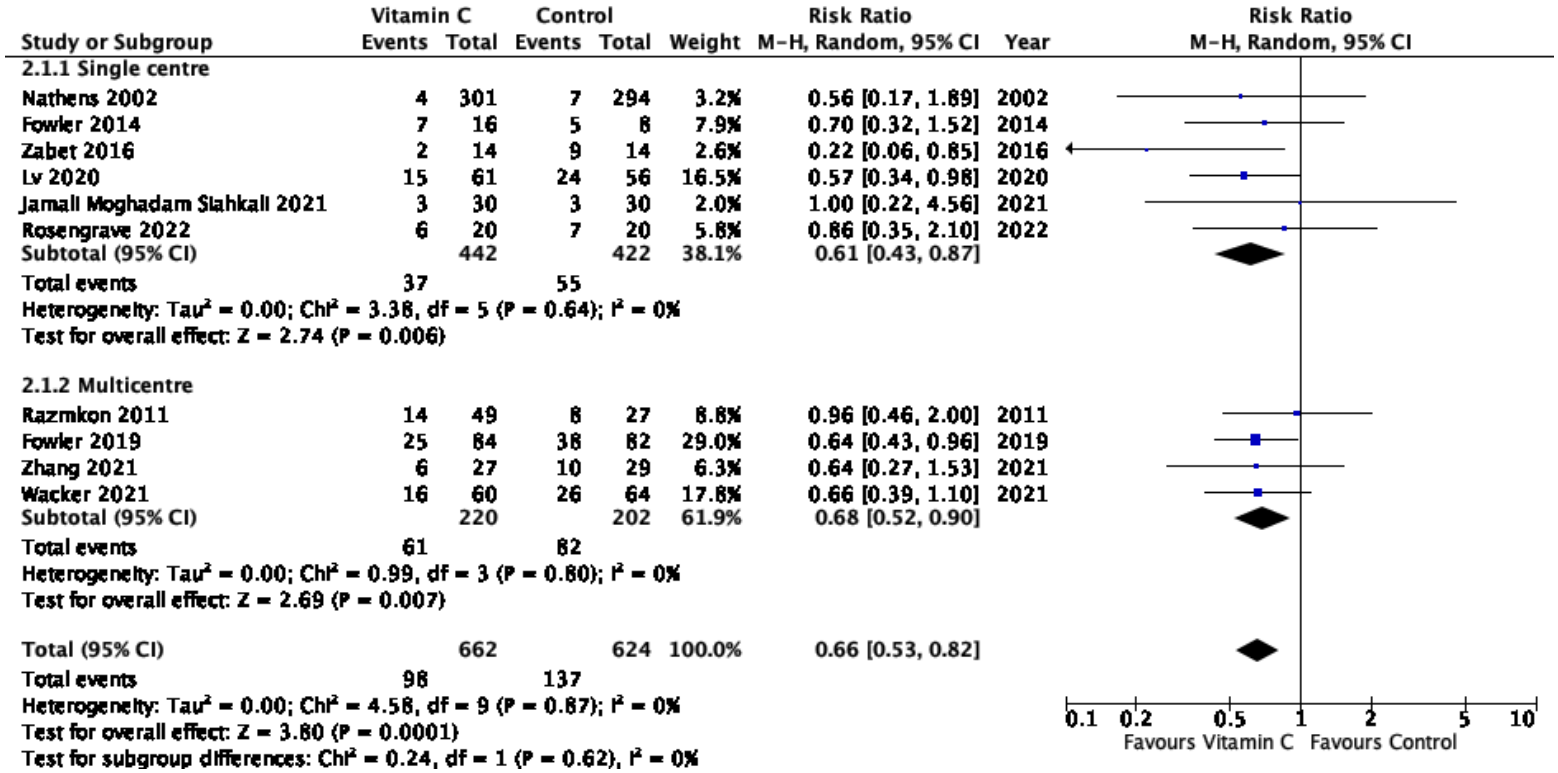
Most Current Systematic Review and Meta-analysis of Parenteral Vitamin C Trials in ICU Setting

Mortality



Most Current Systematic Review and Meta-analysis of Parenteral Vitamin C (Monotherapy) Trials in ICU Setting

Mortality



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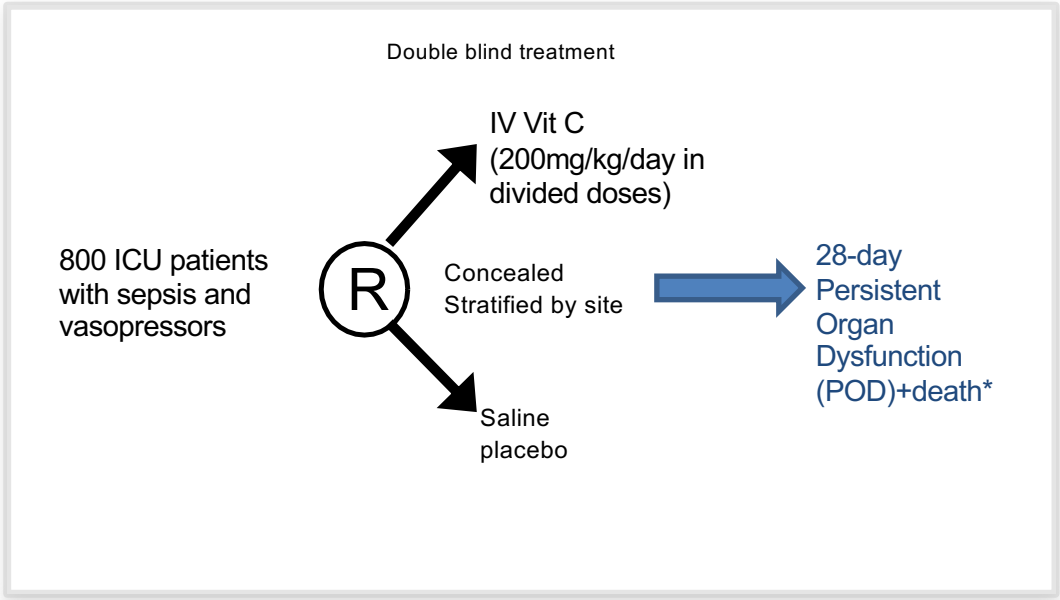
LOVIT

