2015 – A Year of Critical Care

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NEICS Spring Meeting 2016

2015 – A Year of Critical Care

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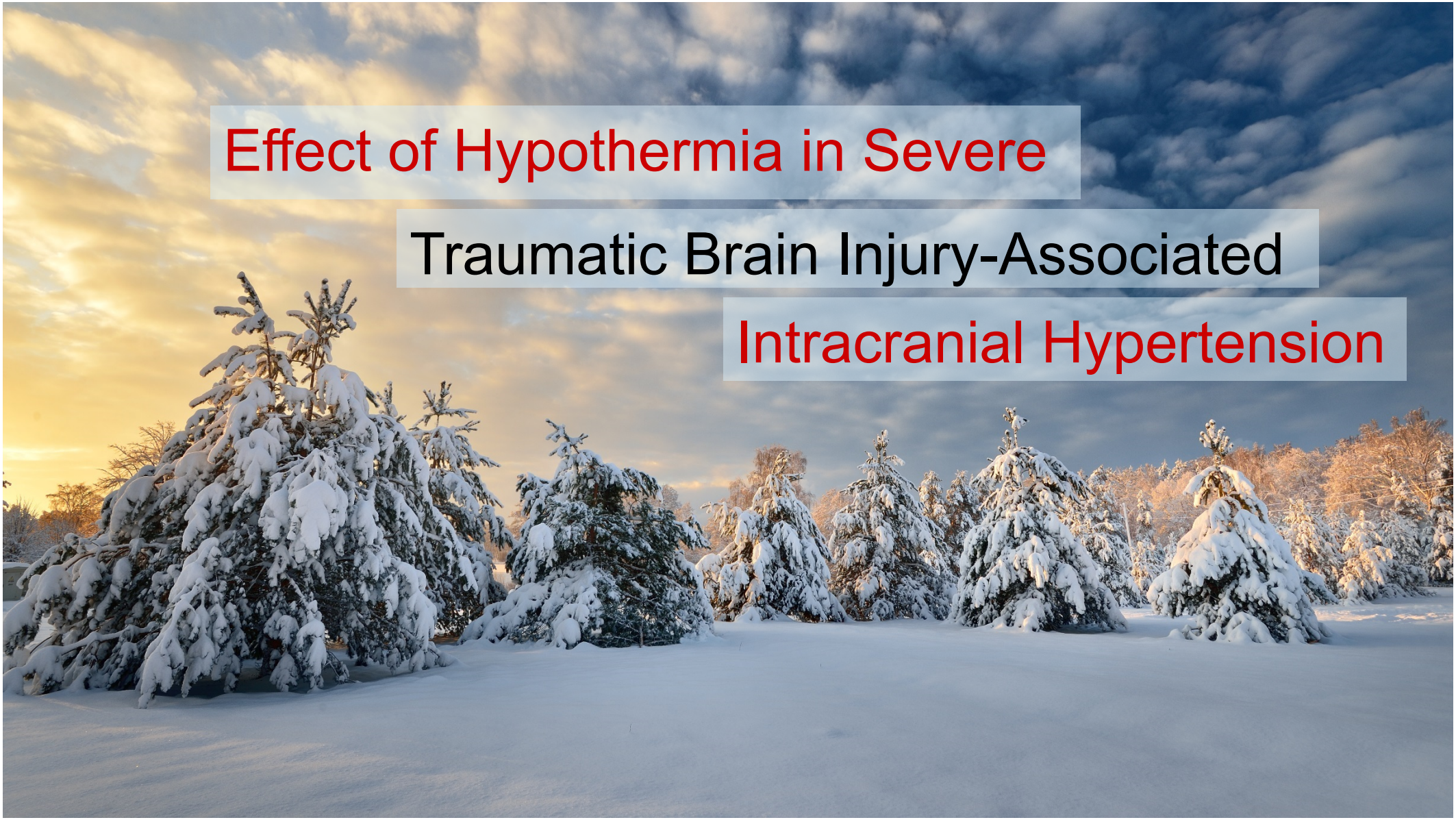
http://bit.do/CCR-NEICS16

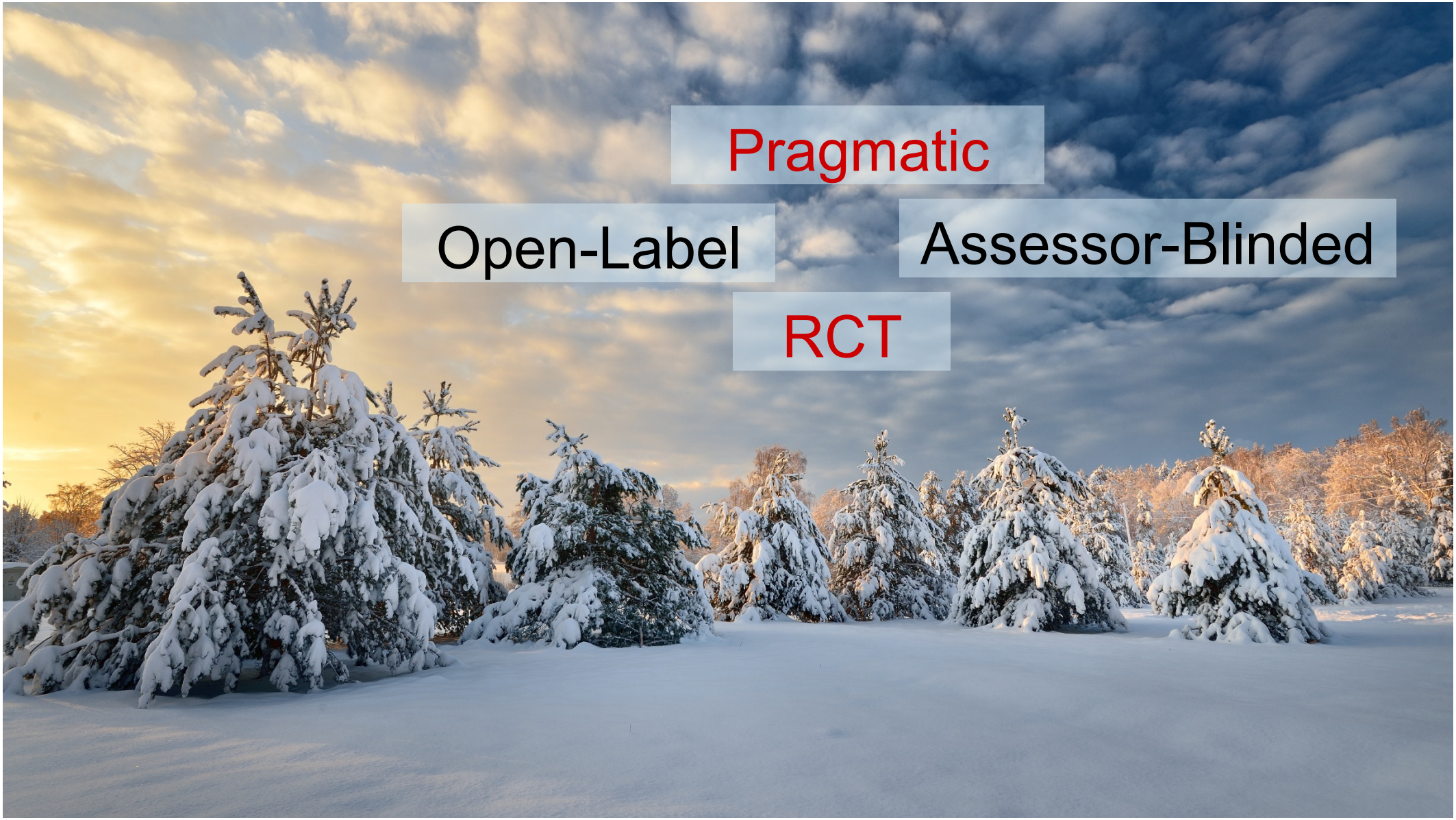

Conflict of
Interest


Health Research Board of Ireland

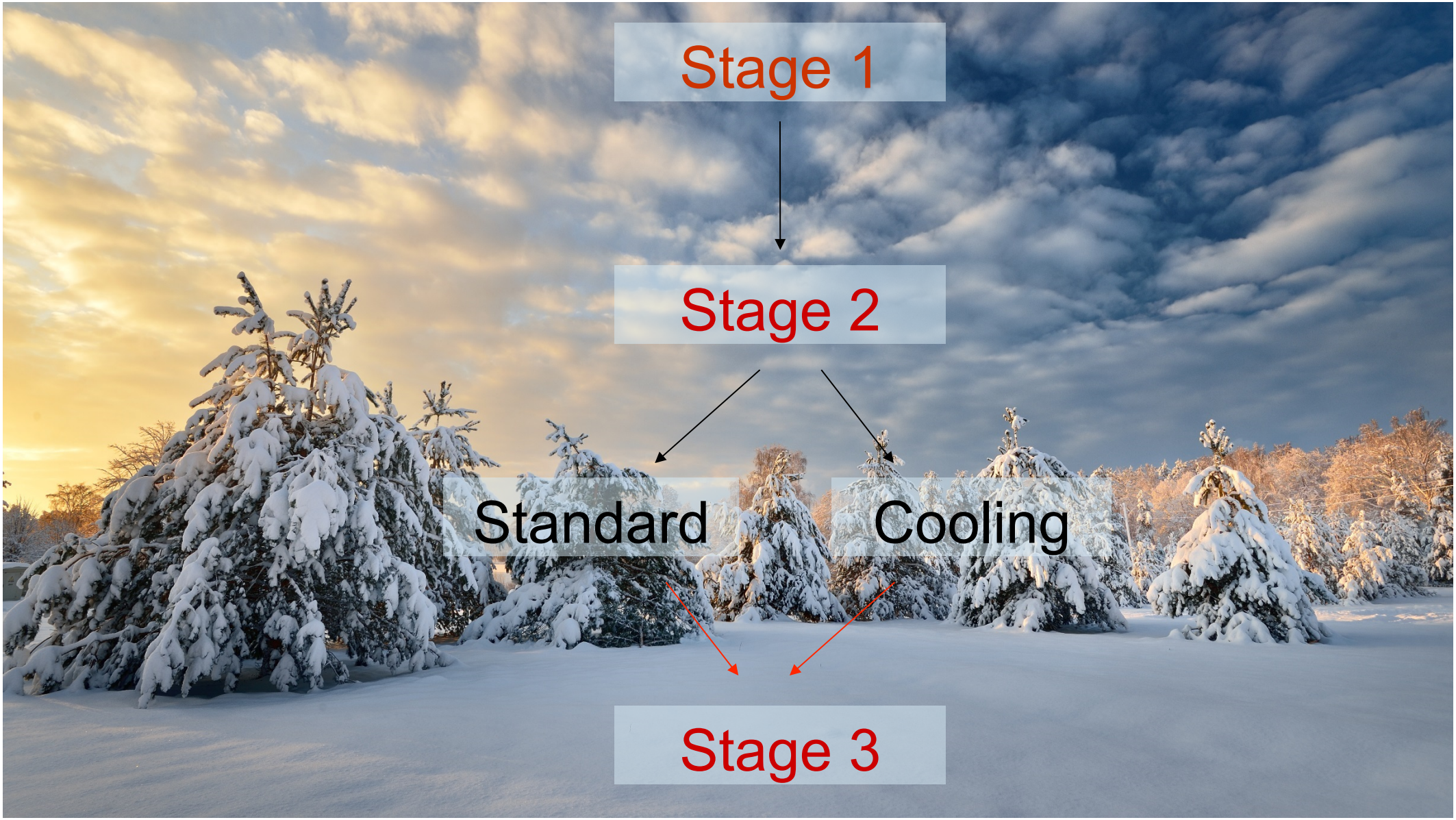

Health Research Board of Ireland
Irish Critical Care Trials Group


Eurotherm

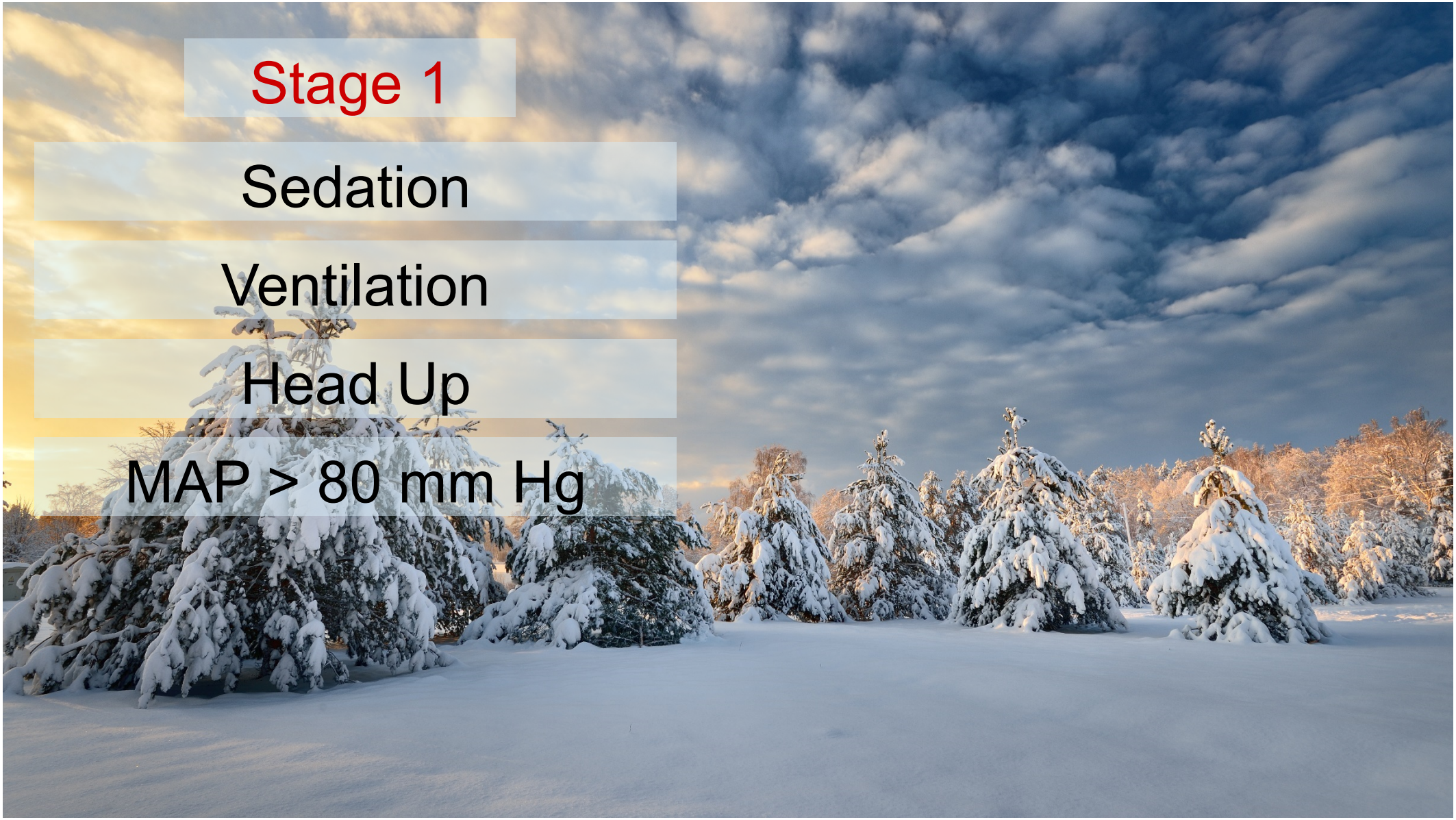

Effect of Hypothermia in Severe
Traumatic Brain Injury-Associated
Intracranial Hypertension

