

Outcomes



Primary Outcomes

- + Persistent Organ Dysfunction + Death at 28 days (composite endpoint of)
 - + Being Alive
 - + Free from Organ Support (Inotropes/vasopressors, renal replacement therapy, mechanical ventilation)





What is POD?

Persistent Organ Dysfunction (POD) +death is a novel composite endpoint that has been previously validated in general intensive care unit (ICU) patients.

POD+death = need for life-sustaining therapies:

- 1. Mechanical ventilation
- 2. Vasopressor therapy
- 3. Mechanical circulatory support
- 4. Continuous renal replacement therapy

Heyland Critical Care 2011



What is POD?

When combined with death, the prevalence of PODs increases the event rate.

ICU day	RE-ENERGIZE Pilot and bridge trial (n=173)							
	In Shock	On Dialysis	MV	Dead	Dead or with POD	Dead or with mPOD		
1	3.5	9.2	40.5	0.0	42.2	41.0		
2	4.6	9.2	41.0	0.0	41.6	41.6		
3	6.4	9.2	40.5	0.0	40.5	40.5		
4	6.4	9.2	39.3	0.6	41.0	39.9		
5	5.2	9.2	39.9	0.6	41.6	40.5		
6	4.6	9.2	39.3	0.6	39.9	39.9		
7	4.0	9.2	39.3	0.6	39.9	39.9		
8	4.6	9.2	39.9	1.2	40.5	40.5		
9	5.7	8.6	37.4	1.1	39.1	38.5		
10	6.4	8.7	35.8	1.2	37.6	37.0		
11	6.4	8.7	35.3	1.7	37.6	36.4		
12	6.4	8.7	34.7	1.7	37.0	36.4		
13	6.9	8.7	32.9	1.7	35.3	34.7		
14	3.5	8.7	31.8	1.7	34.1	33.5		
21	5.2	75	24.3	4.0	28.0	28.3		
28	4.6	6.4	14.5	6.4	23.1	22.0		
60	N/A	2.9	5.8	11.0	N/A	16.8		
90	N/A	1.2	1.7	12.7	N/A	14.5		



Stoppe Burns 2021

VICTORV

What is POD?



Patients alive at day 28 with POD have a higher 6 month-mortality...

Critical Care Nutrition

	Day 28		
	Without mPOD (n=192)	With mPOD (n=37)	P - value
Physical Functioning	63.5 (31.5)	47.6 (31.3)	0.005
Role-Limitations due to physical problems	49.6 (34.7)	33.6 (30.6)	0.01
Pain Index	55.6 (28.8)	49.8 (27.0)	0.26
General Health Perceptions	62.2 (24.6)	51.2 (26.3)	0.02
Vitality	53.2 (23.5)	47.9 (22.8)	0.21
Social Functioning	63.9 (34.4)	51.7 (32.8)	0.05
Role-Limitations due to emotional problems	62.9 (35.6)	51.9 (37.5)	0.09
Mental Health Index	66.4 (23.6)	63.0 (23.3)	0.41
Standardized Physical Component Scale	42.4 (10.8)	36.2 (9.3)	0.002
Standardized Mental Component Scale	43.8 (14.8)	41.0 (14.5)	0.31

...and a lower quality of life. These observations validate that having POD is clinically important. Stoppe Burns 2021

Why POD+death?

By using a more proximal endpoint, such as 28-day POD+death, which has a higher event rate, the sample size requirements and the costs of follow up might be reduced. Table 4: Total size required to achieve 80% power at a two-sided alpha=0.5 for selected outcomes at various effect sizes; RRR: relative risk reduction, SD: standard deviation, A: delta, difference, mPOD: modified Persistent Organ Dysfunction,

Time Point	Observed rate	15% RRR	20% RRR	25% RRR	30% RRR	
Mortality	1					
14	4%	31066	17018	10596	7154	
28	9%	13140	7206	4492	3036	
00	1370	8728	4/92	2990	2022	
90	15%	7404	4066	2538	1718	
mPOD+death						
14	39%	2108	1168	736	502	
28	27%	3580	1974	1236	\$40	
60	18%	5970	3282	2050	1388	
90	17%	6392	3512	2194	1486	
mPOD free days	Mean±SD	25% of mean days with mPOD	∆=1 day	∆=2 days	∆=3 days	
14	7.7±6.4	522 (A=1.6 days)	1288	324	146	
28	17.1±11.8	592 (A=2.7 days)	4372	1094	488	
60	42.3±22.2	792 (Δ=4.4 days)	15474	3870	1720	
90	67.1±31.5	952 (Δ=5.7 days)	31154	7790	3462	
Time to discharge alive (censored at 90 days)						
25% RRR in mortality and 25% increase in daily discharge rate						
25% RRR in mortality and 10% increase in daily discharge rate						
0% RRR in mortality and 25% increase in daily discharge rate						



Stoppe Burns 2021



Secondary Outcomes

- + ICU outcomes (e.g. length of stay, duration of mechanical ventilation, and readmission rates)
- + Hospital outcomes (mortality, length of stay, time-to-discharge alive, bacteremia with gram-negative bacilli)
- + 6-month outcomes (mortality, SF-36, Katz ADL, and Lawton IADL).





Safety Outcomes

- + Routine labs
 - + Glucose, HCO3, Albumin
 - + Urea/Creatinine
 - + LFTs

Nutrition

- + Hemoglobin, Haptoglobin
- + Laboratory Sub-study
 - + Vitamin C levels
 - + Measures of oxidative stress and antioxidant capacity (ORP)
 - + Markers of inflammation (IL-6, IL-10)
- ▲ Markers of acute kidney injury (ILGF7xTIMP and penKID)



Events of Interest

- + New dx of oxalate kidney stones
- + Severe hemolysis
- + Severe acid-base/electrolyte imbalances
- + Refractory hypoglycemia