The **L**essening **O**rgan Injury/Dysfunction with **VIT**amin C (LOVIT) Trial



Vitamin C Systematic Review – Conclusions

Conclusions:

In Critically ill patients, IV vitamin C…

1. may be associated with lower overall mortality.

   The beneficial treatment effect may be greater with the use of high-dose vitamin C used alone (not in combination with thiamine or corticosteroids) in both sepsis and non-sepsis (including burns).

1. has no effect on ICU, hospital LOS or ventilation outcomes in critically ill patients.
2. may facilitate faster resolution of shock or less use of vasopressor but the heterogeneous nature of the data and conflicting results preclude firm conclusions.
3. may have a positive impact on the resolution of SOFA scores
4. appears to be safe.

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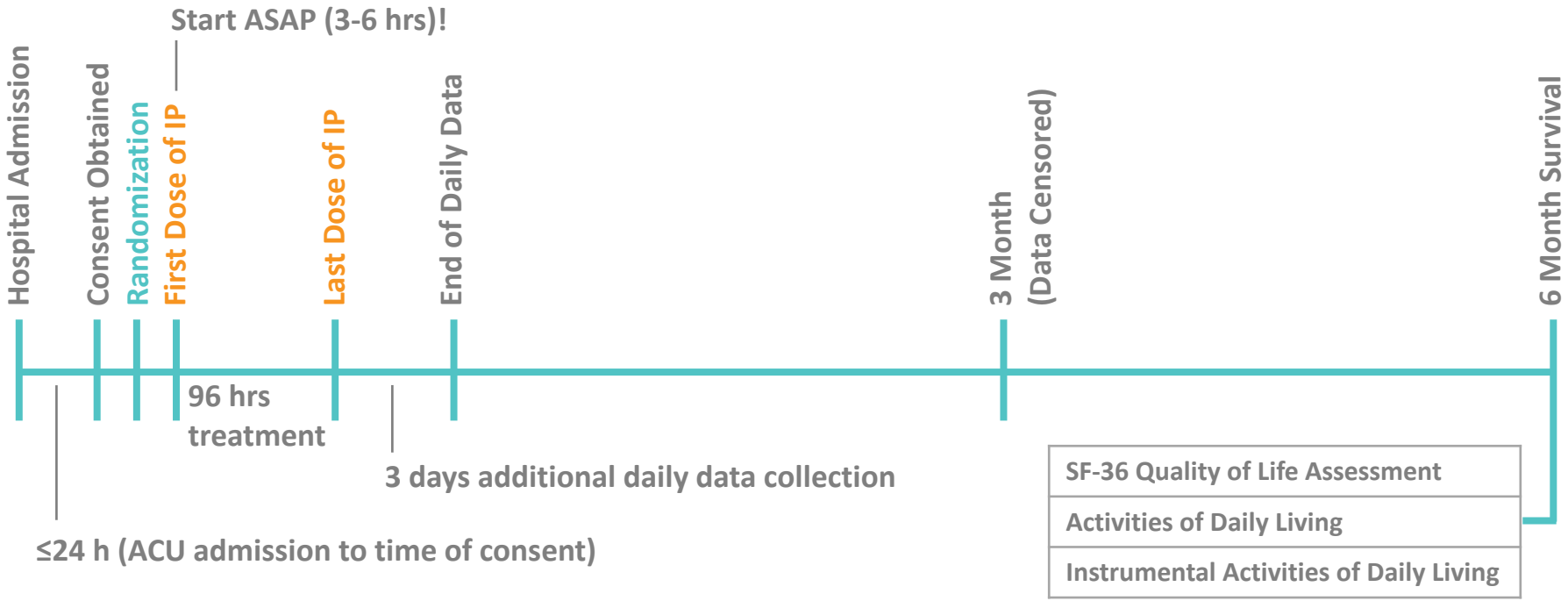
VIT VICTORY

Queen's University

Overall Aim

The overall aim of the VICToRY study is to reduce the burden of illness associated with significant burn injury using a naturally occurring substance, vitamin C!

Study Overview



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Potential Impact

If the VICToRY pilot trial is feasible, we will move right into the phase III trial. If the larger phase III trial shows positive results, we can immediately implement this simple, inexpensive product around the world in both hospitals and 'in the field' settings. Thus, we will:

+ Save lives
+ Reduce infections
+ Shorten stays in hospital
+ Improve the physical recovery of burn injured victims
+ Save money

Thank you for your interest and support

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Questions

Presentation Outline

2. **Site Investigator Responsibilities**
3. **Patient Eligibility (Inclusion/Exclusion Criteria)**
4. Obtaining Consent
5. Randomizing a Patient
6. IP Administration
7. Study Blood Work
8. Pharmacy Procedures (Investigational Product-IP)
9. Data Collection and Data Entry
10. Serious Adverse Event Reporting
11. **Outcomes**
12. Data Quality Checks, Queries, and Monitoring

VIT VICTORY