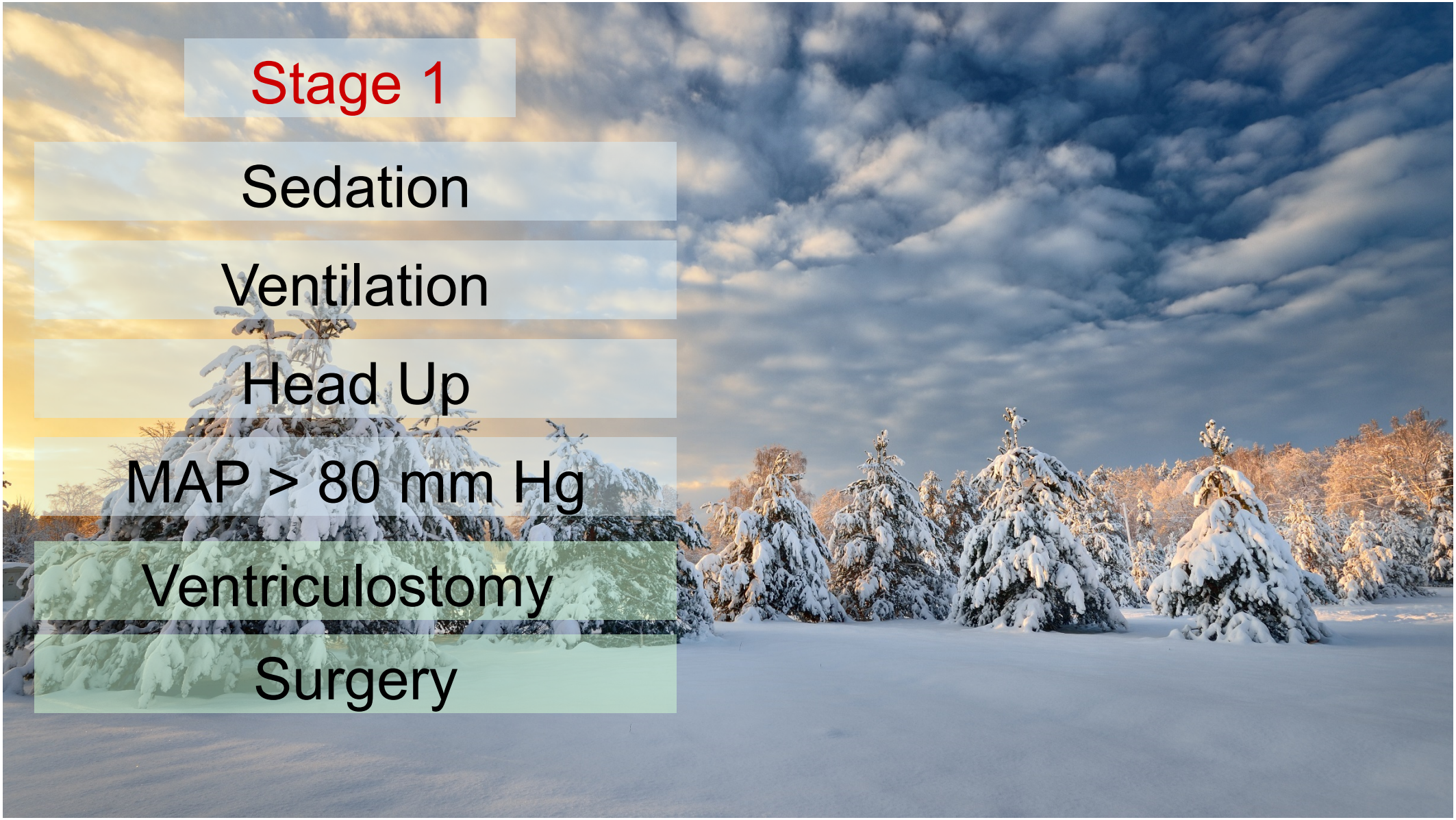

Pragmatic
Open-Label
Assessor-Blinded
RCT

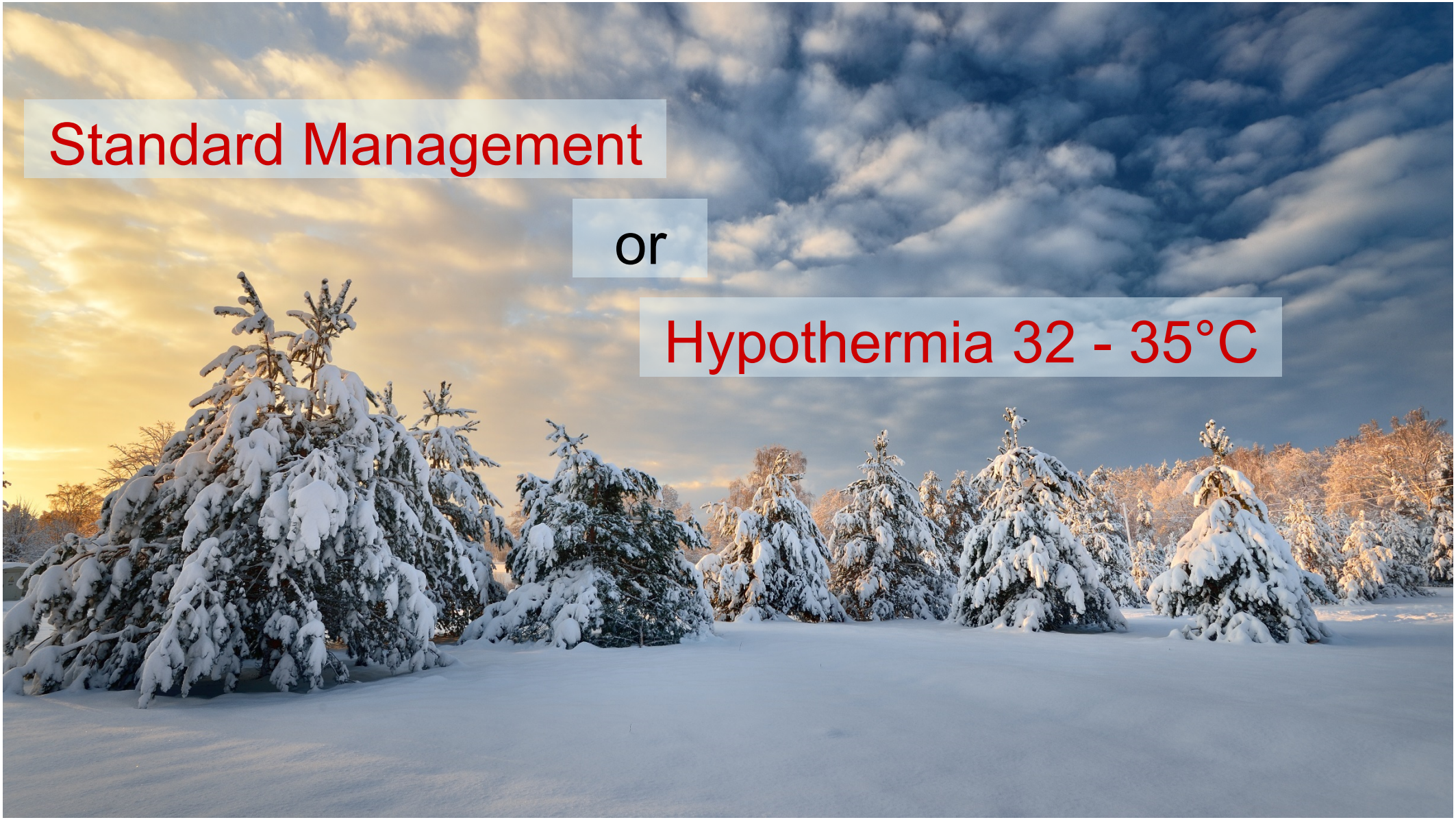

ICP > 20 mmHg > 5 min

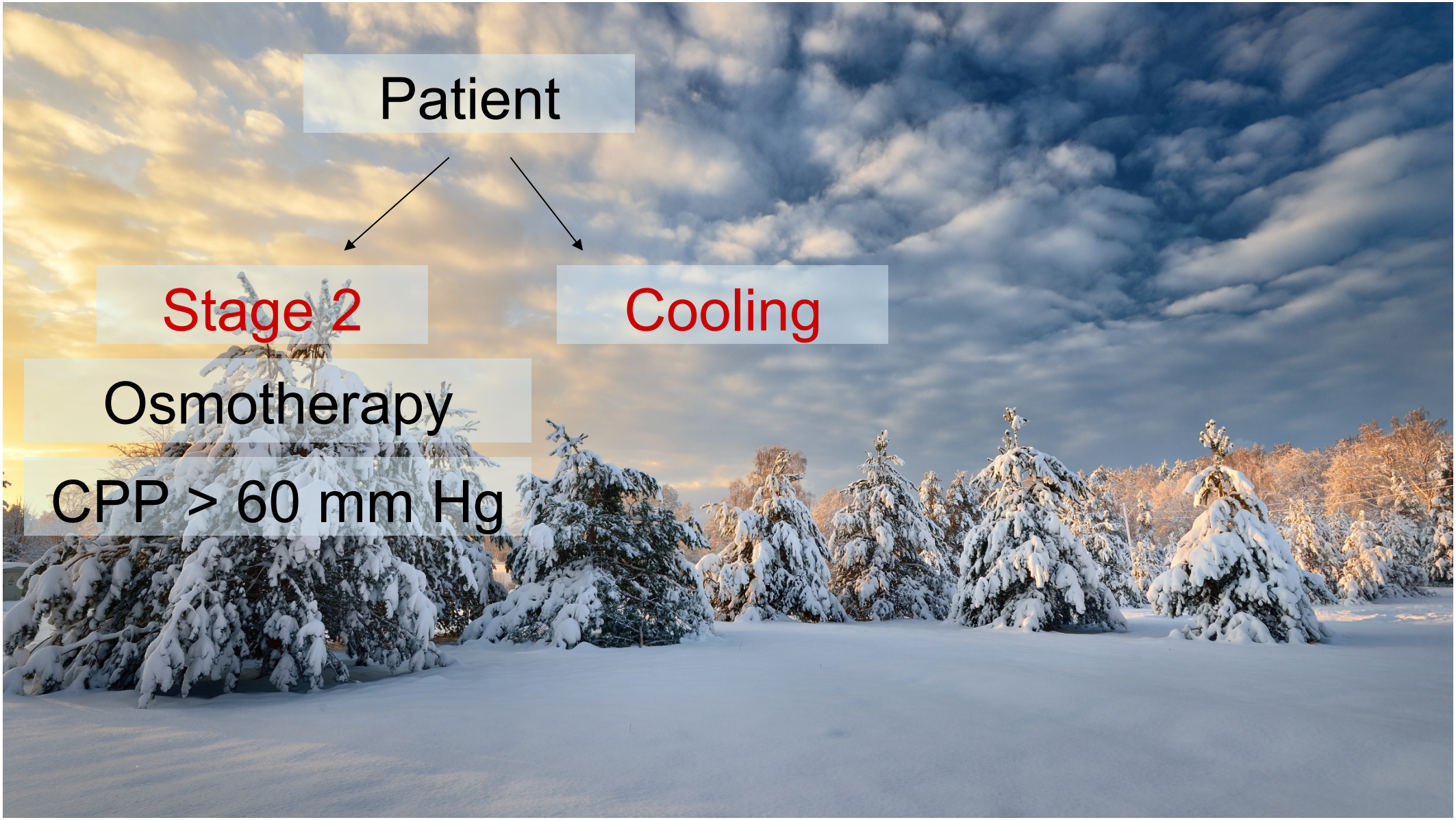

Stage 1
Stage 2
Standard
Cooling
Stage 3

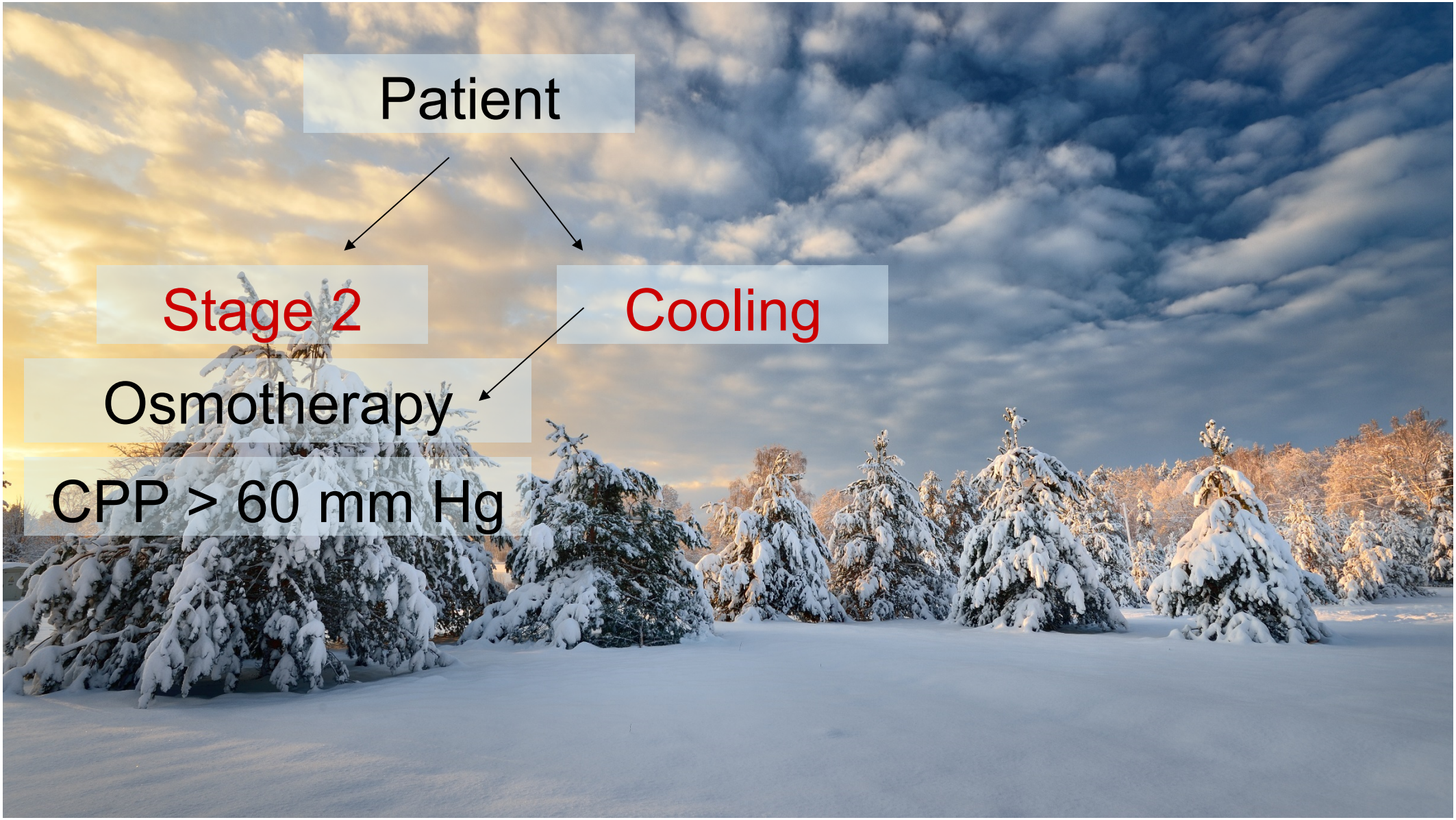

Stage 1

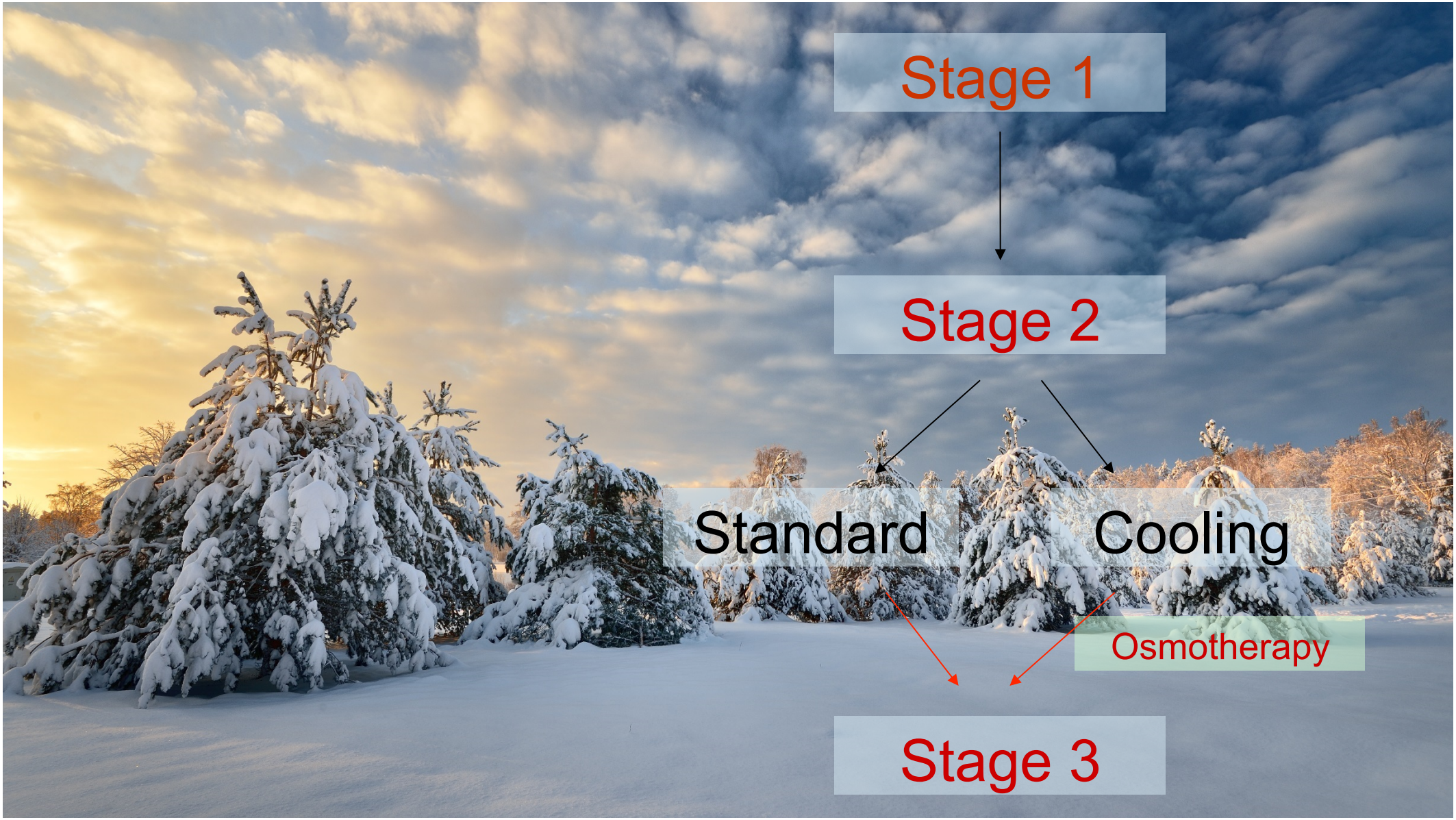

Stage 1
Sedation
Ventilation
Head Up
MAP > 80 mm Hg

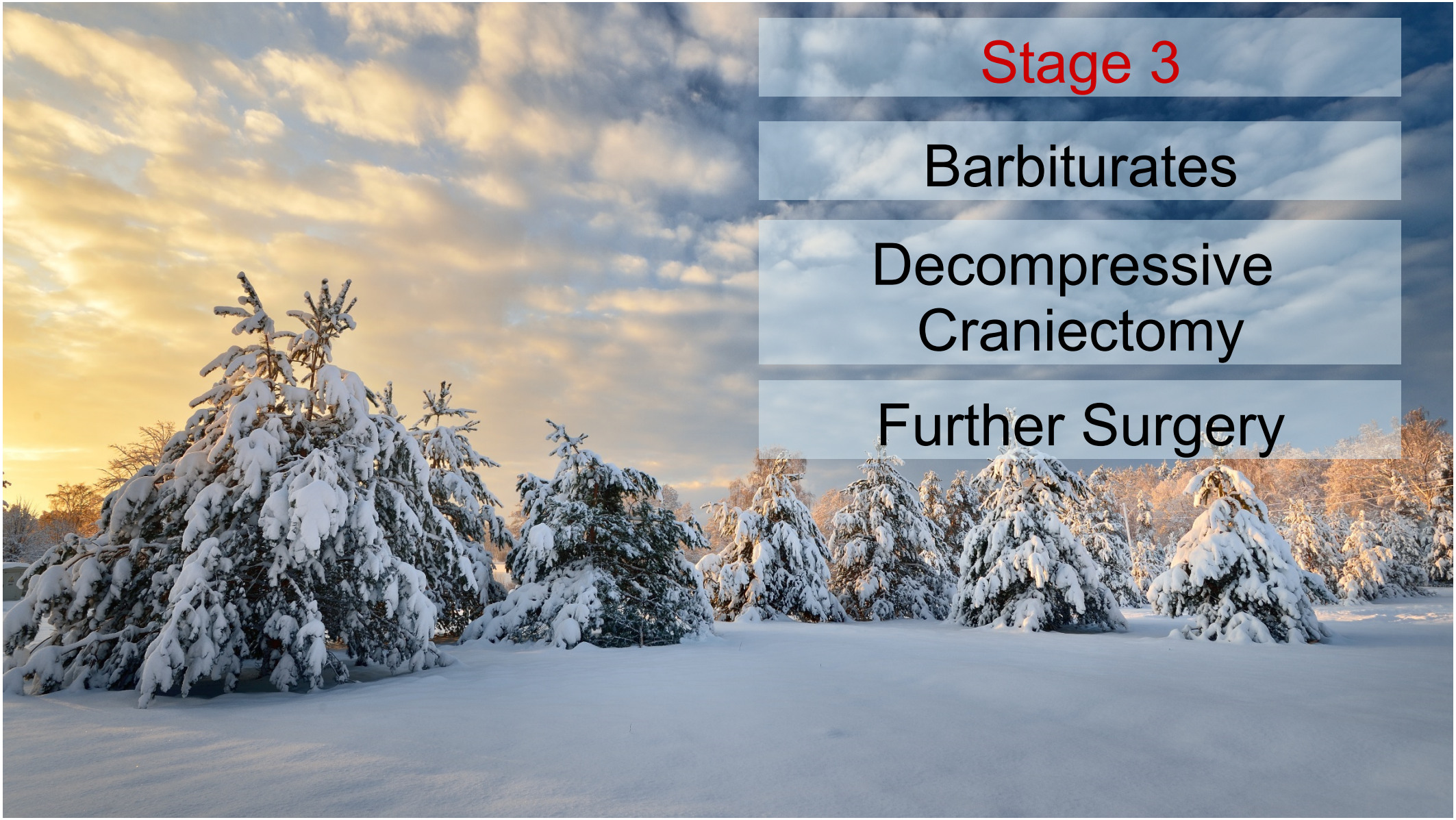

Stage 1
Sedation
Ventilation
Head Up
MAP > 80 mm Hg
Ventriculostomy
Surgery

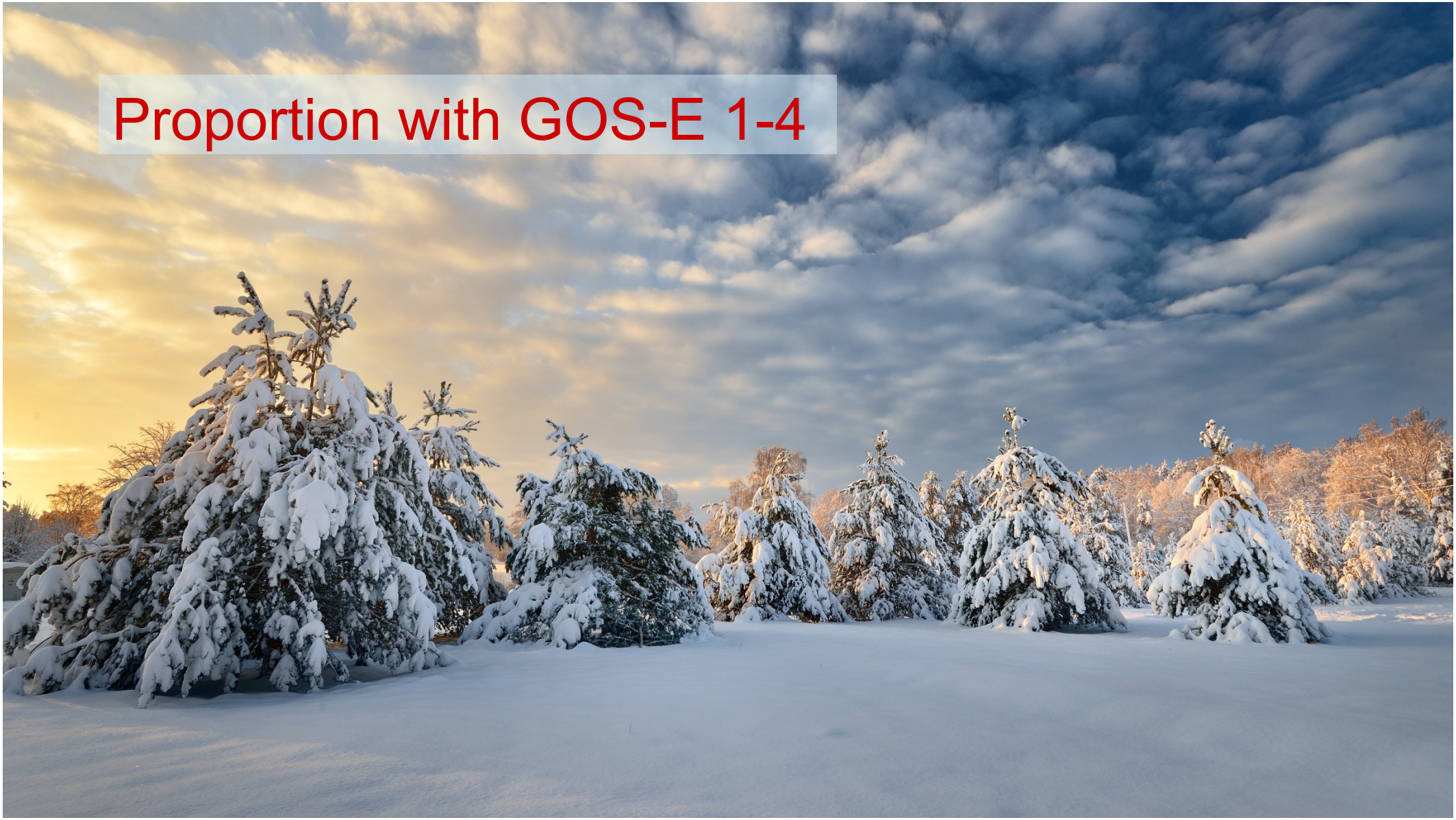

Standard Management
or
Hypothermia 32 - 35°C

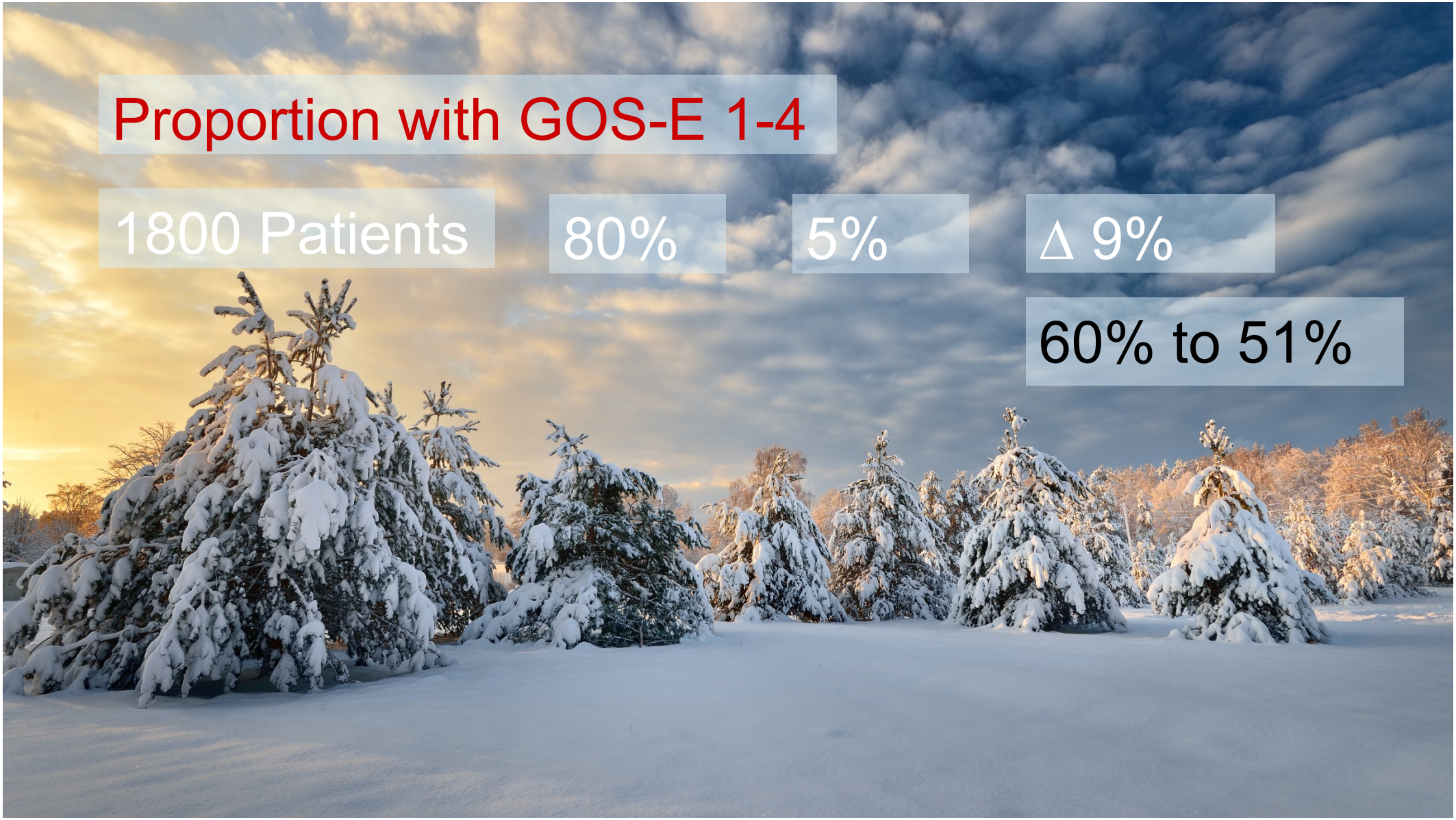

Patient
Stage 2
Cooling
Osmotherapy
CPP > 60 mm Hg

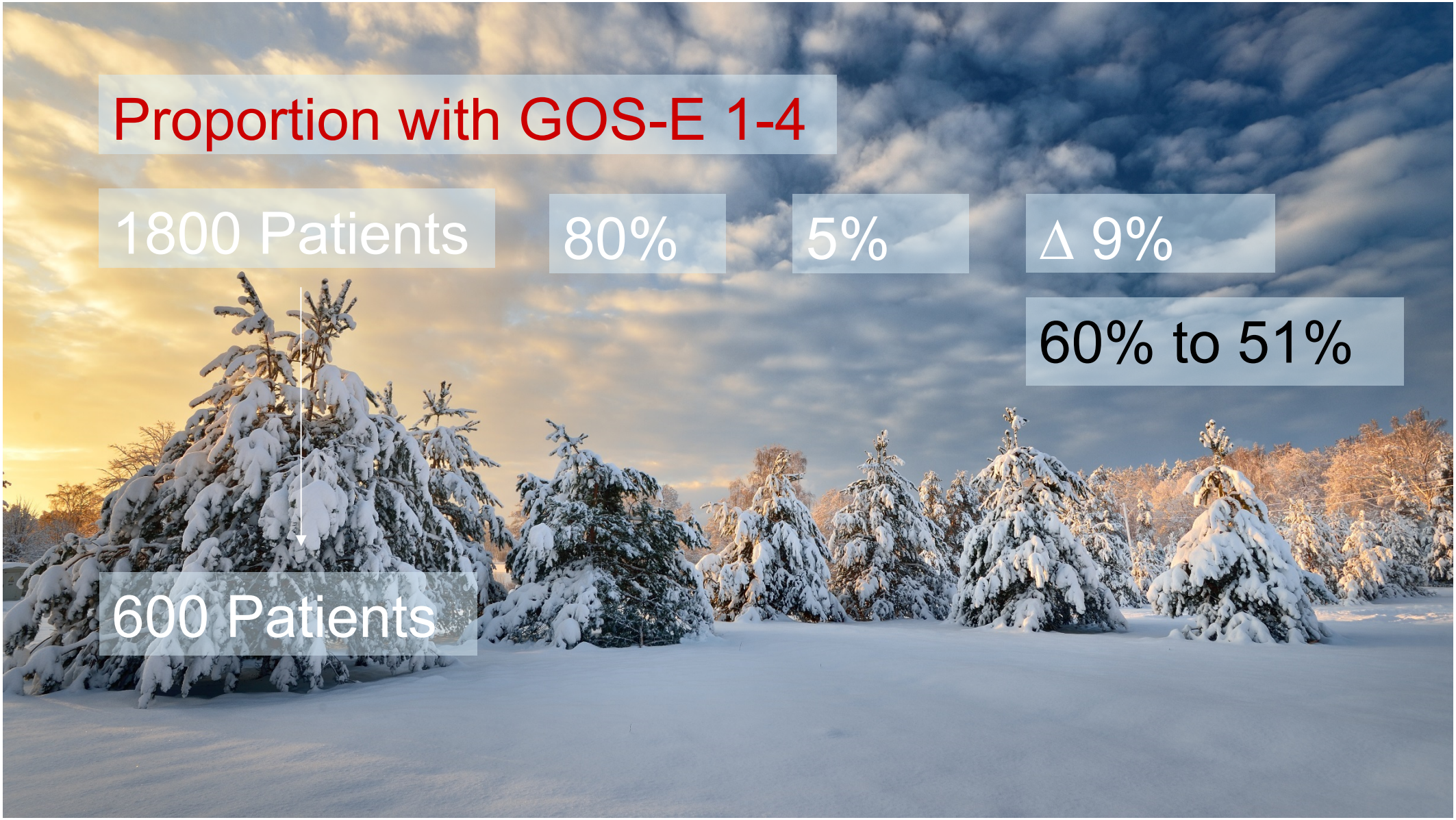

Patient
Stage 2
Cooling
Osmotherapy
CPP > 60 mm Hg


Stage 1
Stage 2
Standard
Cooling
Osmotherapy
Stage 3

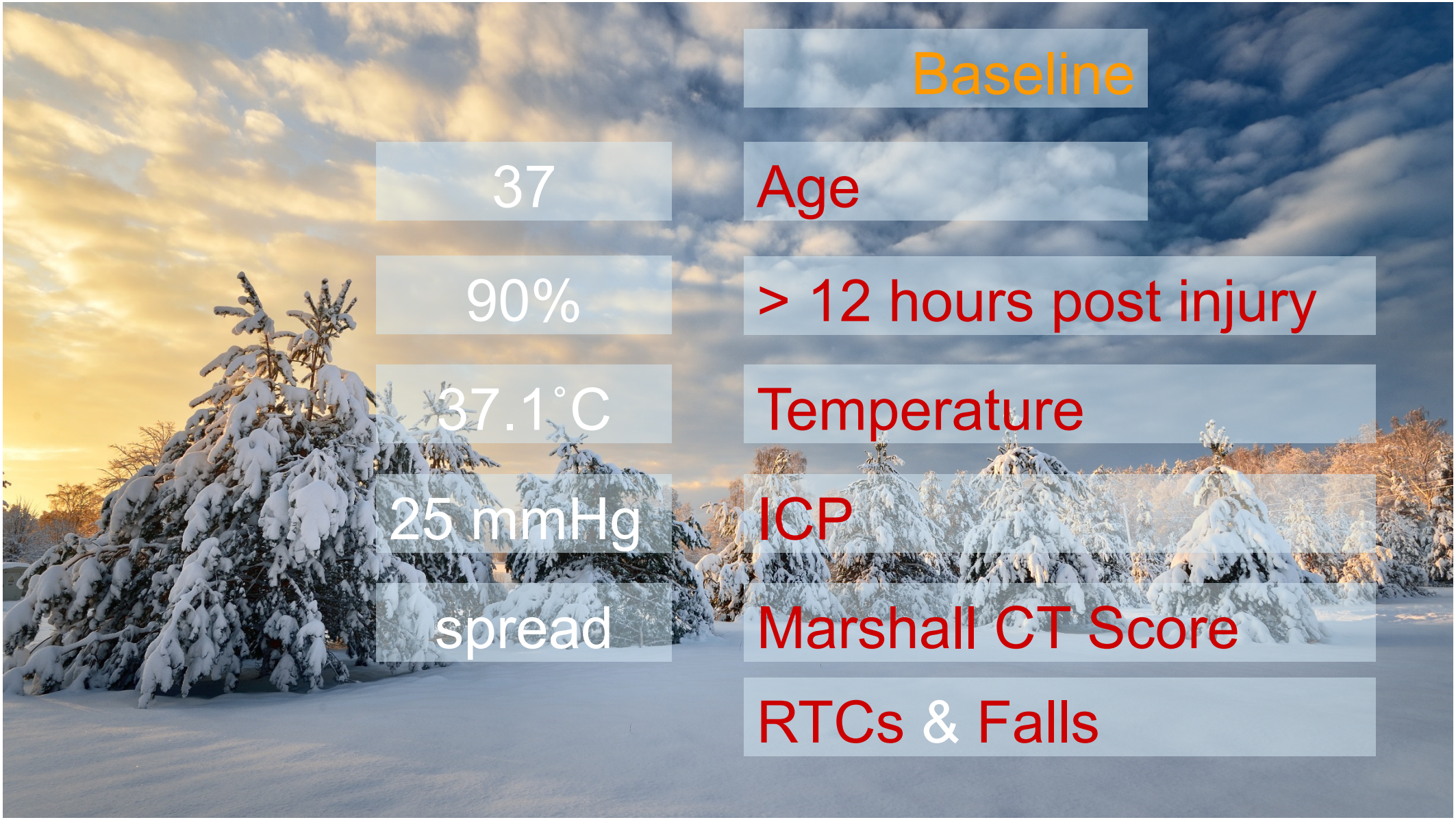

Stage 3
Barbiturates
Decompressive Craniectomy
Further Surgery

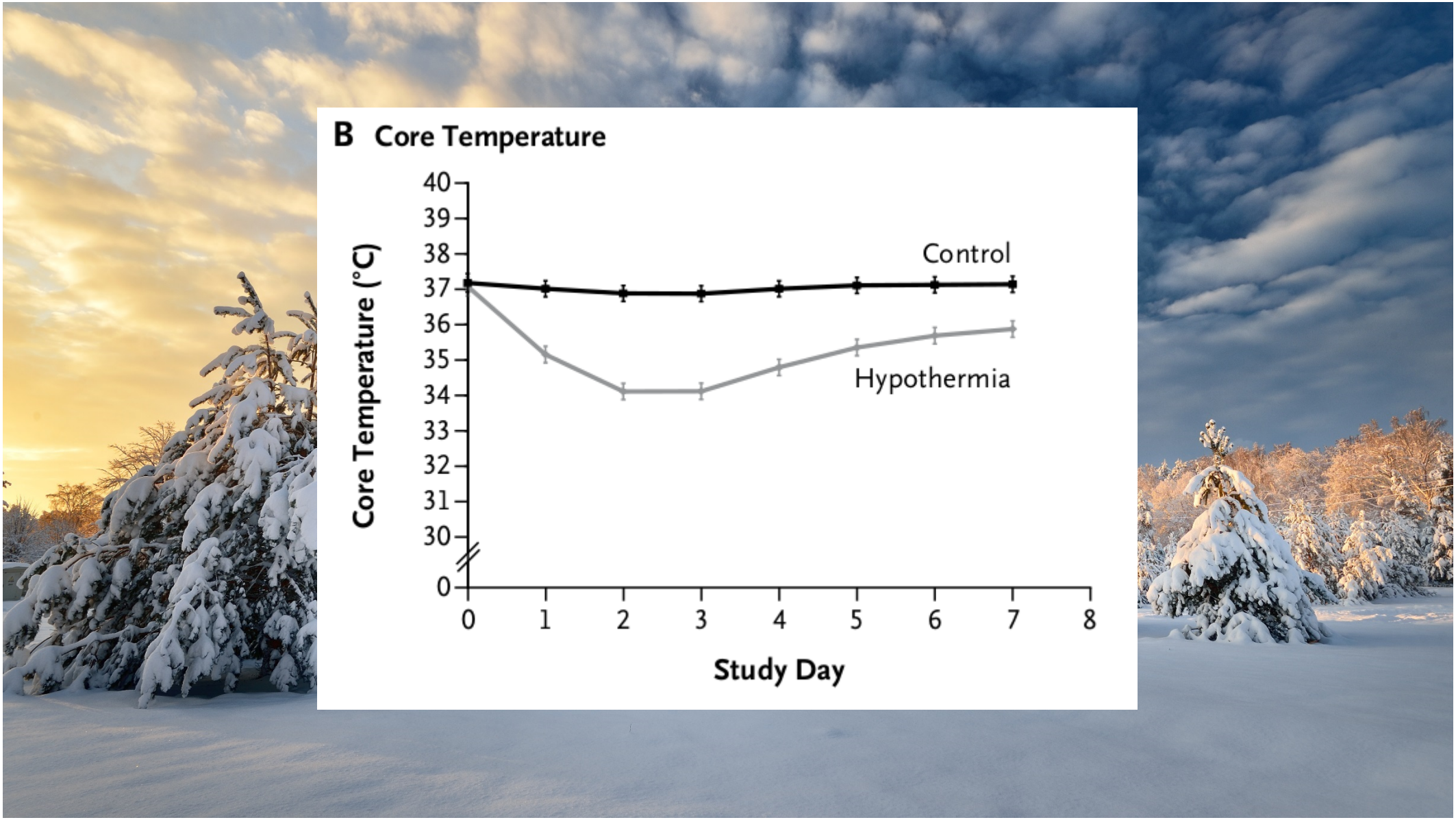

Proportion with GOS-E 1-4

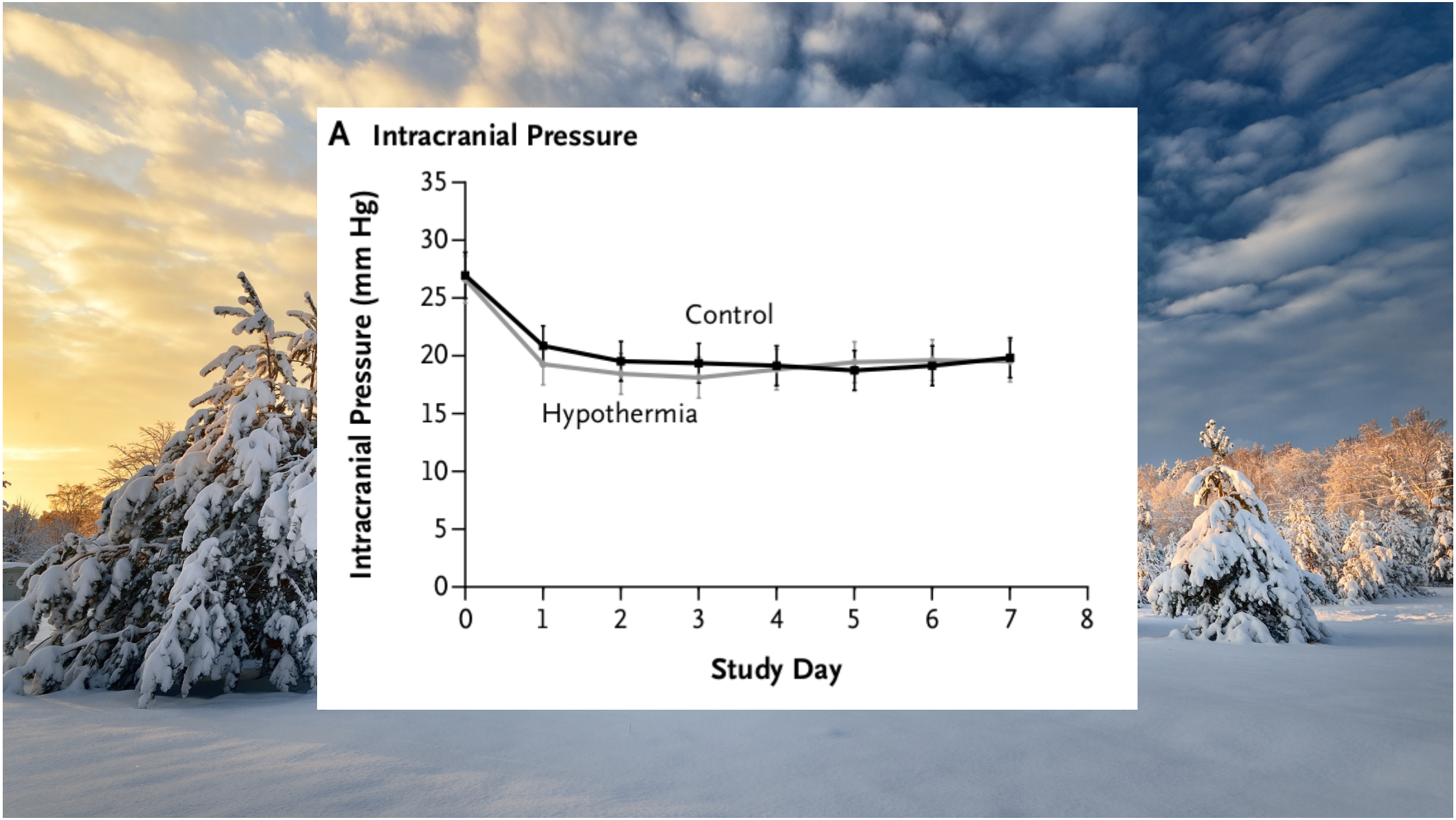

Proportion with GOS-E 1-4
1800 Patients
80%
5%
Δ 9%
60% to 51%

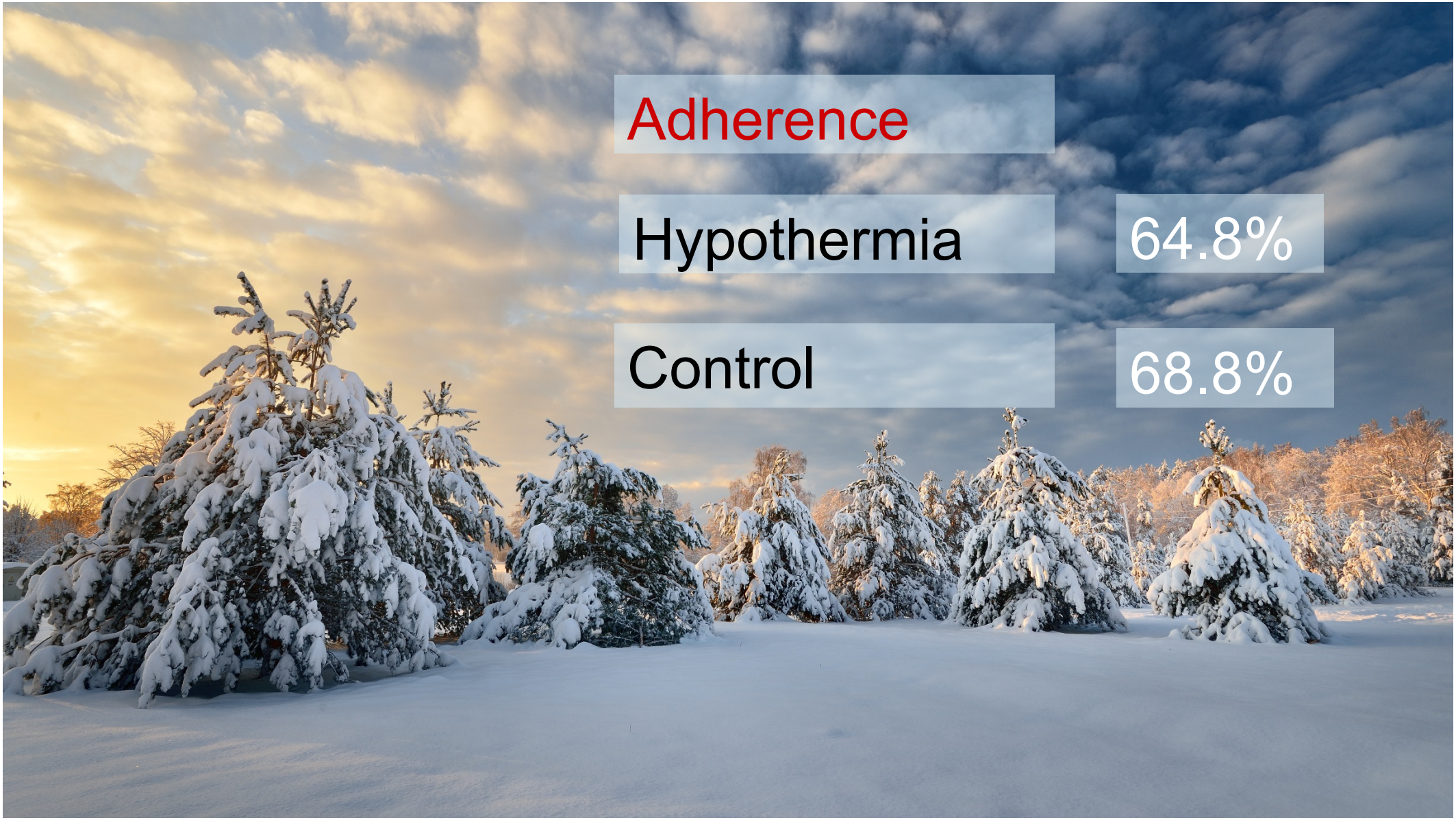

Proportion with GOS-E 1-4
1800 Patients
80%
5%
Δ 9%
60% to 51%
600 Patients

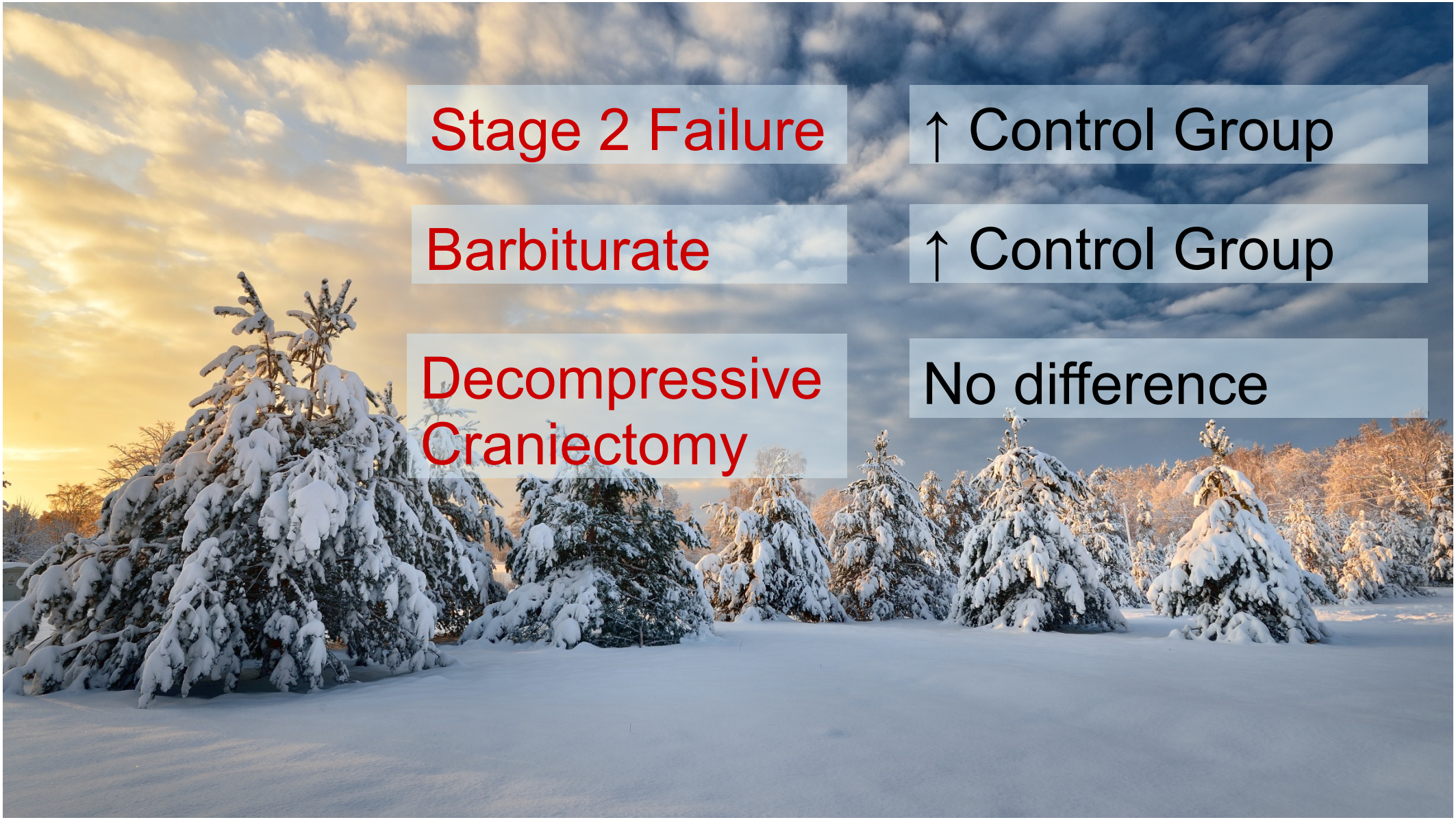

387 patients
47 centres
18 countries


Baseline
37
Age
90%
> 12 hours post injury
37.1˚C
Temperature
25 mmHg
ICP
spread
Marshall CT Score
RTCs & Falls


B Core Temperature
Core Temperature (°C)
40
39
38
37
36
35
34
33
32
31
30
0
Control
Hypothermia
0
1
2
3
4
5
6
7
8
Study Day

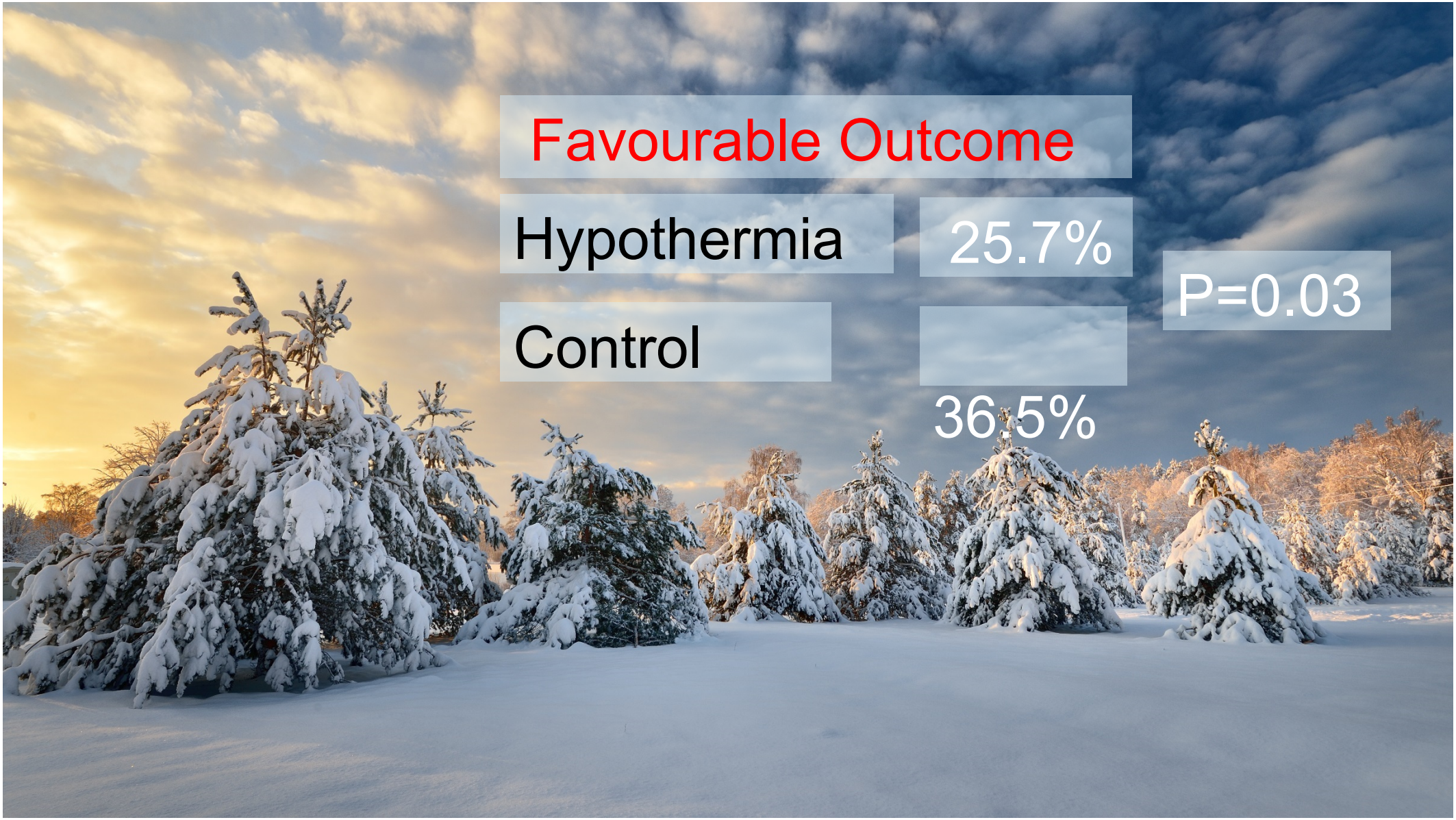

A Intracranial Pressure
Intracranial Pressure (mm Hg)
35
30
25
20
15
10
5
0
Control
Hypothermia
0
1
2
3
4
5
6
7
8
Study Day

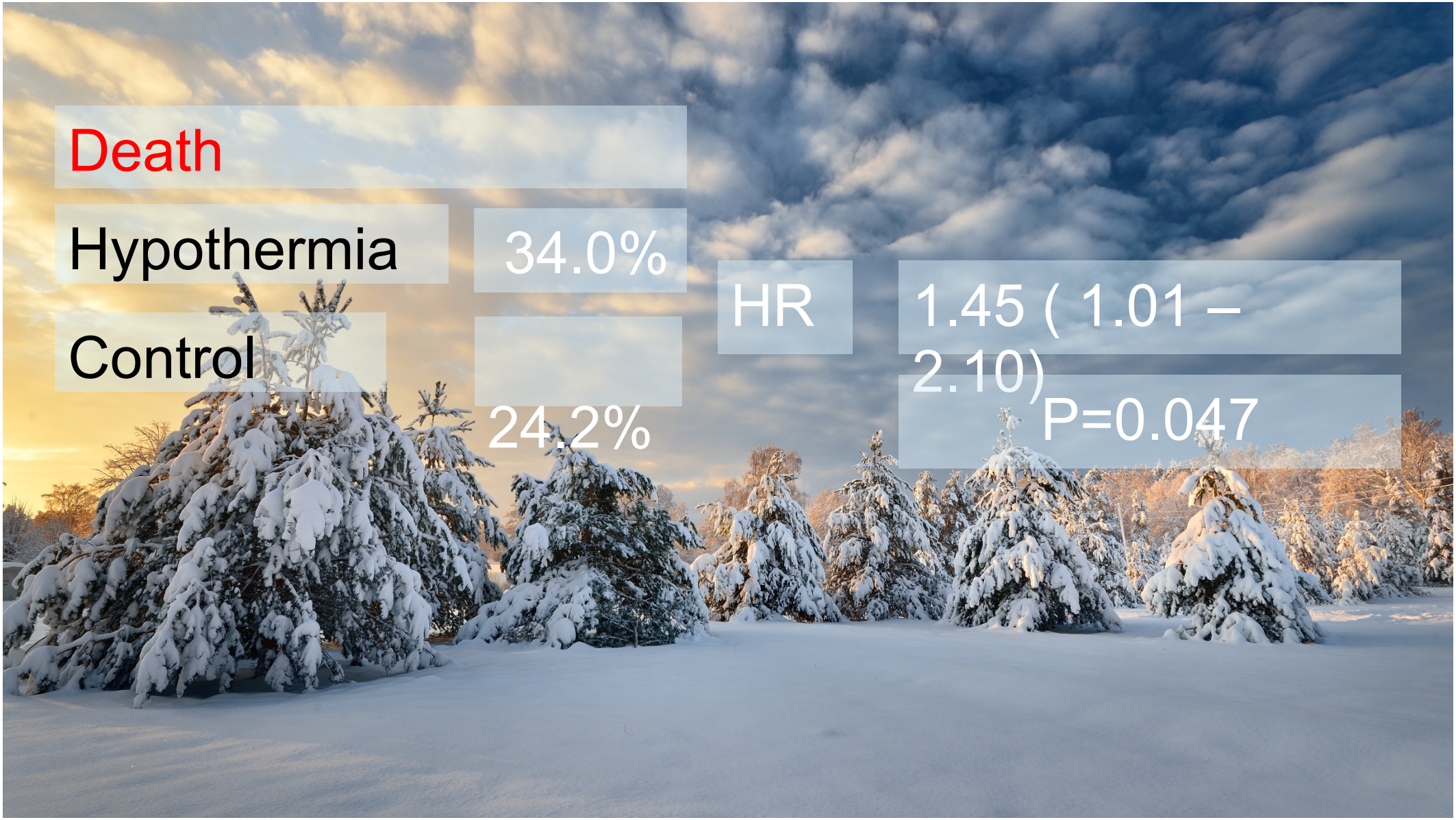

Adherence
Hypothermia
64.8%
Control
68.8%


Stage 2 Failure
↑ Control Group
Barbiturate
↑ Control Group
Decompressive Craniectomy
No difference


Primary Outcome
EGOS 1 - 4
acOR
1.53 (1.02 to 2.30)
P=0.04


Primary Outcome
EGOS 1 - 4
acOR
1.53 (1.02 to 2.30)
P=0.04
EGOS 5 - 8
cOR
1.55 (1.05 to 2.29)
P=0.03

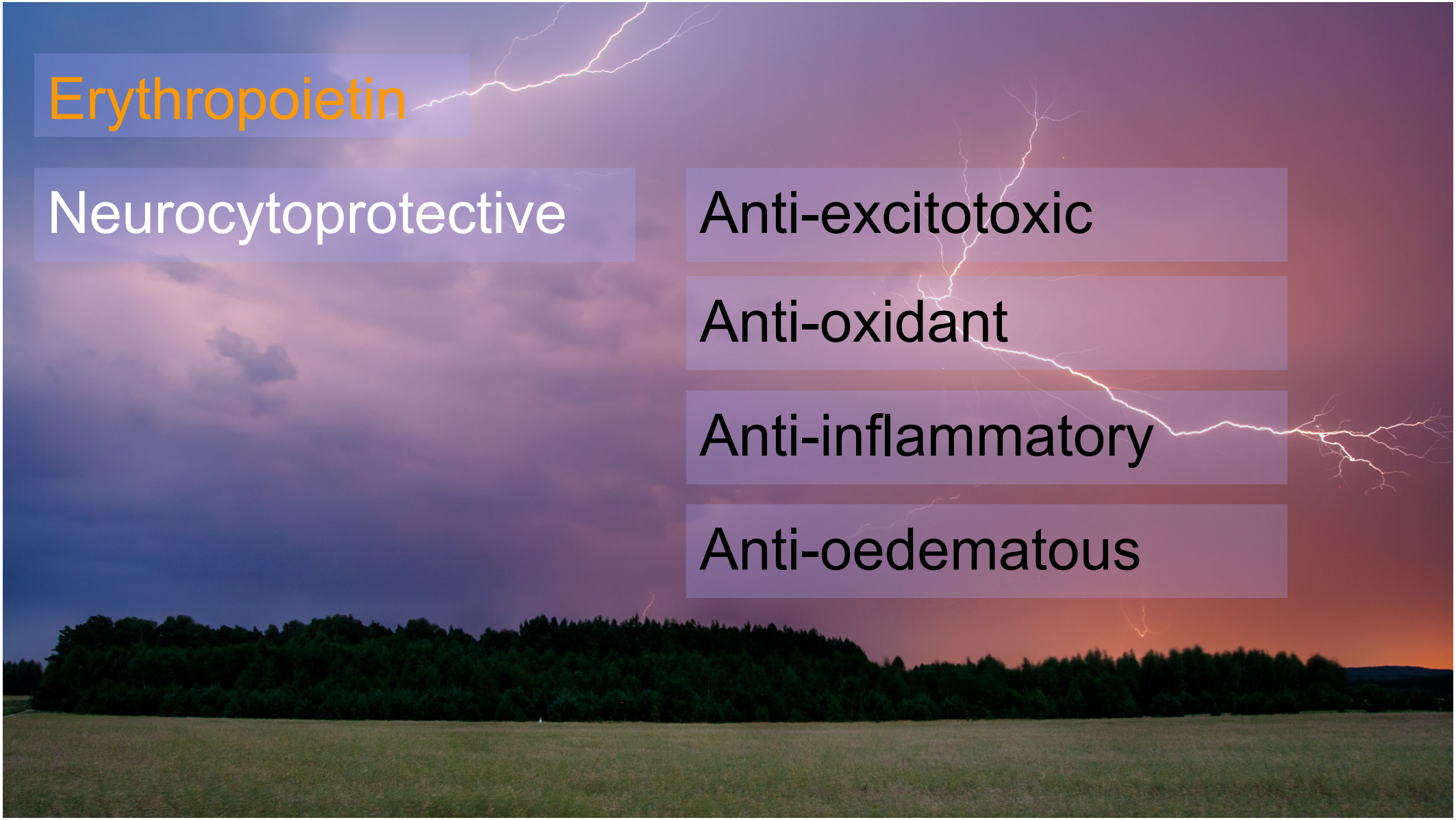

Favourable Outcome
Hypothermia
25.7%
P=0.03
Control
36.5%


Death
Hypothermia
34.0%
Control
24.2%
HR
1.45 (1.01 – 2.10)
P=0.047


Methodologically strong
Limitations some
Overall controversial

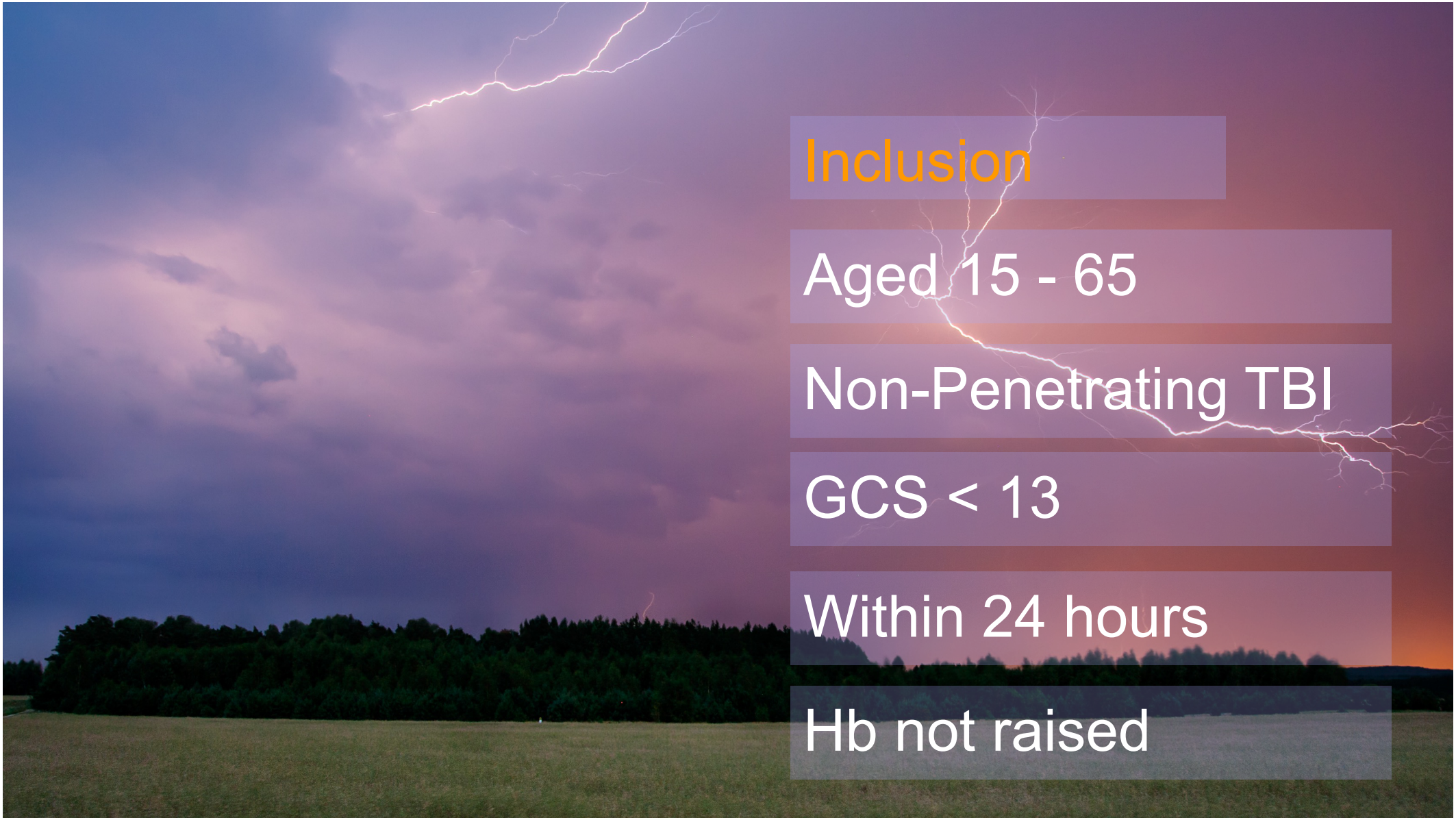

EPO-TBI


Erythropoietin in Traumatic Brain Injury


Erythropoietin
Neurocytoprotective
Anti-excitotoxic
Anti-oxidant
Anti-inflammatory
Anti-oedematous


Erythropoietin
vs
Placebo

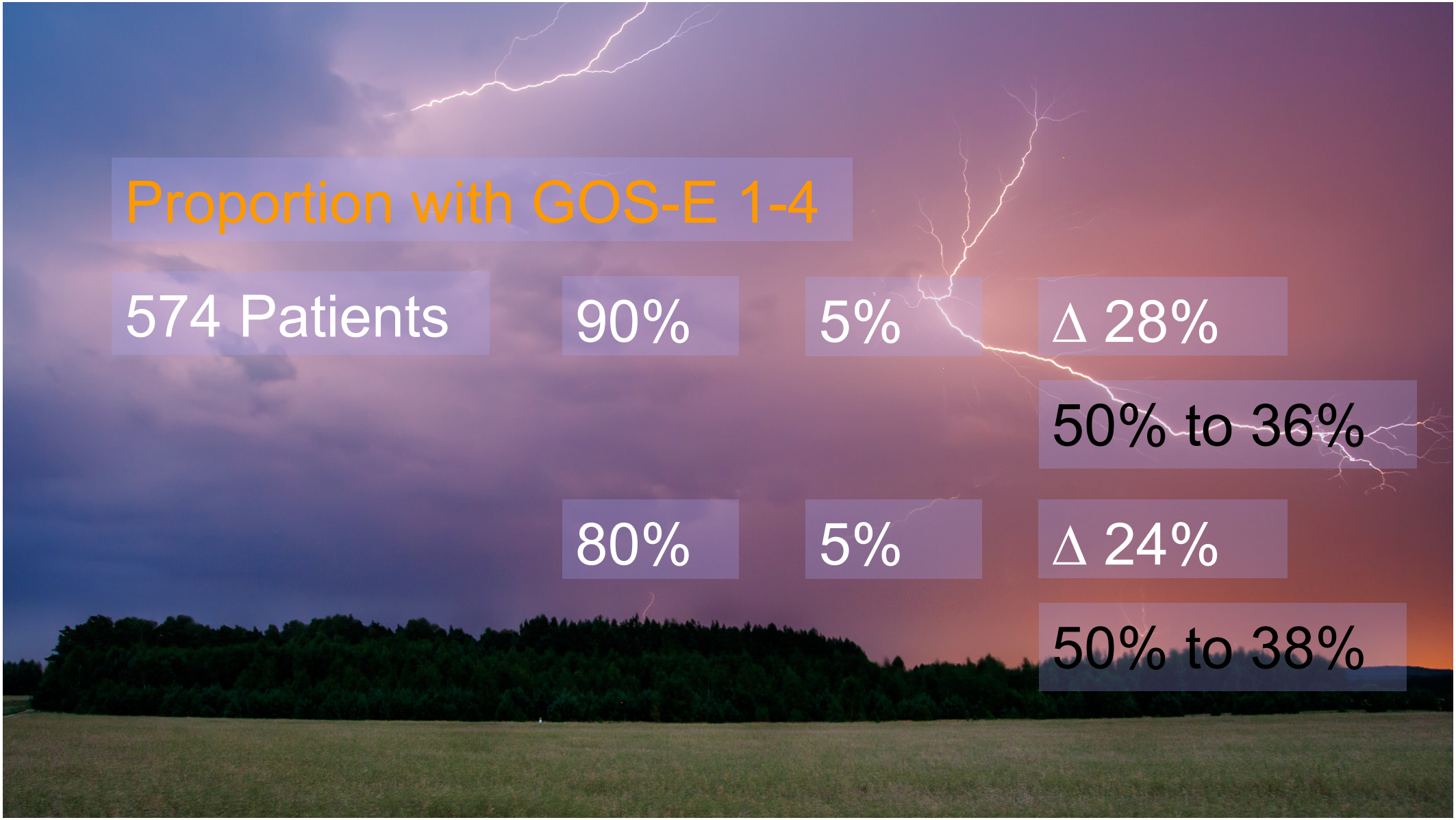

Design
International
Stratified
Double-Blind
Placebo controlled
Randomised trial

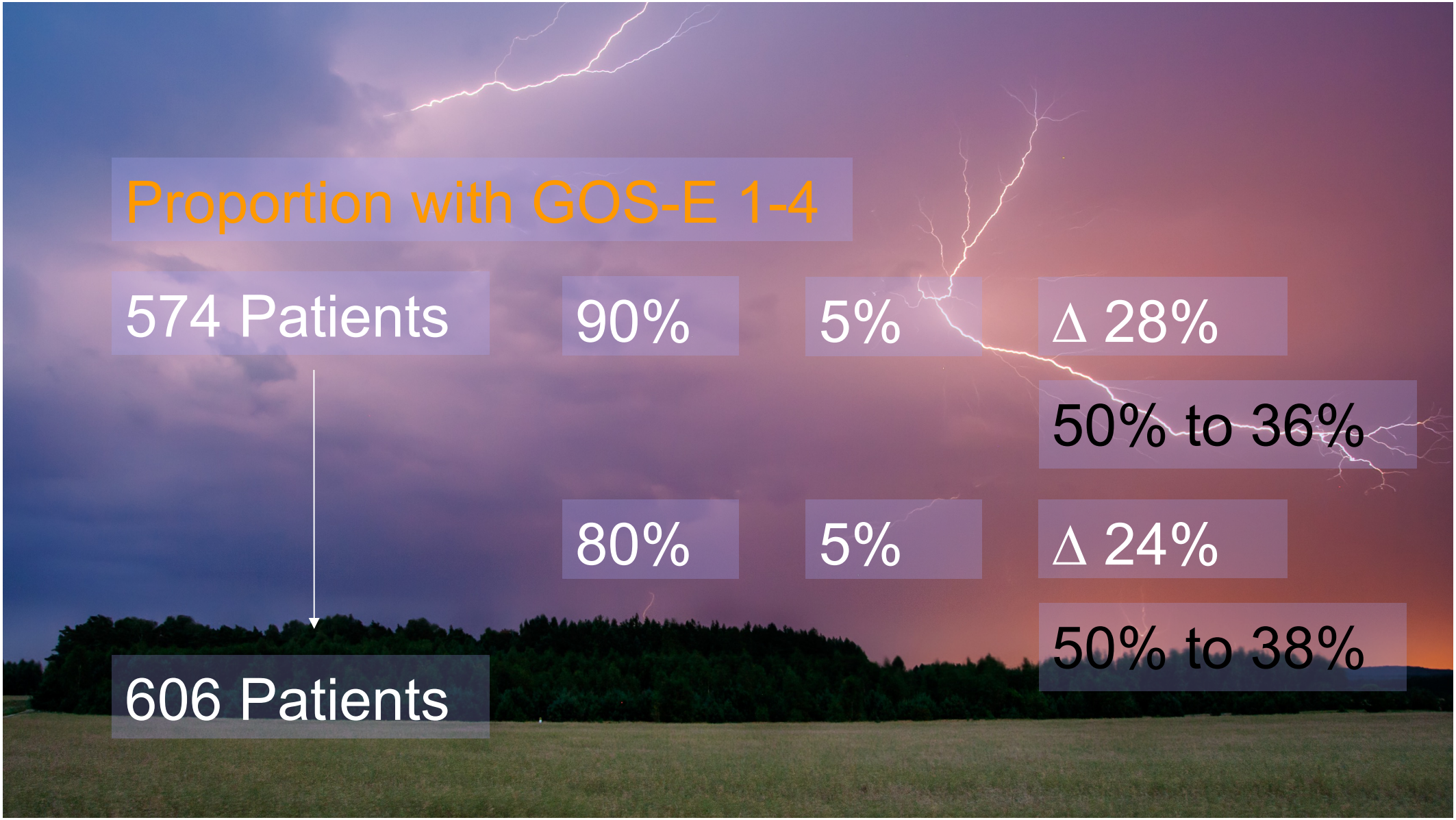

Inclusion
Aged 15 - 65
Non-Penetrating TBI
GCS < 13
Within 24 hours
Hb not raised


Safety Measures
Stopping critieria
DVT Screening

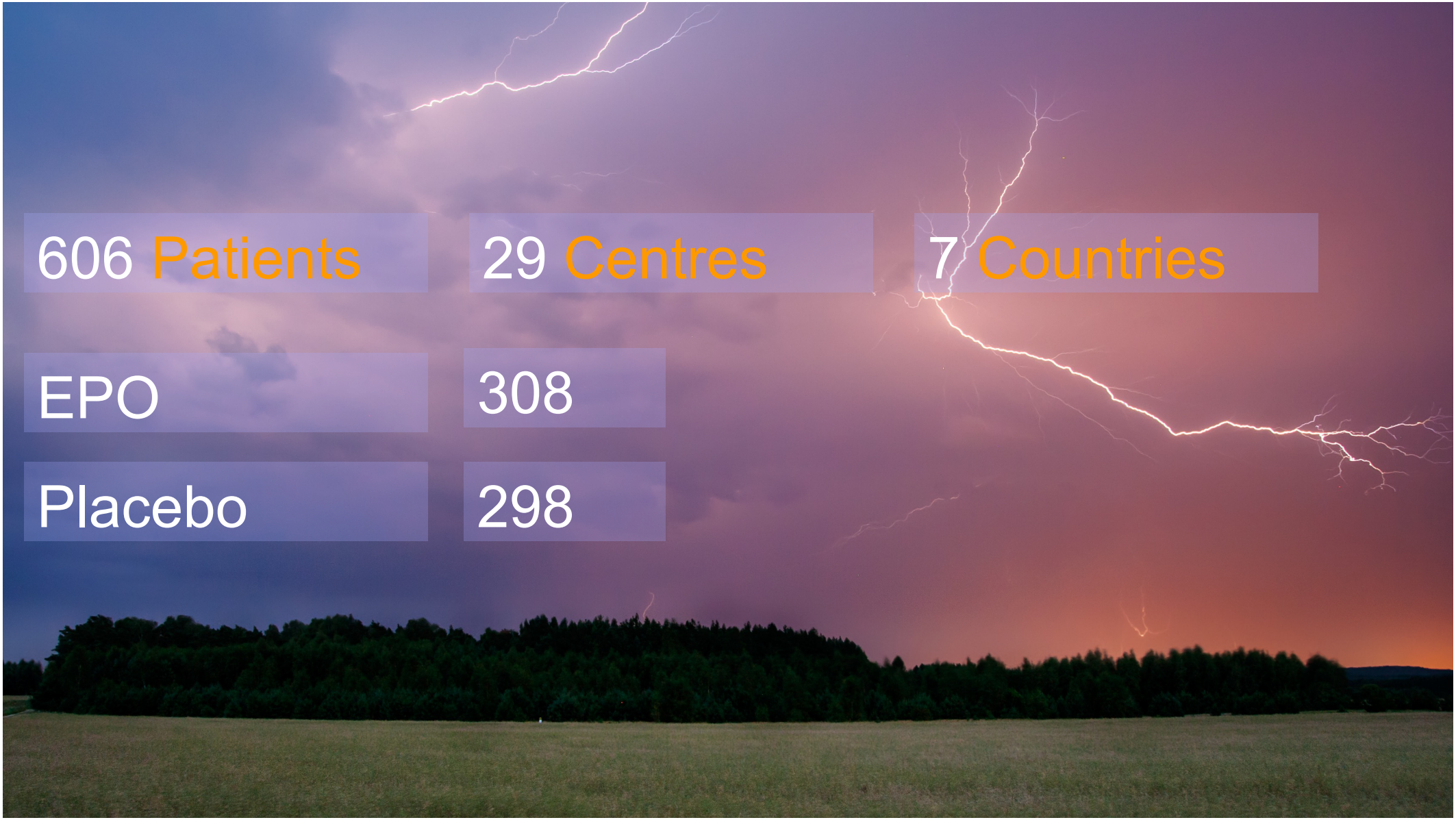

Proportion with GOS-E 1-4

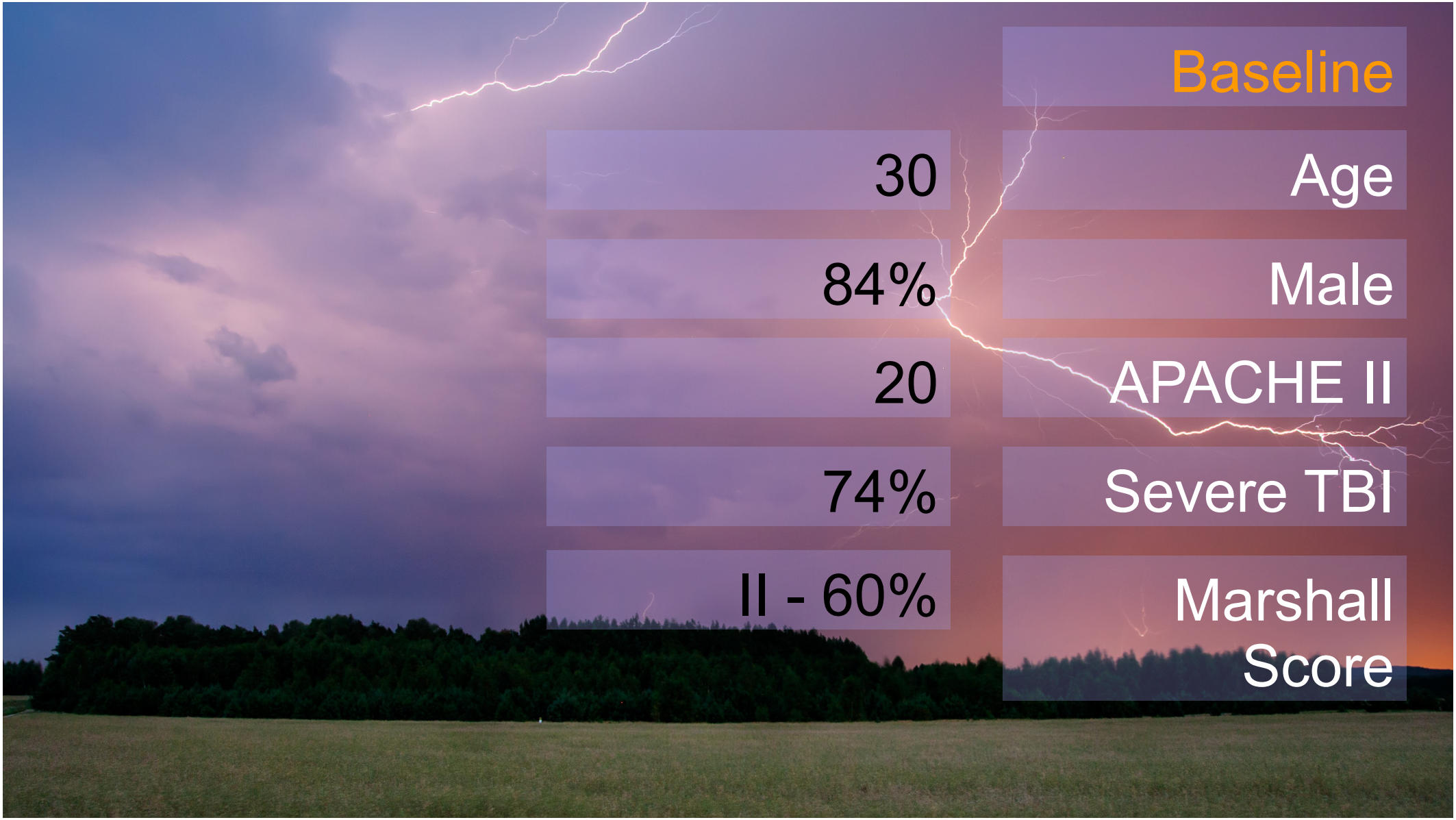

Proportion with GOS-E 1-4
574 Patients
90%
5%
Δ 28%
50% to 36%

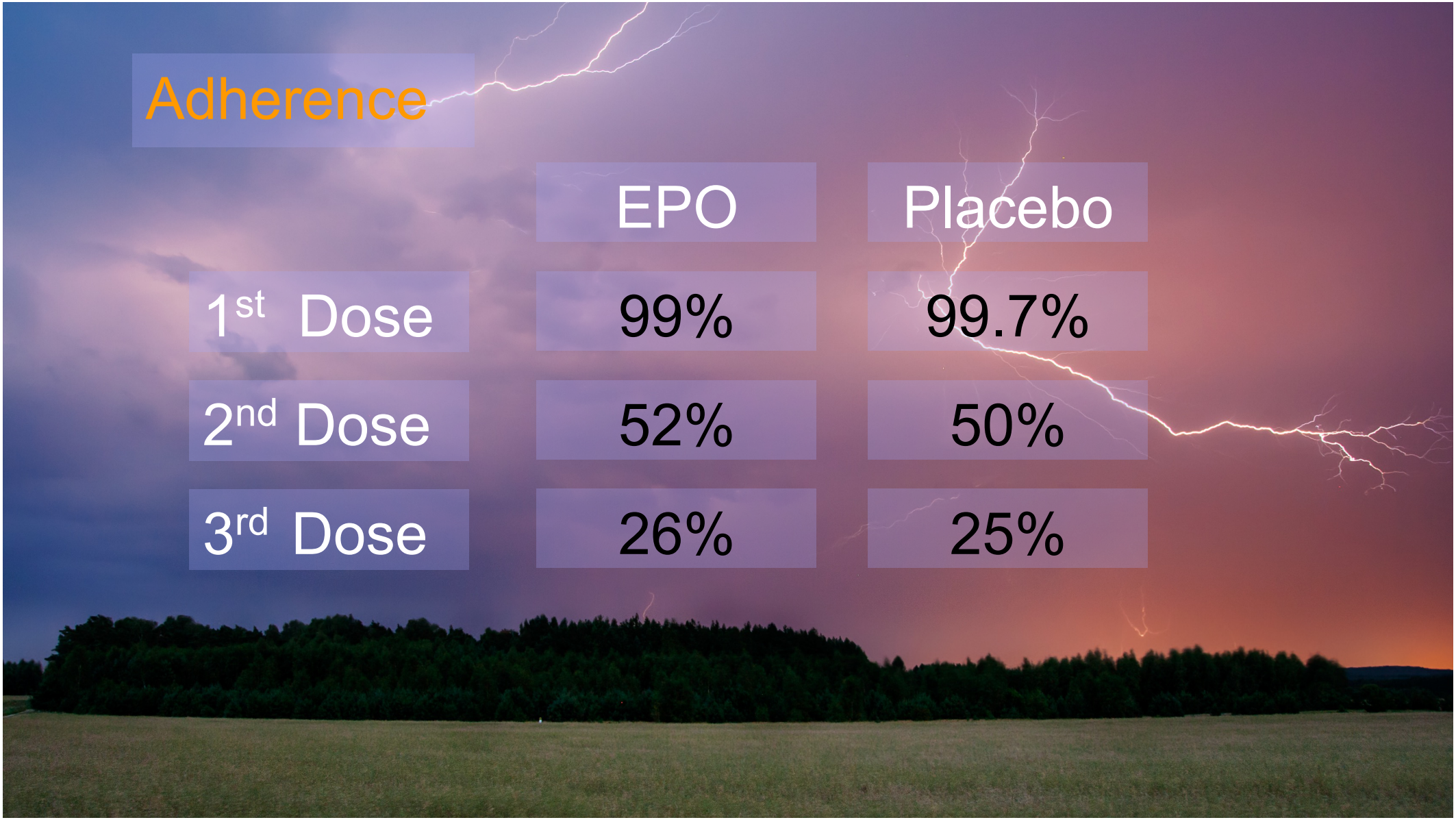

Proportion with GOS-E 1-4
574 Patients
90%
5%
Δ 28%
50% to 36%
80%
5%
Δ 24%
50% to 38%

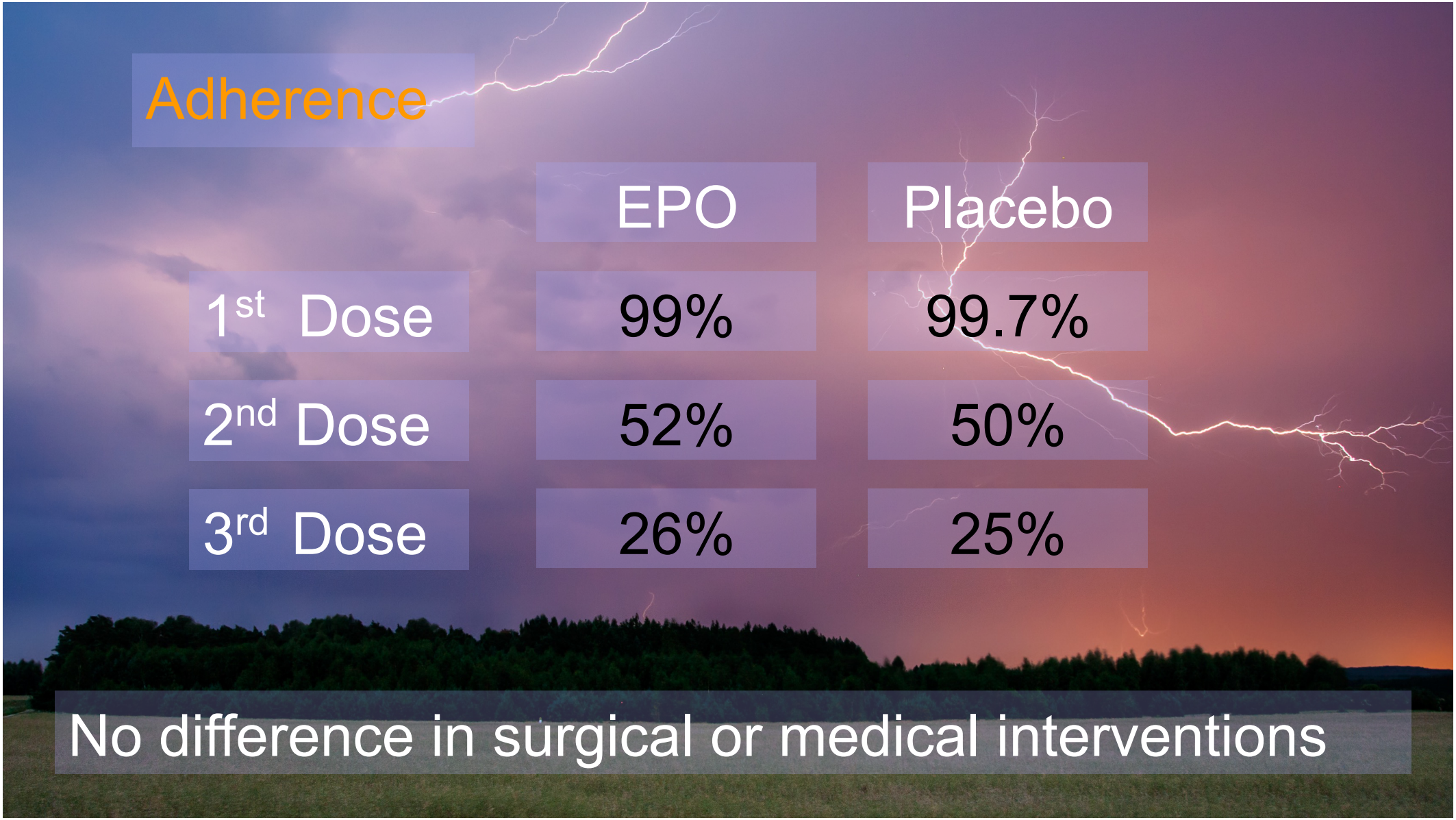

Proportion with GOS-E 1-4
574 Patients
90%
5%
Δ 28%
50% to 36%
606 Patients
80%
5%
Δ 24%
50% to 38%


606 Patients
29 Centres
7 Countries


606 Patients
29 Centres
7 Countries
EPO
308
Placebo
298


Baseline
30
Age
84%
Male
20
APACHE II
74%
Severe TBI
II - 60%
Marshall Score


Adherence
EPO
Placebo
1st Dose
99%
99.7%
2nd Dose
52%
50%
3rd Dose
26%
25%


Adherence
EPO
Placebo
1st Dose
99%
99.7%
2nd Dose
52%
50%
3rd Dose
26%
25%
No difference in surgical or medical interventions

GOS-E 1 - 4

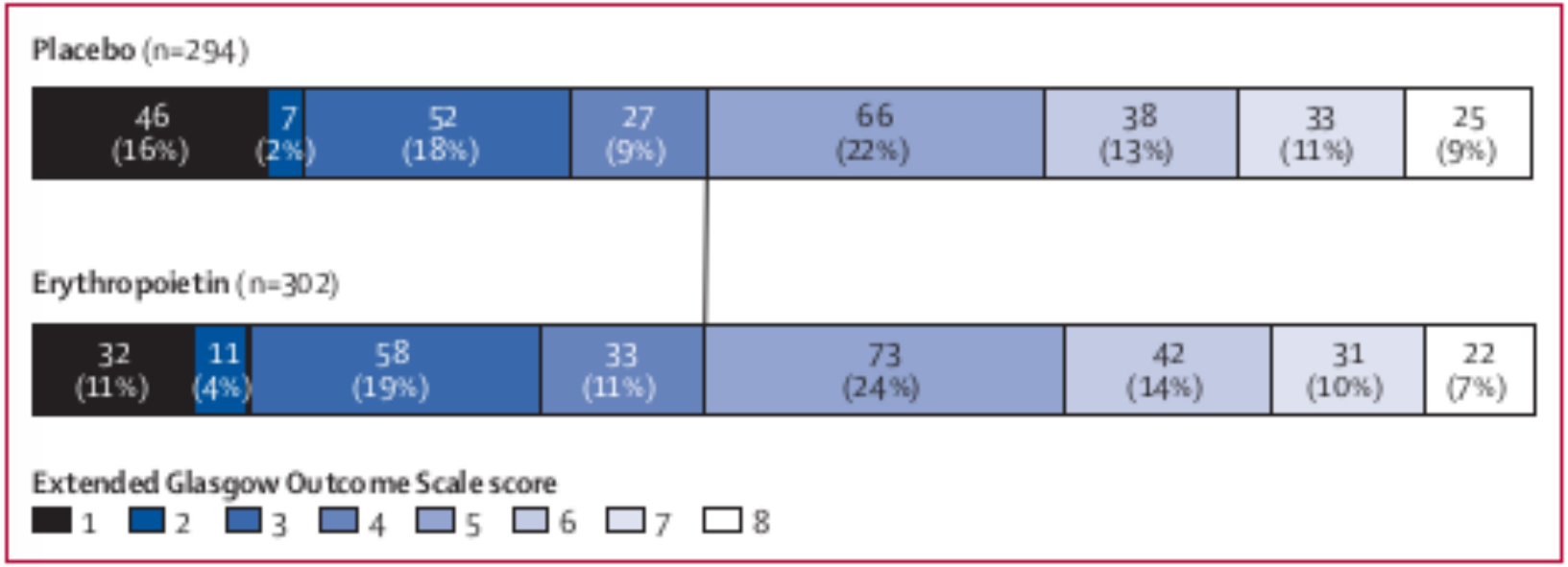


Figure 2: Distribution of Extended Glasgow Outcome Scale scores

RR 0.99, 95% CI 0.83 – 1.18; P=0.90

Day 180 Mortality

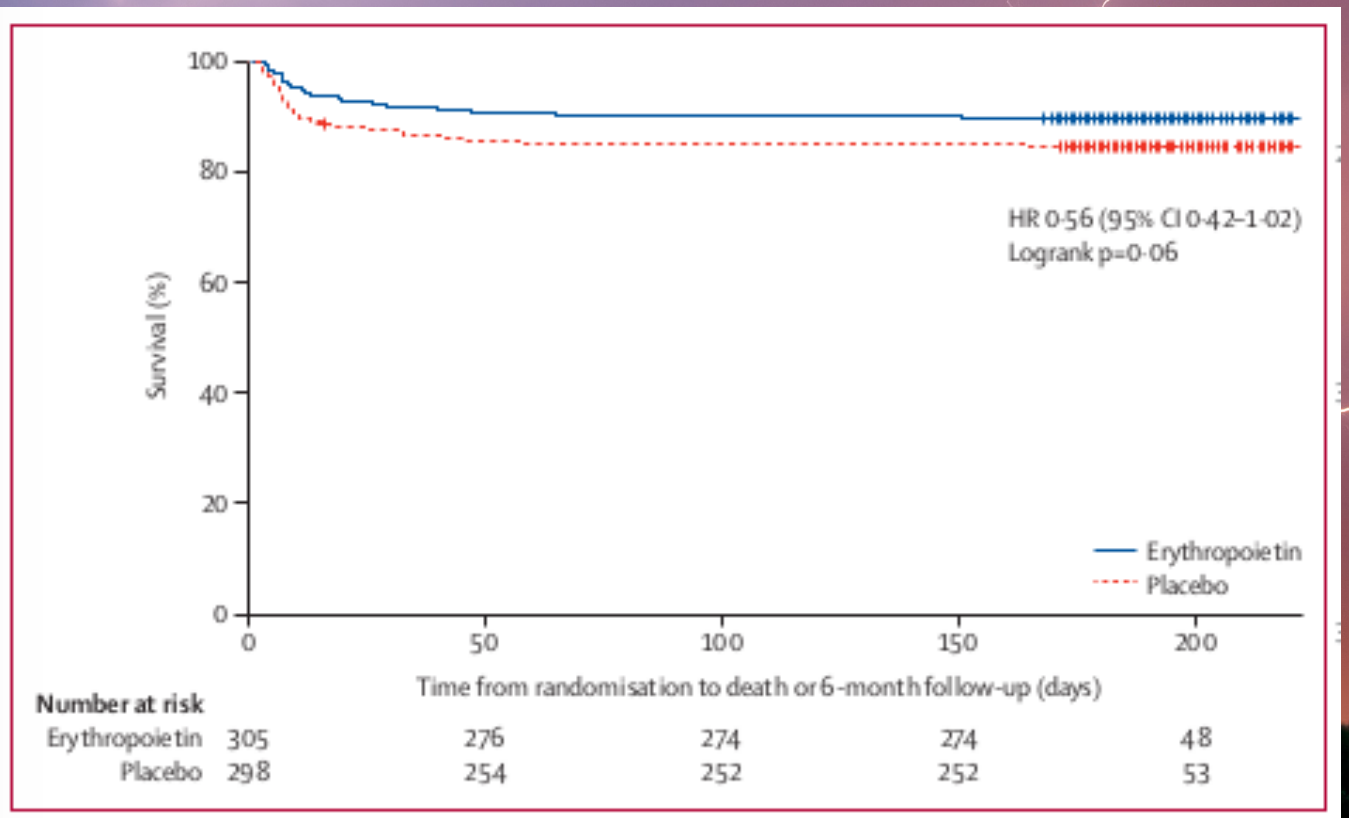
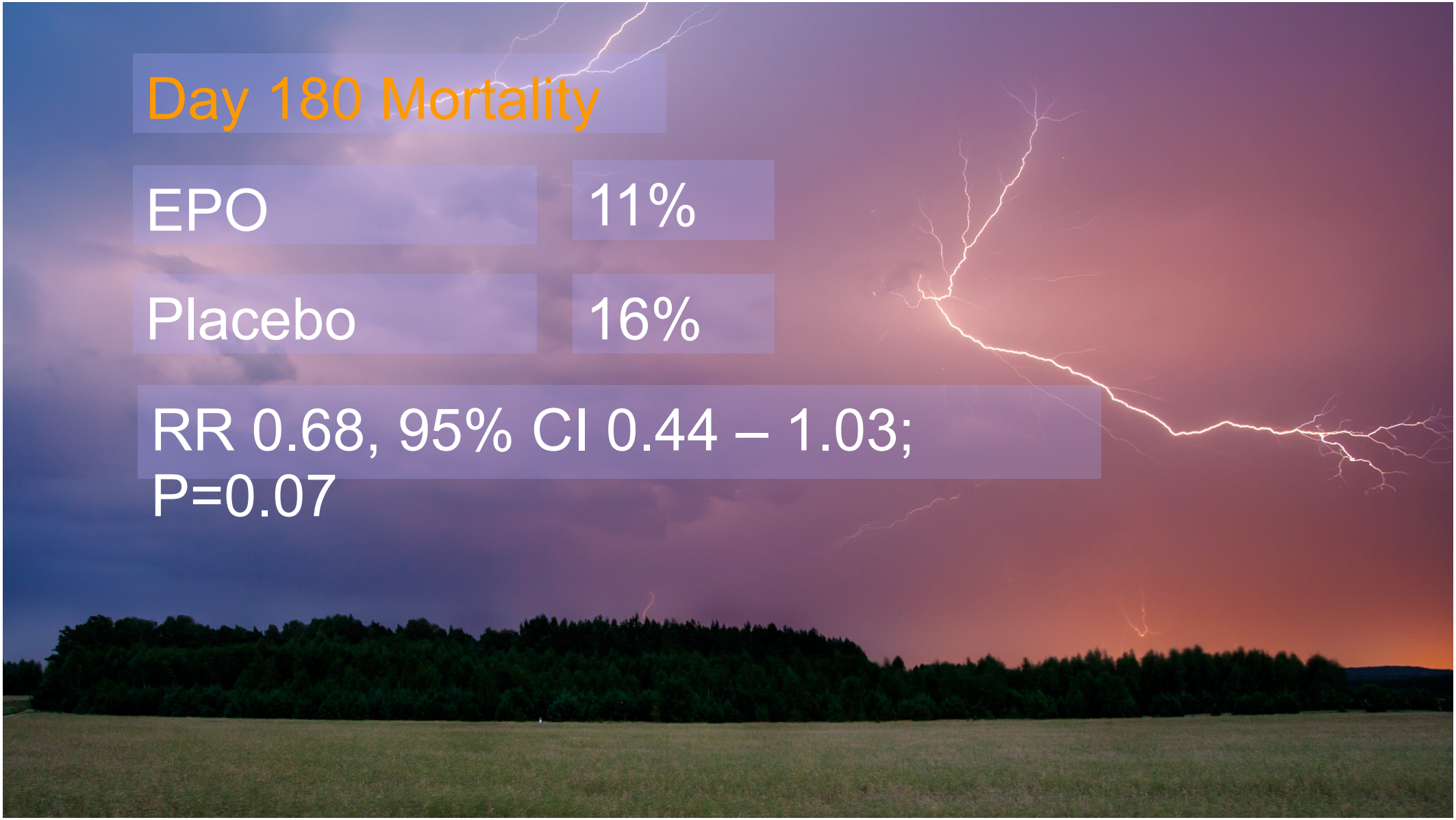
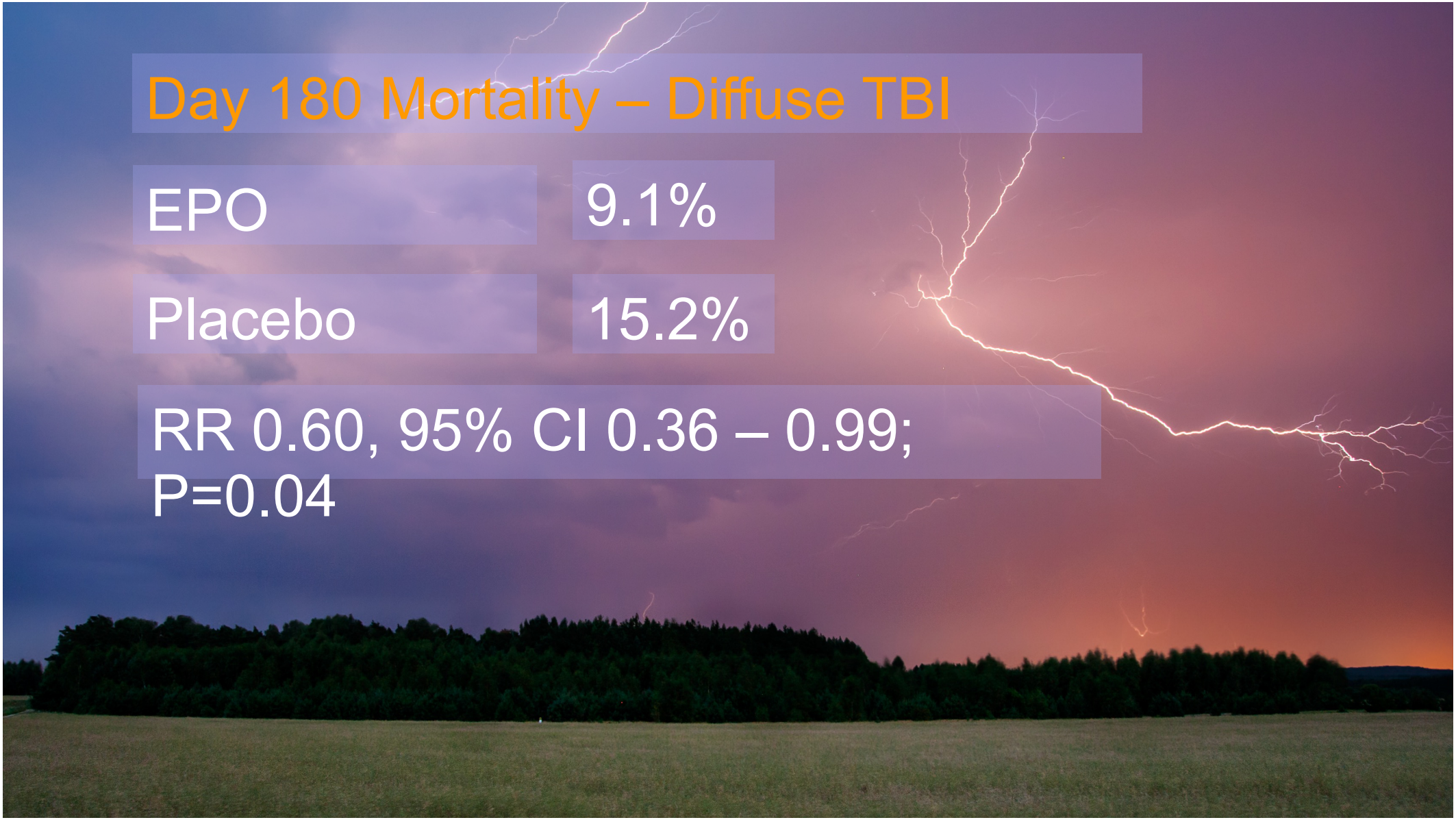
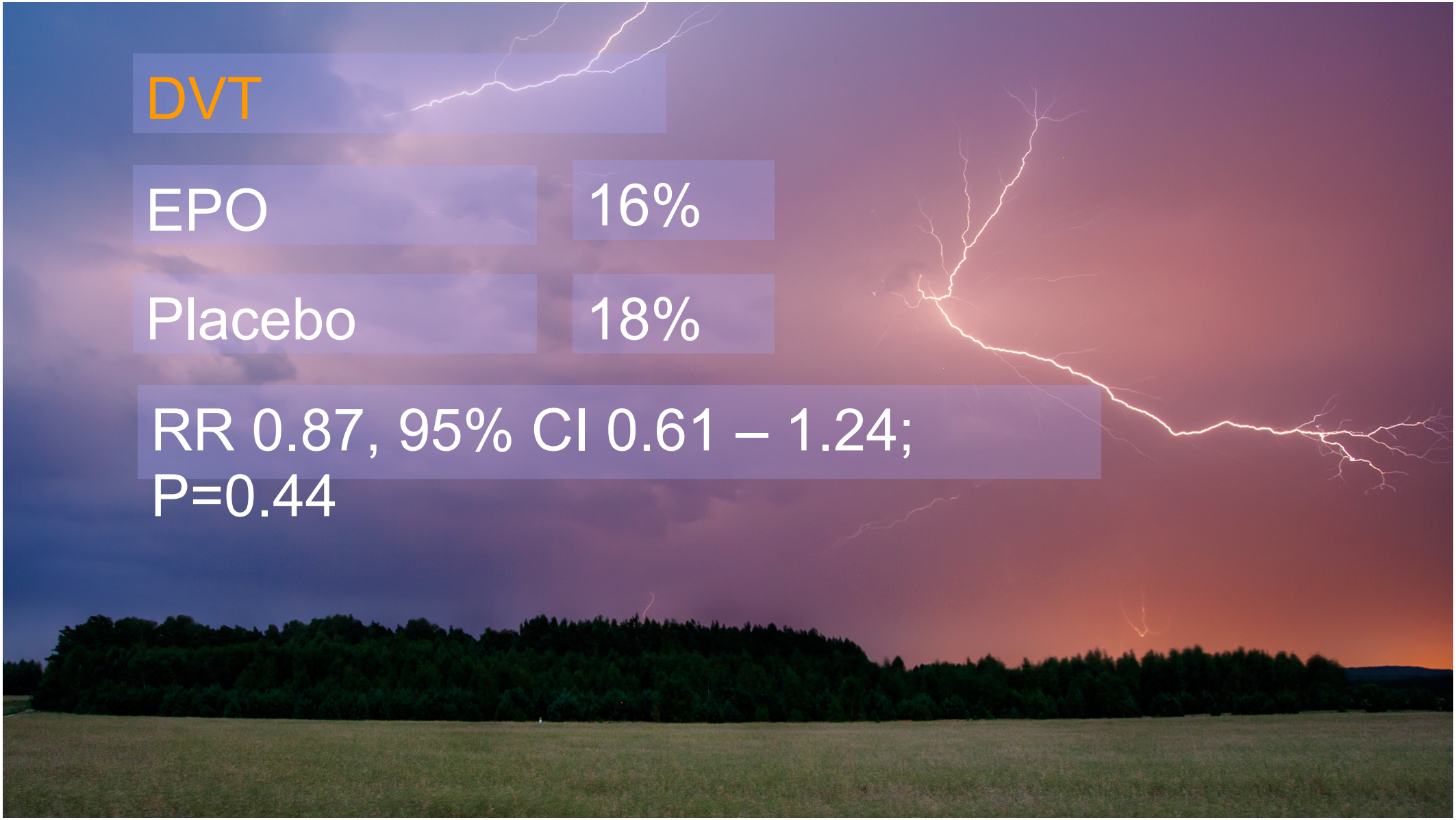


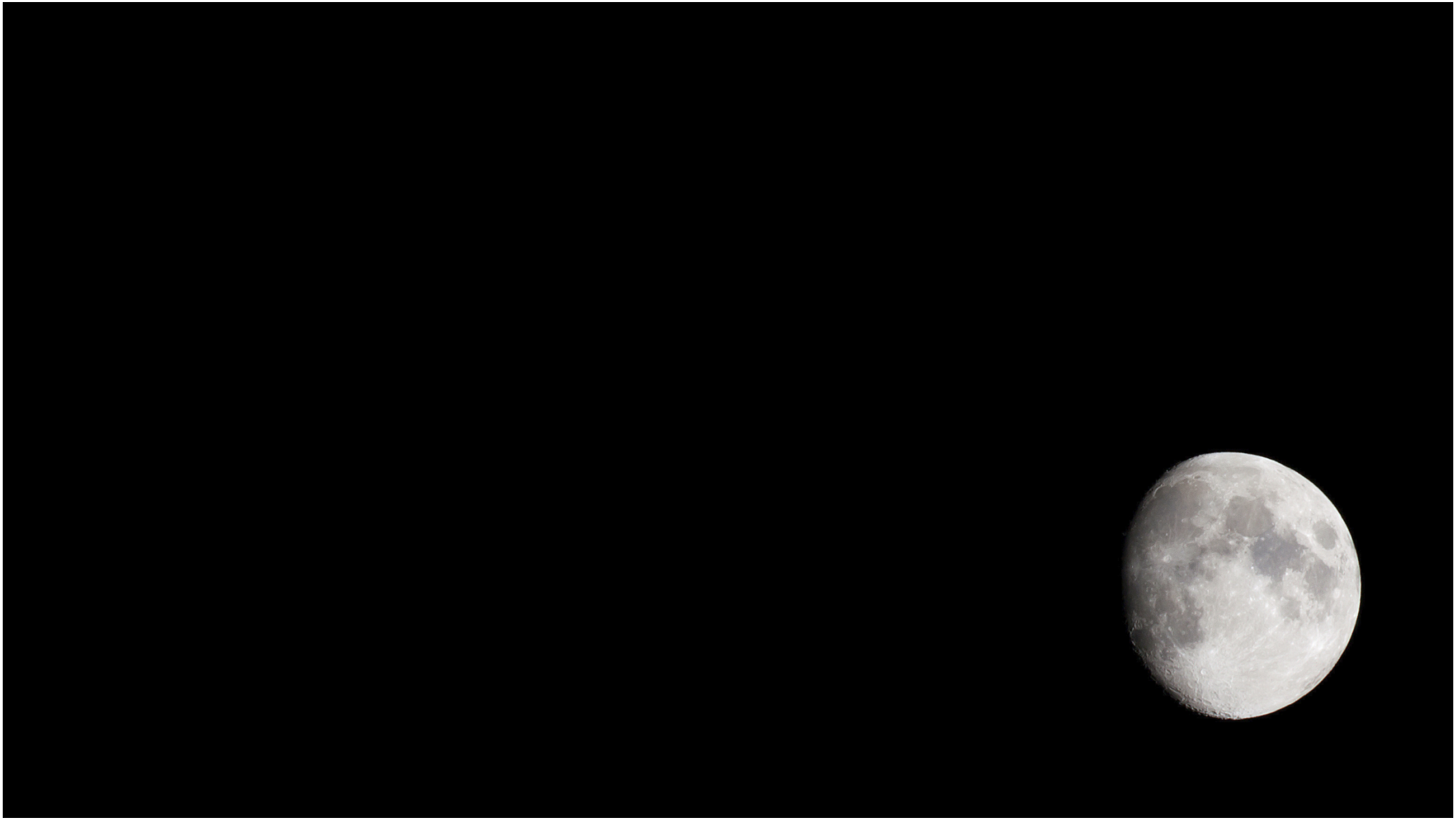
Figure 3: Kaplan–Meier estimates of the unadjusted probability of death at 6 months in patients receiving erythropoietin or placebo


Day 180 Mortality
EPO
11%
Placebo
16%
RR 0.68, 95% CI 0.44 – 1.03;
P=0.07


Day 180 Mortality – Diffuse TBI
EPO
9.1%
Placebo
15.2%
RR 0.60, 95% CI 0.36 – 0.99;
P=0.04


DVT
EPO
16%
Placebo
18%
RR 0.87, 95% CI 0.61 – 1.24;
P=0.44


Methodologically Excellent
Limitations Few
Overall Impressive




PROPPR

Blood product ratios in traumatic haemorrhage

Plasma : Platelets : RBCs

1:1:1 vs 1:1:2

Boxes

Boxes

1:1:1

1 platelets | 6 FFP | 6 RBCs

	Boxes
1:1:1	1 platelets | 6 FFP | 6 RBCs
1:1:2	3 FFP | 6 RBCs

	Boxes
1:1:1	1 platelets | 6 FFP | 6 RBCs
1:1:2	3 FFP | 6 RBCs
	1 platelets | 3 FFP | 6 RBCs

Sequence

Sequence

1:1:1

1 platelets 6 x (1 RBCs | 1 FFP)

	Sequence
1:1:1	1 platelets 6 x (1 RBCs | 1 FFP)
1:1:2	3 x (2 RBCs | 1 FFP) + 1 platelets

End Point

Cessation of requirement for blood

Surgeon

Radiologist

Mortality

Mortality

580 Patients

0.044

Δ 10%

21% to 11%

Mortality

580 Patients

0.044

Δ 10%

21% to 11%

0.044

Δ 12%

35% to 23%

Mortality

580 Patients

0.044

Δ 10%

21% to 11%

680 Patients

0.044

Δ 12%

35% to 23%

Mortality

580 Patients	95%	0.044	Δ 10%
			21% to 11%
680 Patients	92%	0.044	Δ 12%
			35% to 23%

1:1:1	338
1:1:2	342

1:1:1	1:1:2	Baseline
34.5	34	Age
78%	83%	Male
26.5	26	ISS
-8	-8.5	Base Excess
27.5	25.4	Time to Recruitment

1:1:1 vs 1:1:2

Plasma : RBCs

Platelets : RBCs

	1:1:1	vs	1:1:2
Plasma : RBCs	1.0		0.5
Platelets : RBCs			

	1:1:1	vs	1:1:2
Plasma : RBCs	1.0		0.5
Platelets : RBCs	1.5		0.4

Blood Products during Intervention

Blood Products during Intervention

1:1:1	15
1:1:2	16

Blood Products after Intervention

Blood Products after Intervention

1:1:1	1
1:1:2	2

Blood Products at 24 hours

Blood Products at 24 hours	1:1:1	25
	1:1:2	19

Blood Products at 24 hours

1:1:1

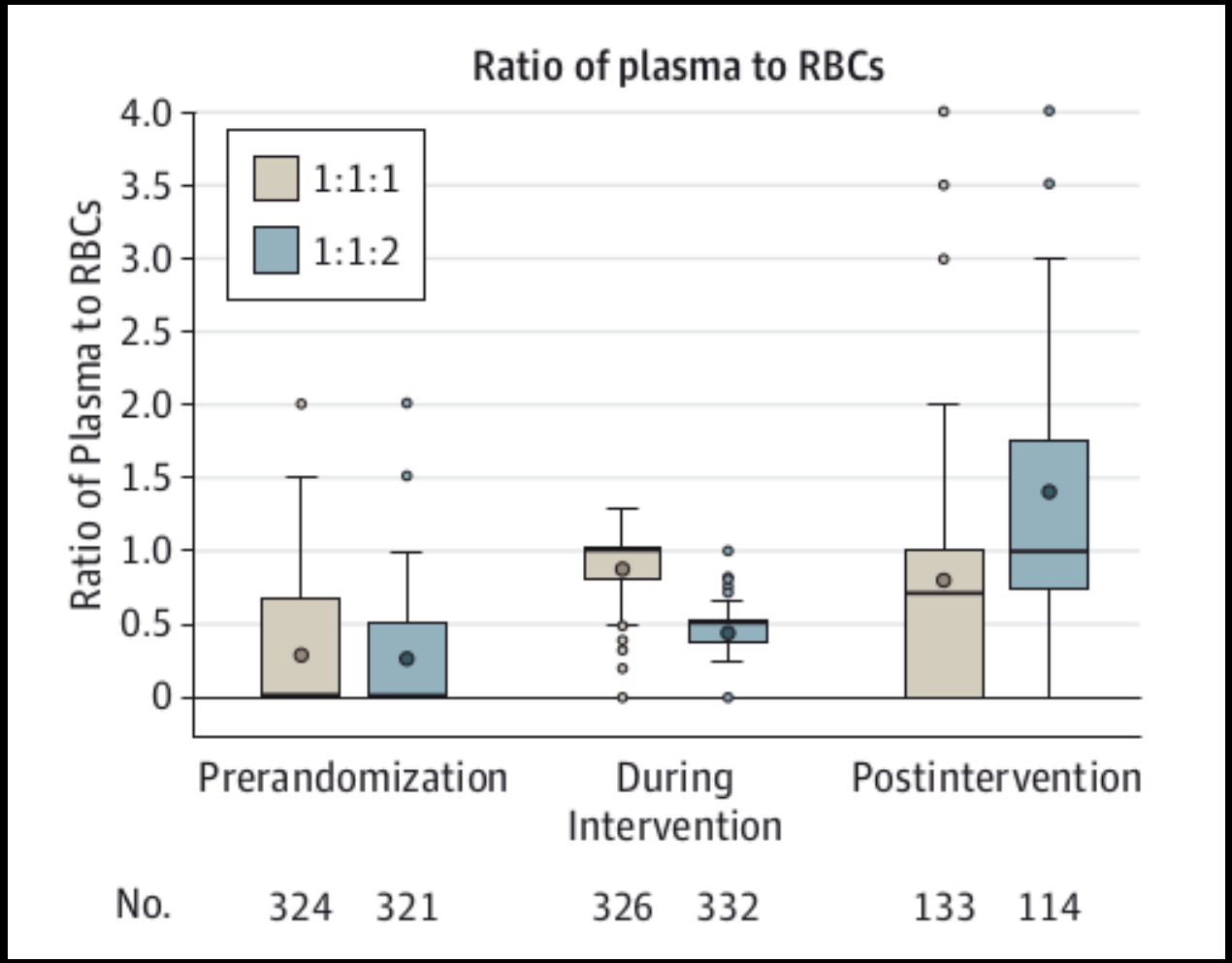
1:1:2

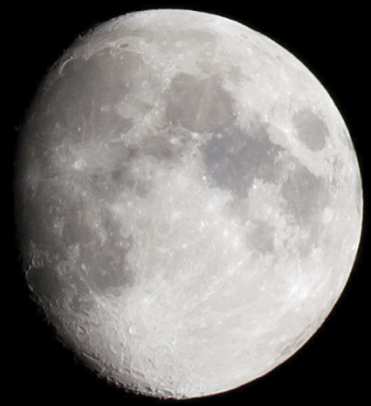
Blood Products at 24 hours

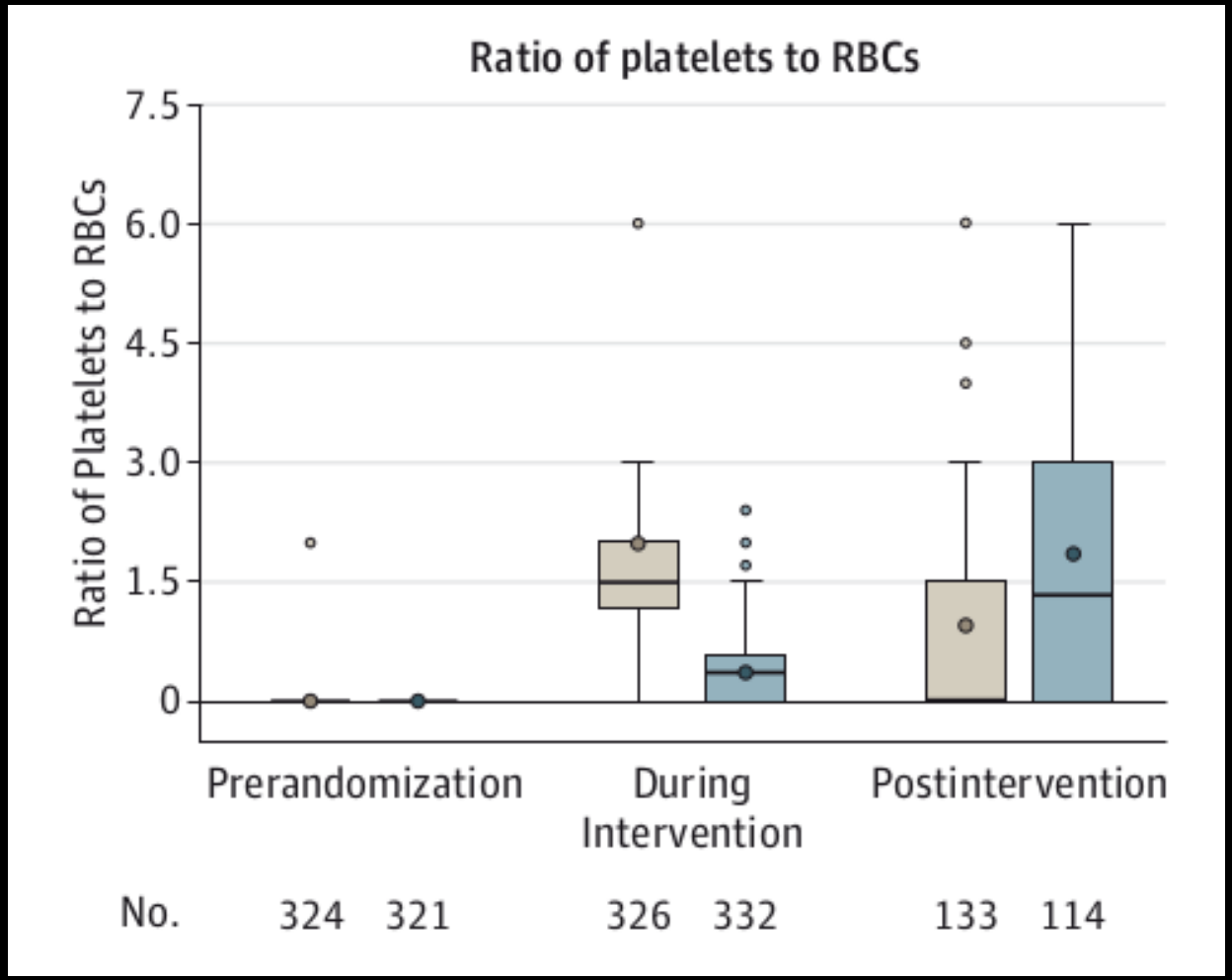
	1:1:1	1:1:2	
Plasma	7	5	P<0.001

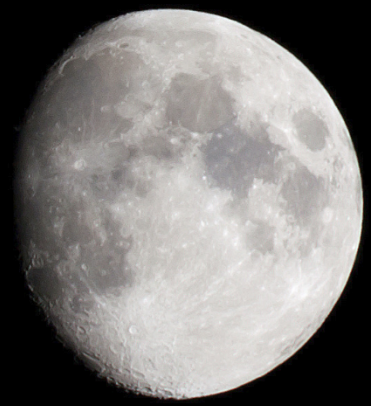
Blood Products at 24 hours

	1:1:1	1:1:2	
Plasma	7	5	P<0.001
Platelets	12	6	P<0.001


Ratio of plasma to RBCs
Ratio of Plasma to RBCs
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
1:1:1
1:1:2
Prerandomization
During Intervention
Postintervention
No.
324
321
326
332
133
114




Ratio of platelets to RBCs
Ratio of Platelets to RBCs
7.5
6.0
4.5
3.0
1.5
0
Prerandomization
During Intervention
Postintervention
No.
324
321
326
332
133
114



Mortality

1:1:1

1:1:2

Mortality	1:1:1	1:1:2
24 Hours	12.7%	17.0%

Mortality	1:1:1	1:1:2
24 Hours	12.7%	17.0%
30 Days	22.4%	26.1%

Deaths from Exsanguination at 24 hours

Deaths from Exsanguination at 24 hours

1:1:1	1:1:2
9.2%	14.6%

Deaths from Exsanguination at 24 hours

1:1:1	1:1:2
9.2%	14.6%

difference −5.4%

95% CI, −10.4% to −0.5%

P = 0.03

Haemostasis

Haemostasis

1:1:1	1:1:2	
86.1%	78.1%	p = 0.006

Methodologically robust

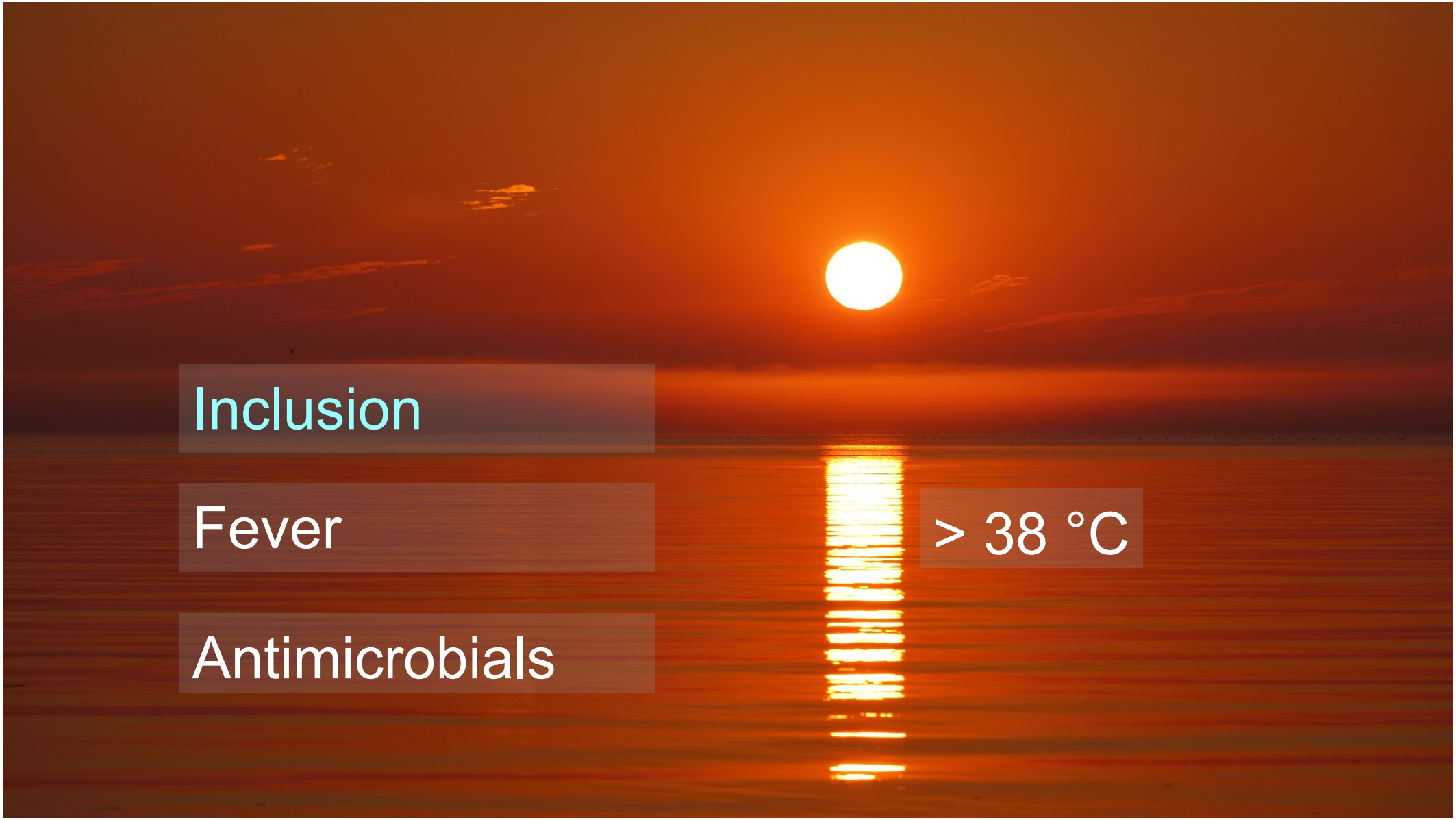
Limitations few

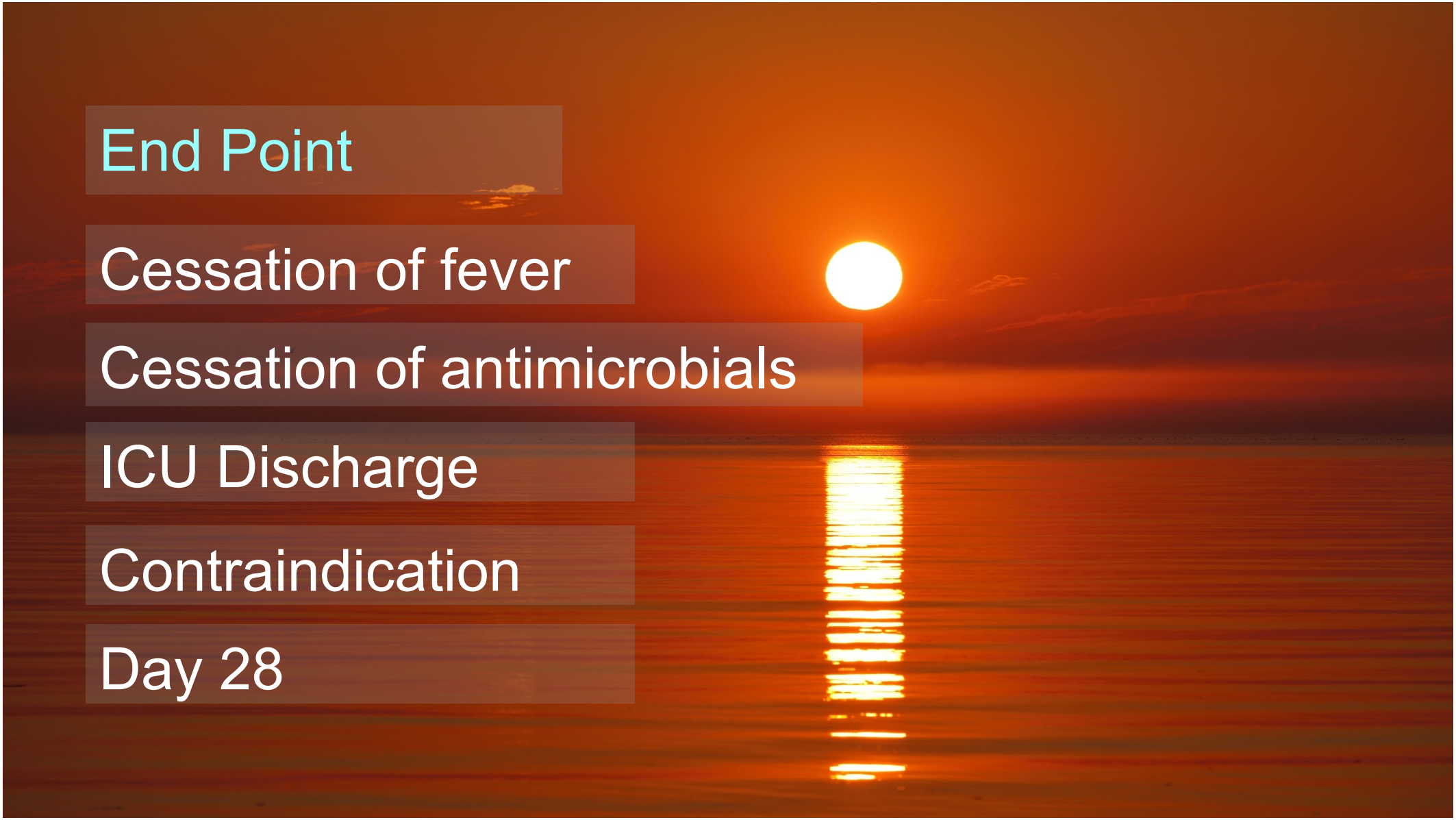
Overall outstanding


HEAT

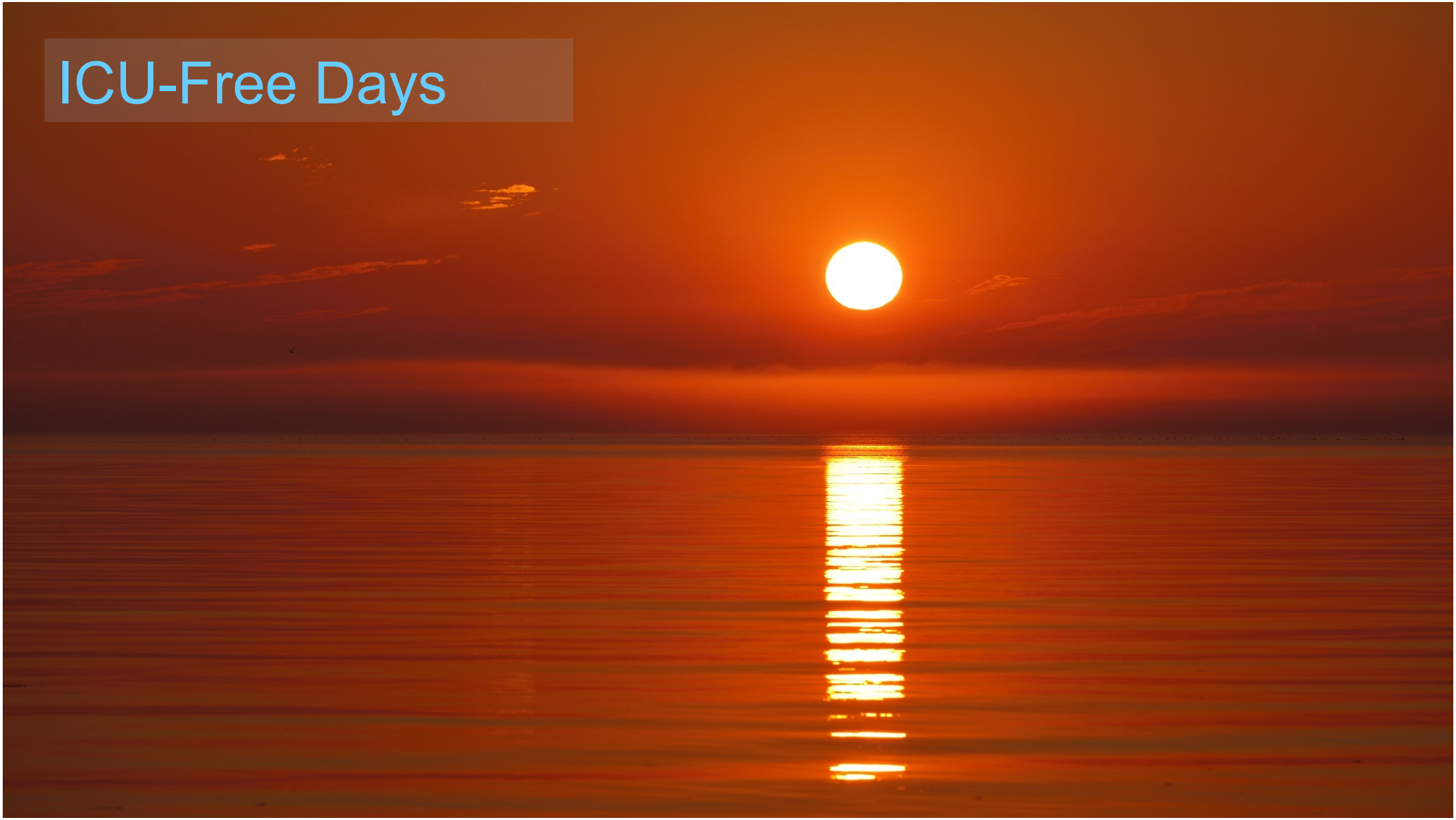

Paracetamol in fever from
suspected infection

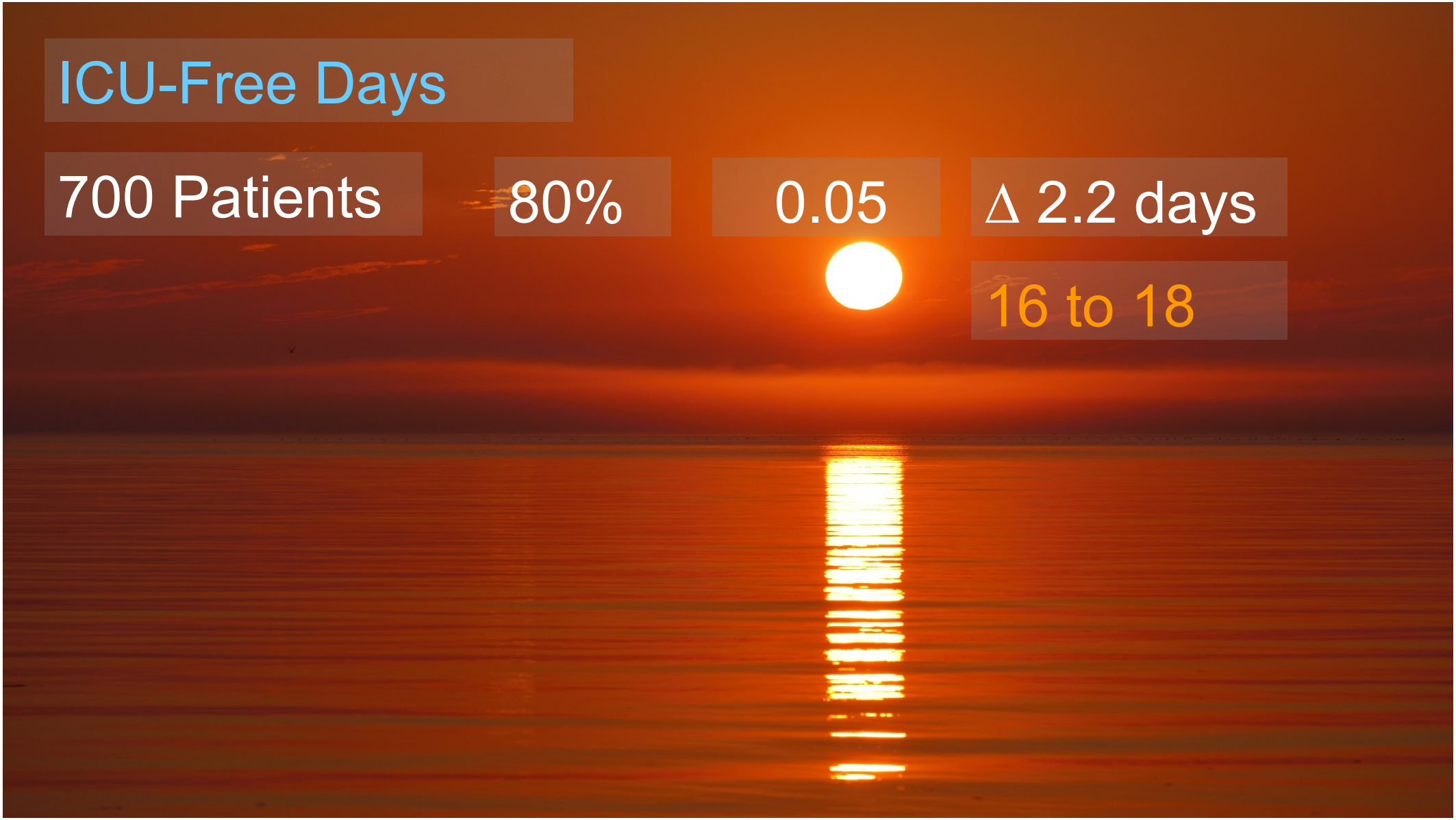

Paracetamol
vs
Placebo

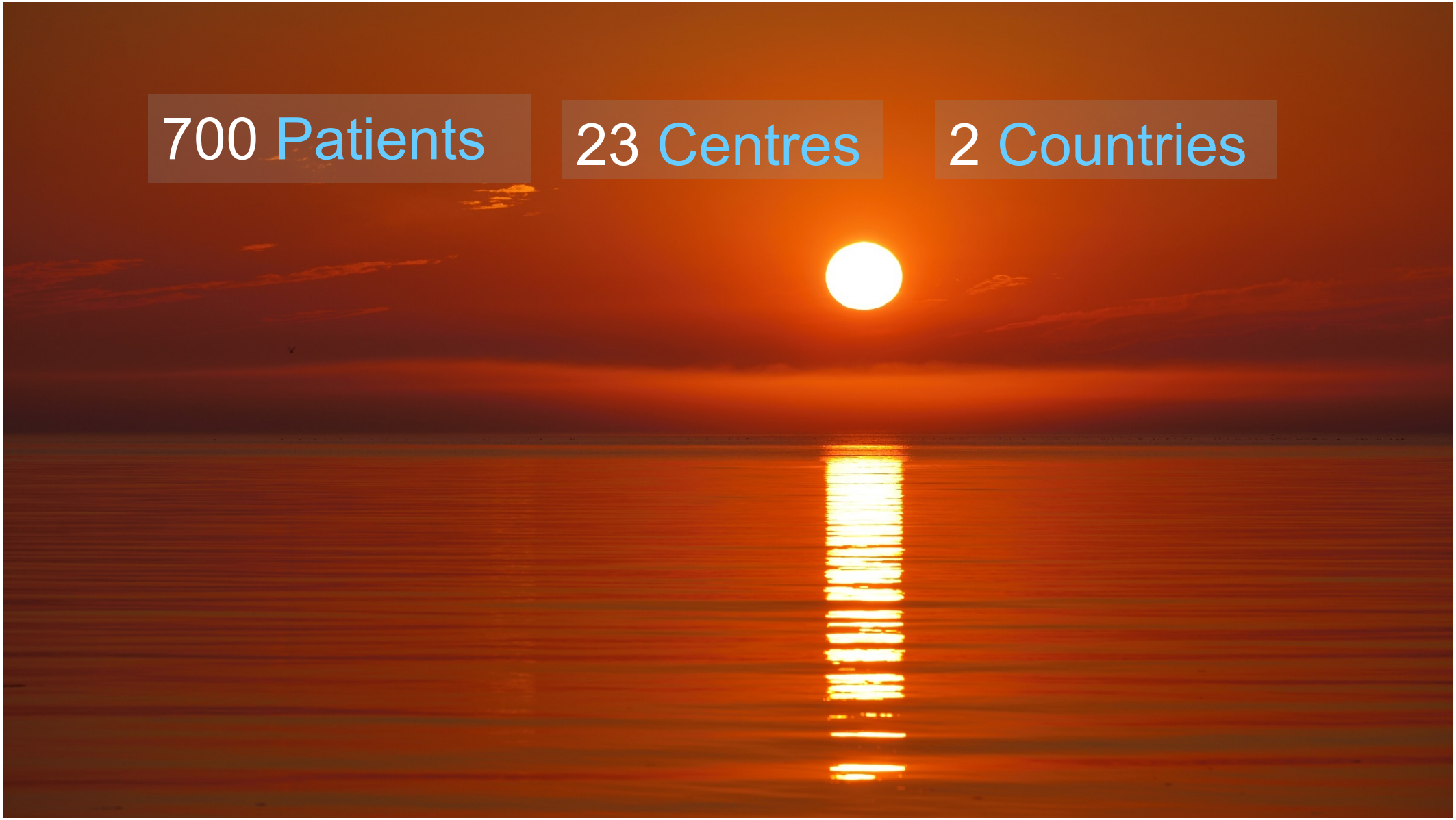

Inclusion
Fever
> 38 °C
Antimicrobials


End Point
Cessation of fever
Cessation of antimicrobials
ICU Discharge
Contraindication
Day 28

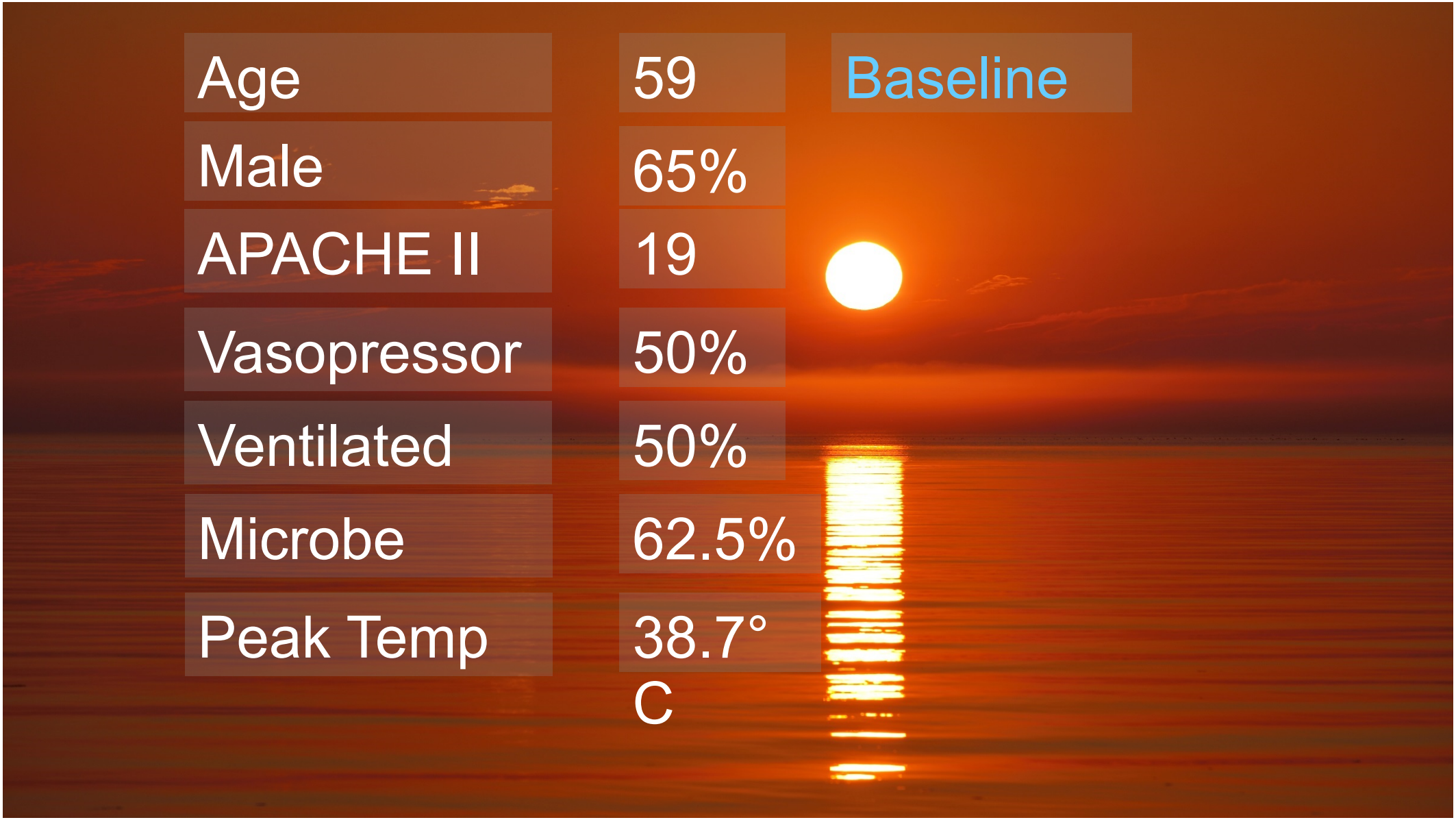

Confounders
Rescue pyrexia management
Open label paracetamol


ICU-Free Days

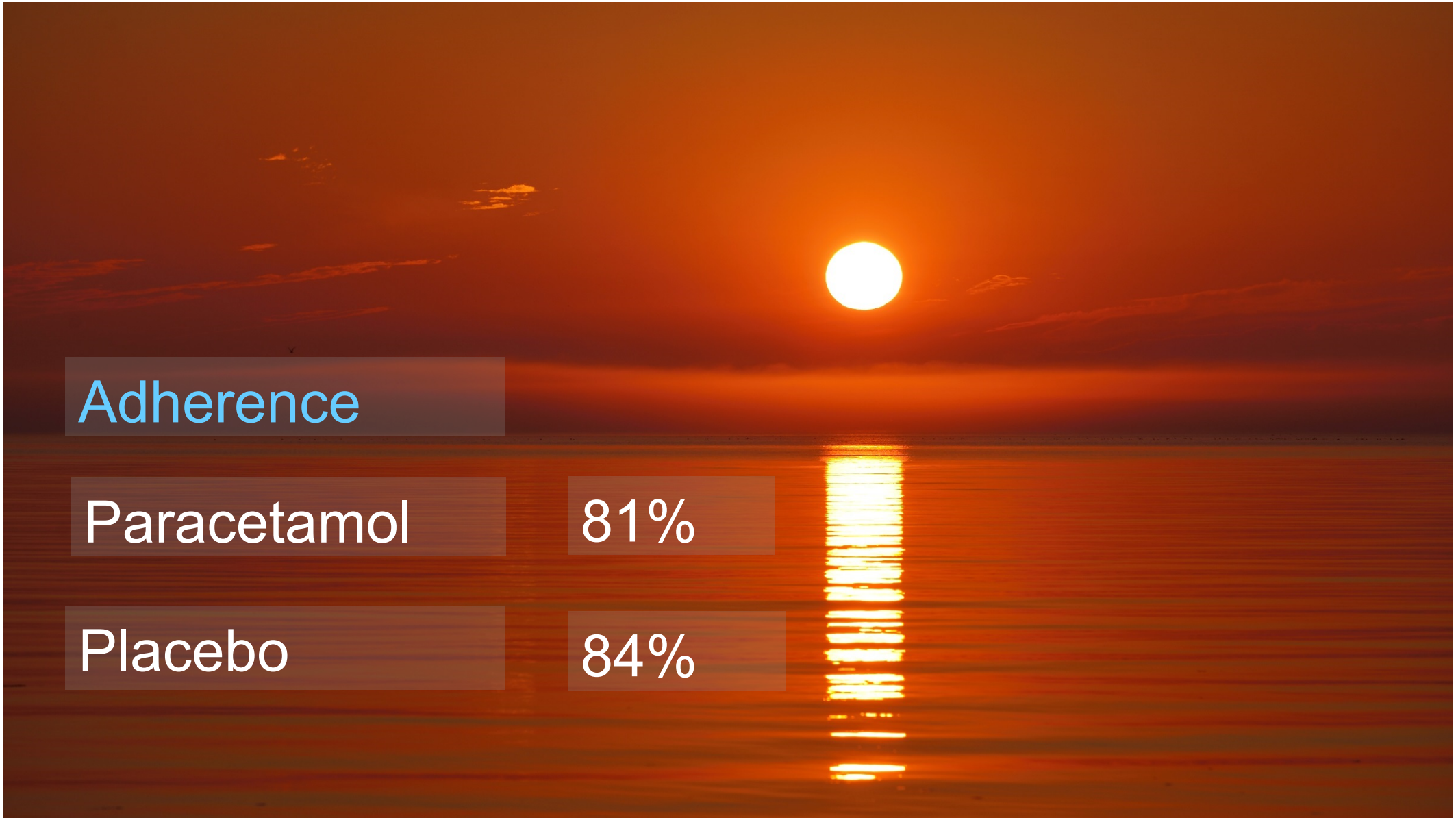

ICU-Free Days
700 Patients
80%
0.05
Δ 2.2 days
16 to 18

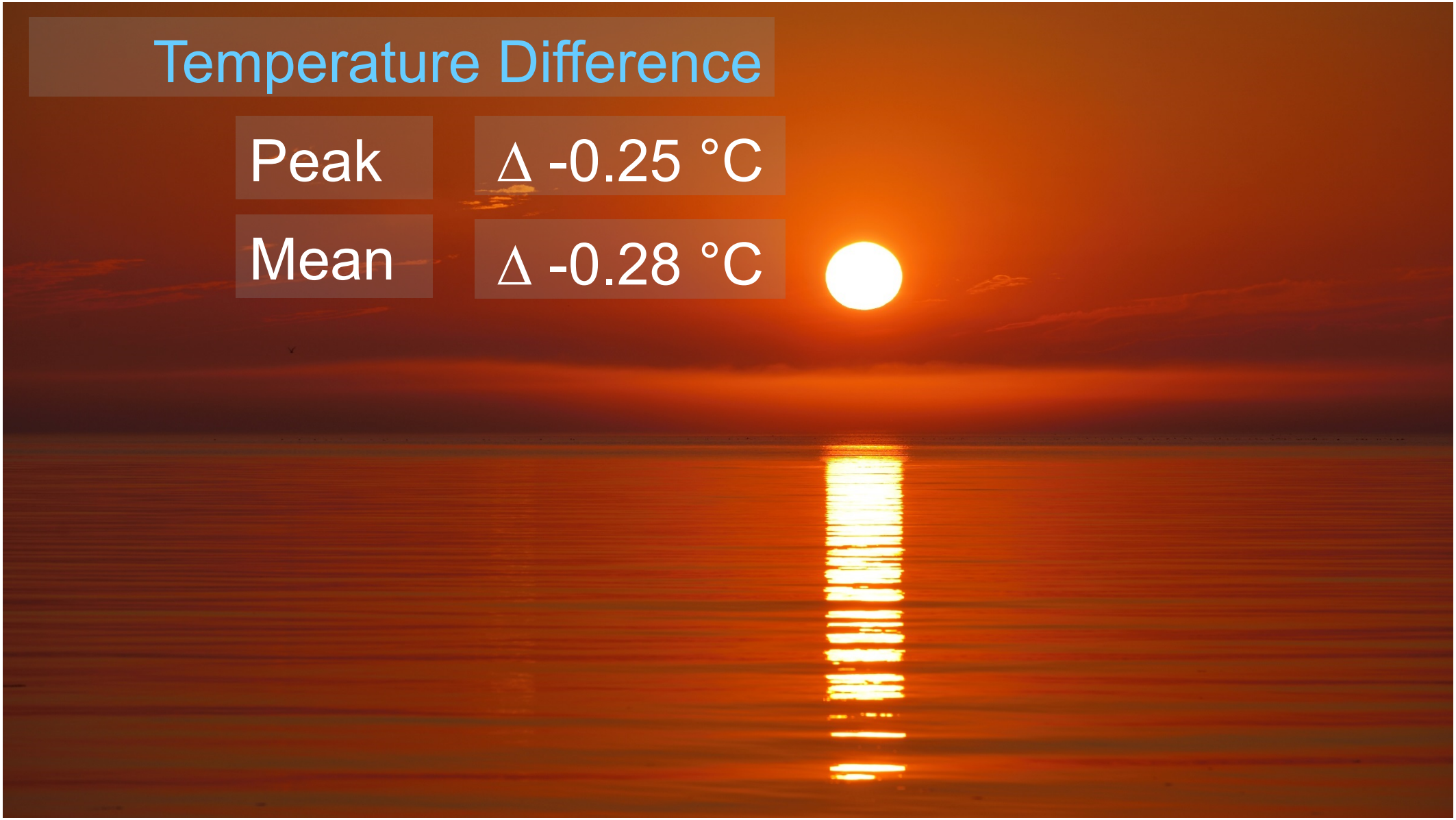

700 Patients
23 Centres
2 Countries


Paracetamol
346
Placebo
344


Age
59
Baseline
Male
65%
APACHE II
19
Vasopressor
50%
Ventilated
50%
Microbe
62.5%
Peak Temp
38.7° C


Doses
Paracetamol
8
Placebo
9


Adherence
Paracetamol
81%
Placebo
84%


Temperature Difference
Peak
Δ -0.25 °C
Mean
Δ -0.28 °C

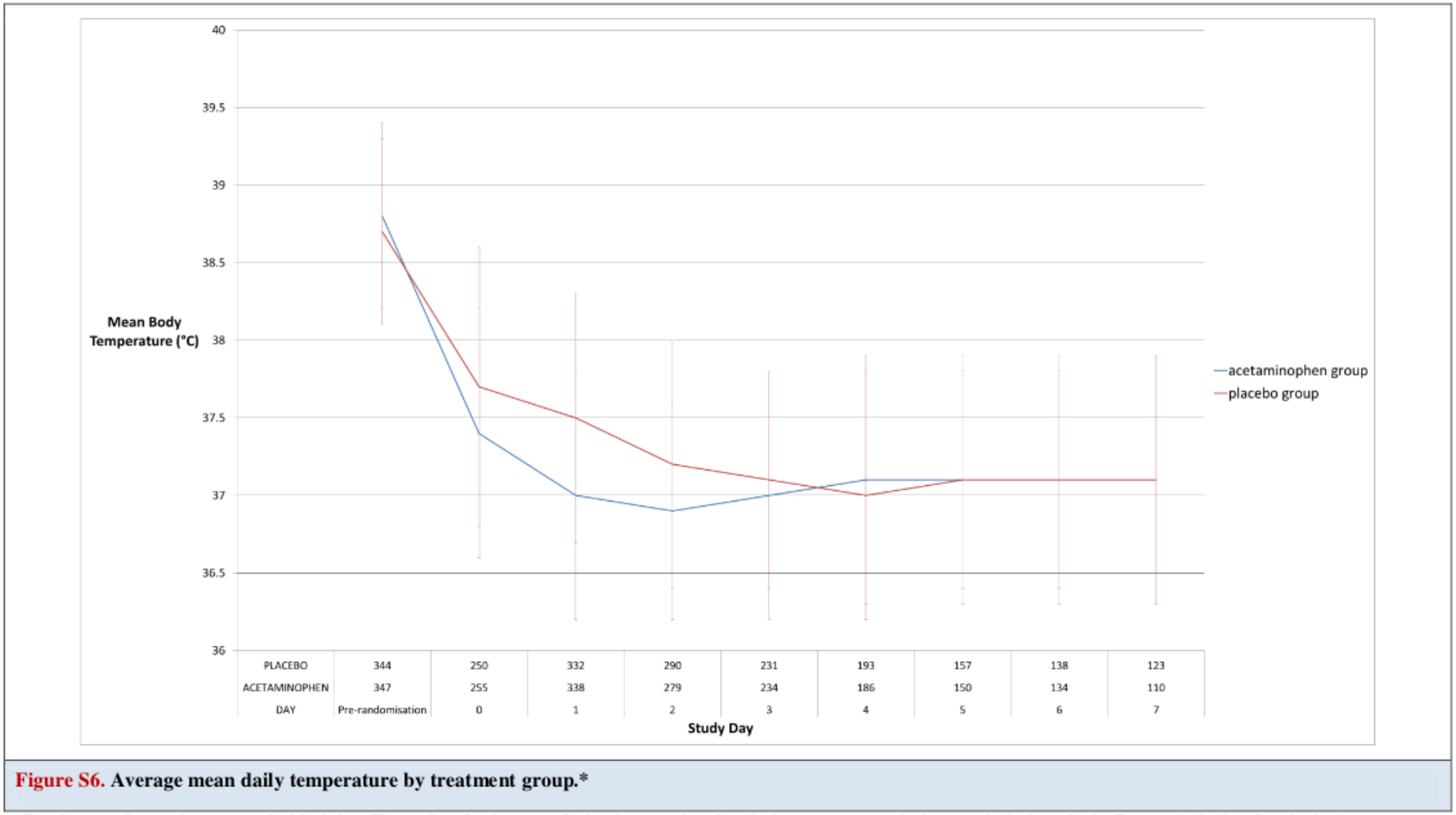
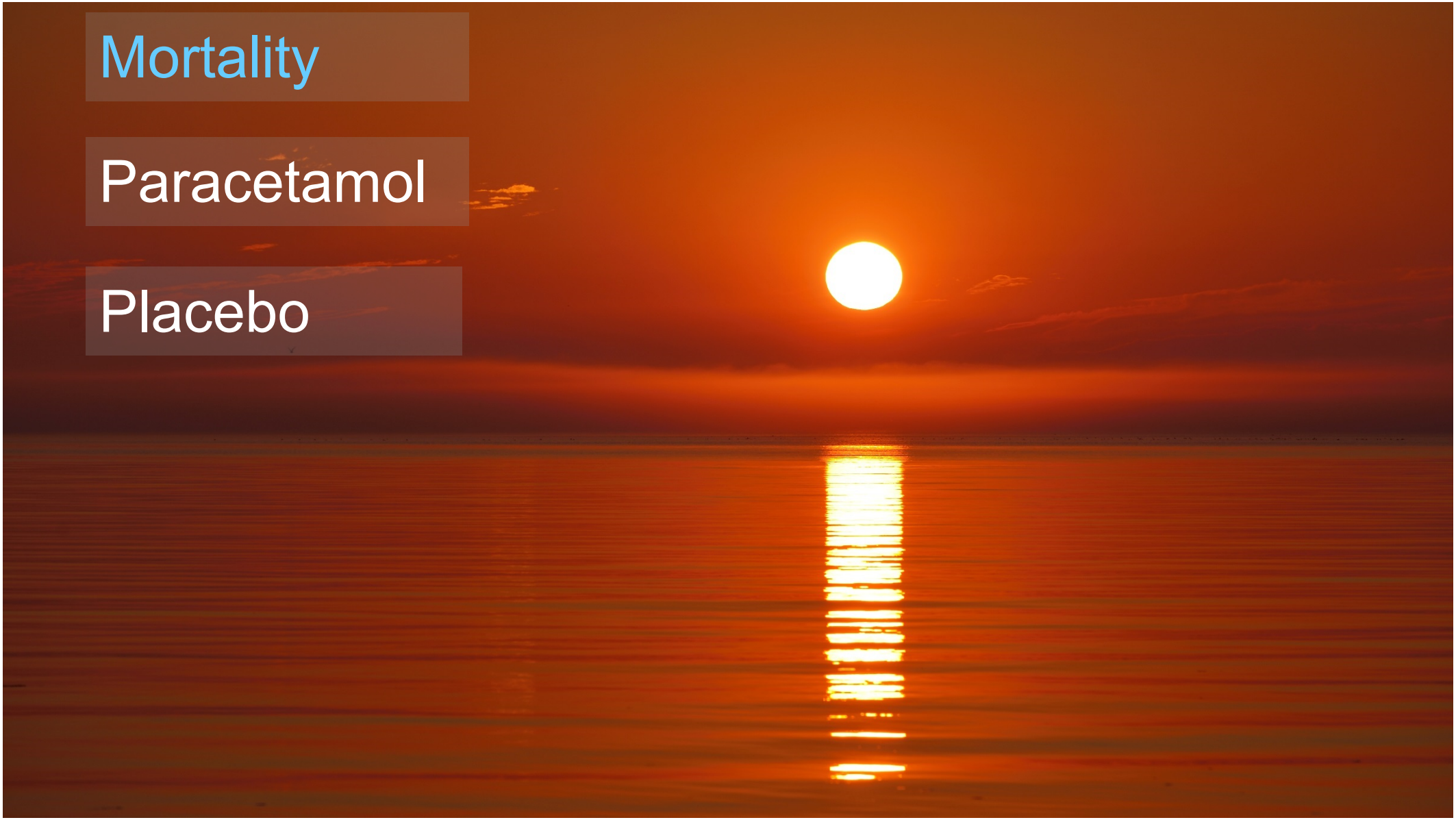


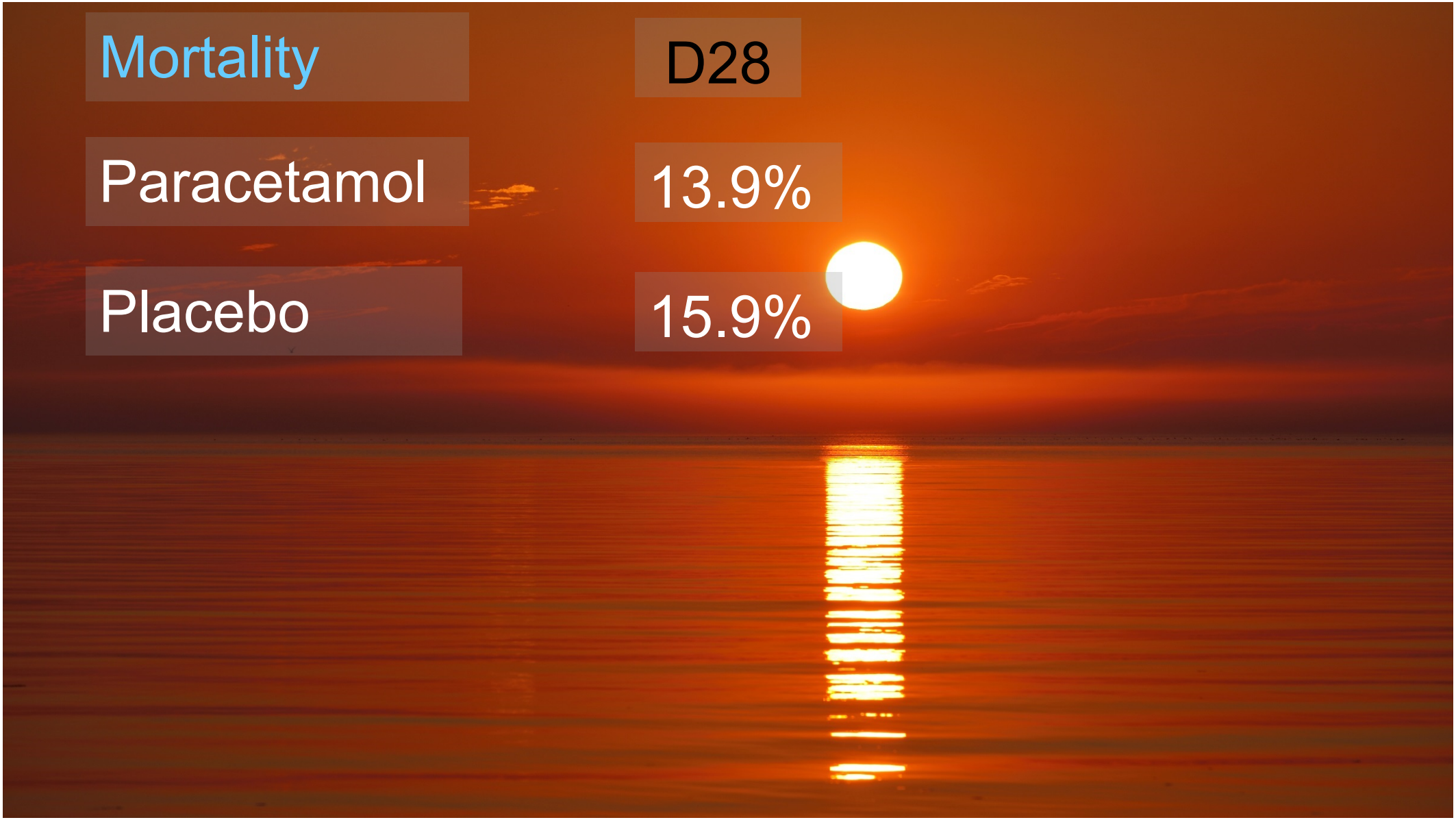
Figure S6. Average mean daily temperature by treatment group.*

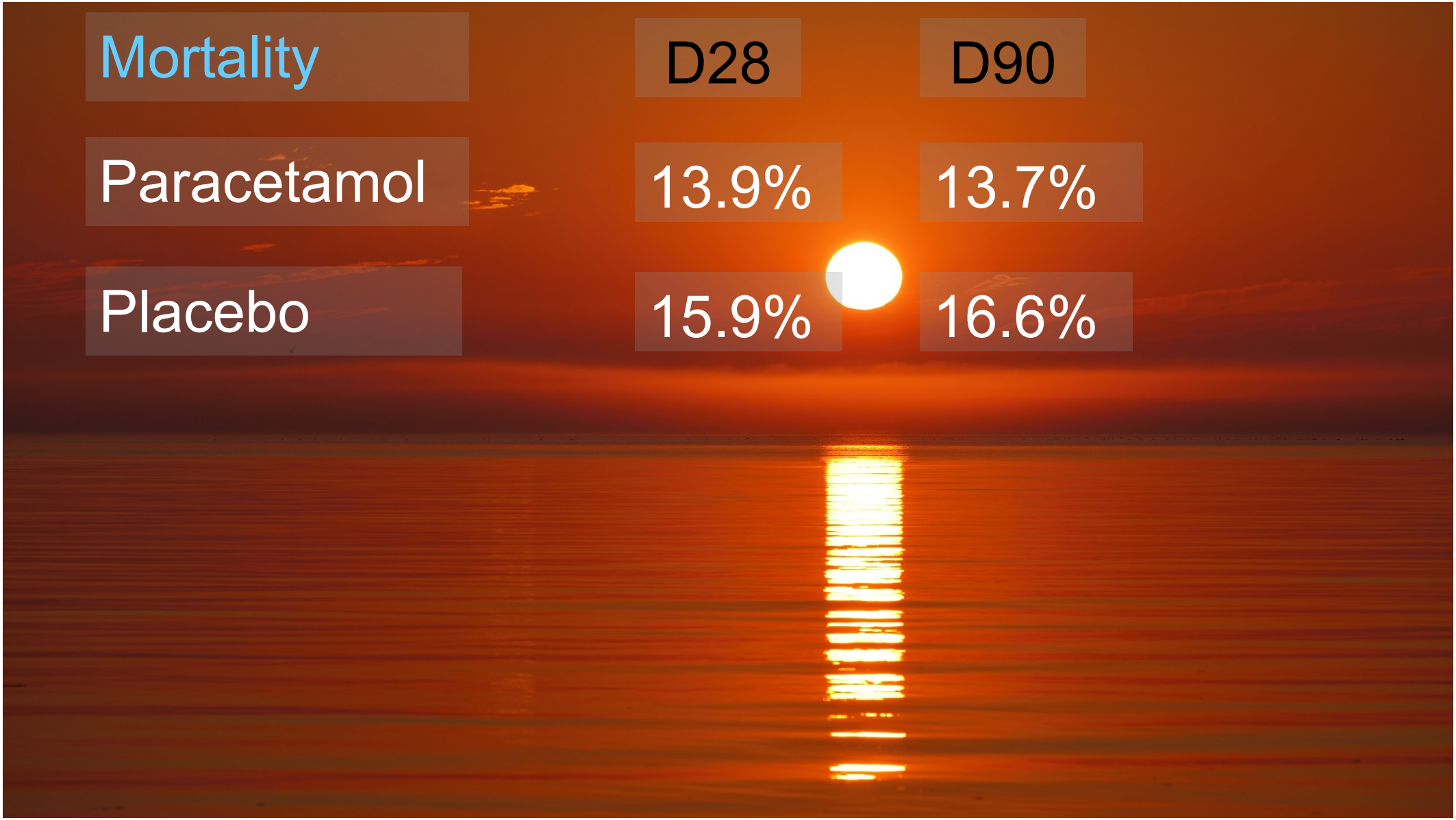
*Error bars are plus or minus one standard deviation. The number of patients contributing data to each study point by treatment group is shown on the horizontal axis. Day zero is the day of randomization.


ICU-Free Days
Paracetamol
23
IQR 13 - 25
Placebo
22
IQR 12 - 25


ICU-Free Days
Δ 0 days; 96.2% CI, 0 to 1; P = 0.07


Mortality
Paracetamol
Placebo


Mortality
D28
Paracetamol
13.9%
Placebo
15.9%


Mortality
D28
D90
Paracetamol
13.9%
13.7%
Placebo
15.9%
16.6%


Contamination
30%


Methodologically good
Limitations several
Overall good

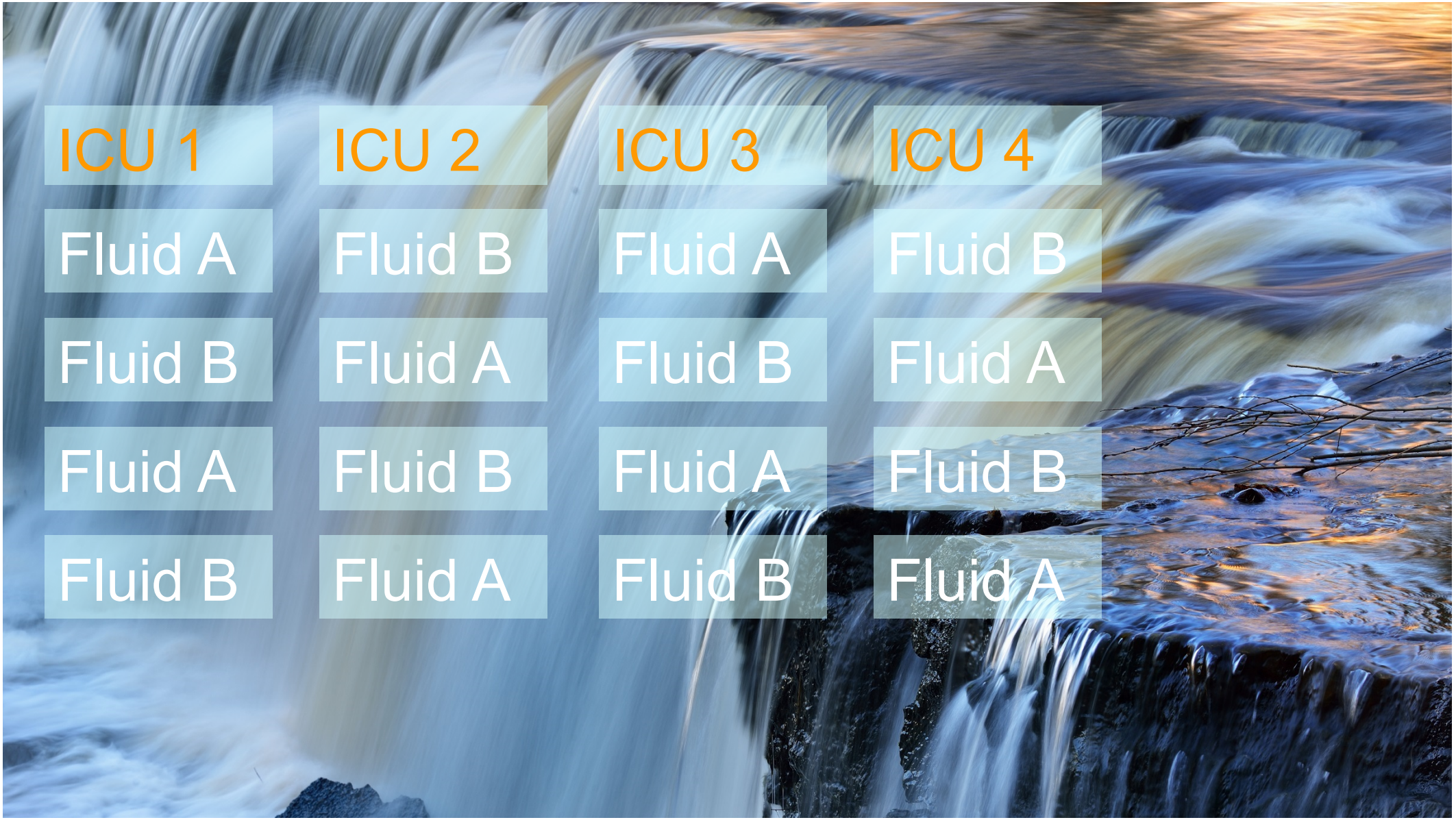

SPLIT


Effect of plasma-lyte 148 vs 0.9% saline
on AKI in ICU patients


Saline harmful
Hyperchloraemia
Metabolic acidosis

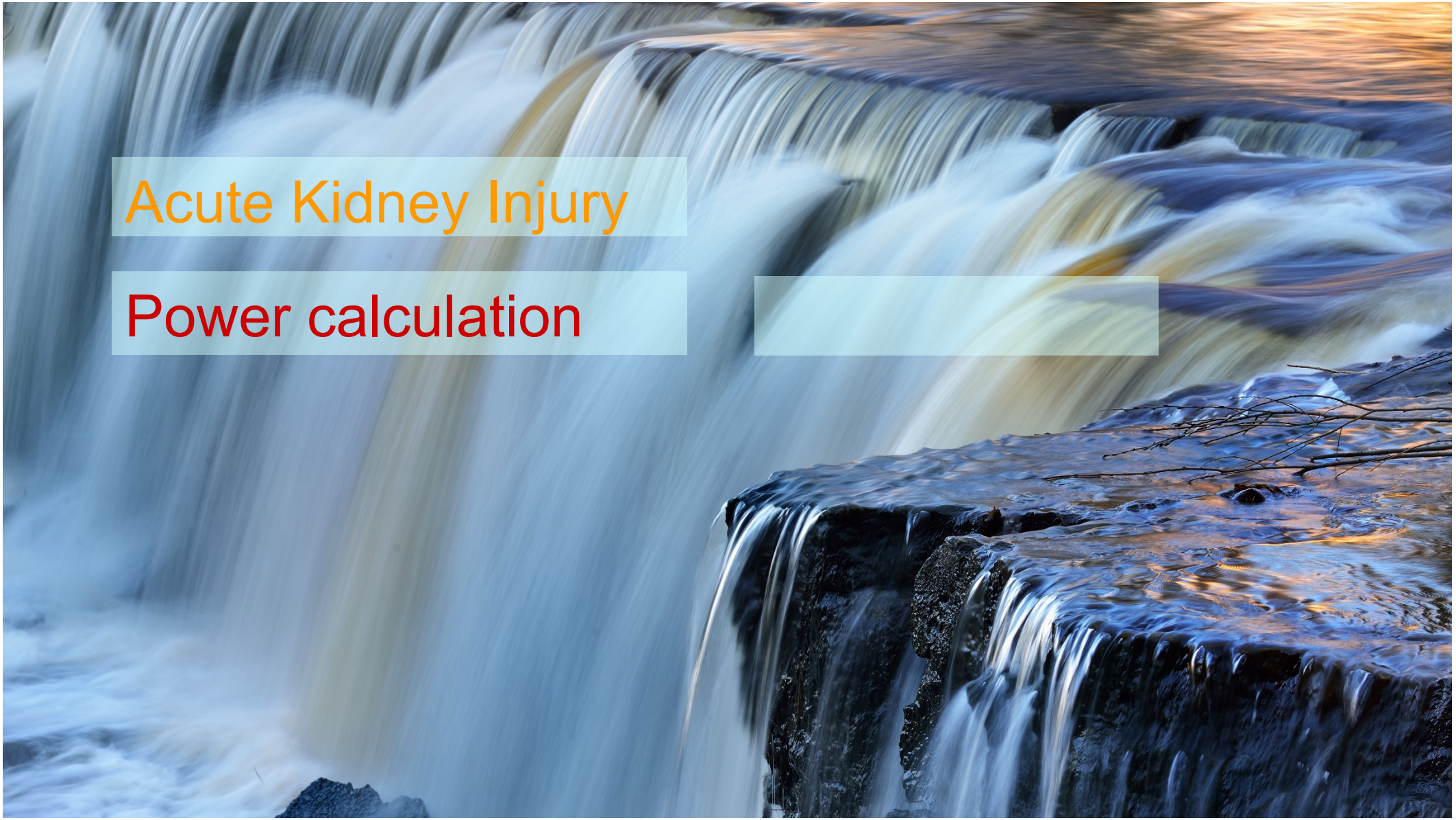

Inclusion
ICU Patient
Crystalloid requirement


Design
Investigator Initiated
Multicentre
Blinded
Cluster-Randomised
Double-Crossover


ICU 1
ICU 2
ICU 3
ICU 4
Fluid A
Fluid B
Fluid A
Fluid B
Fluid B
Fluid A
Fluid B
Fluid A
Fluid A
Fluid B
Fluid A
Fluid B
Fluid B
Fluid A
Fluid B
Fluid A


Fluid Therapy
Study fluid encouraged
Open-label crystalloid
Clinician determined

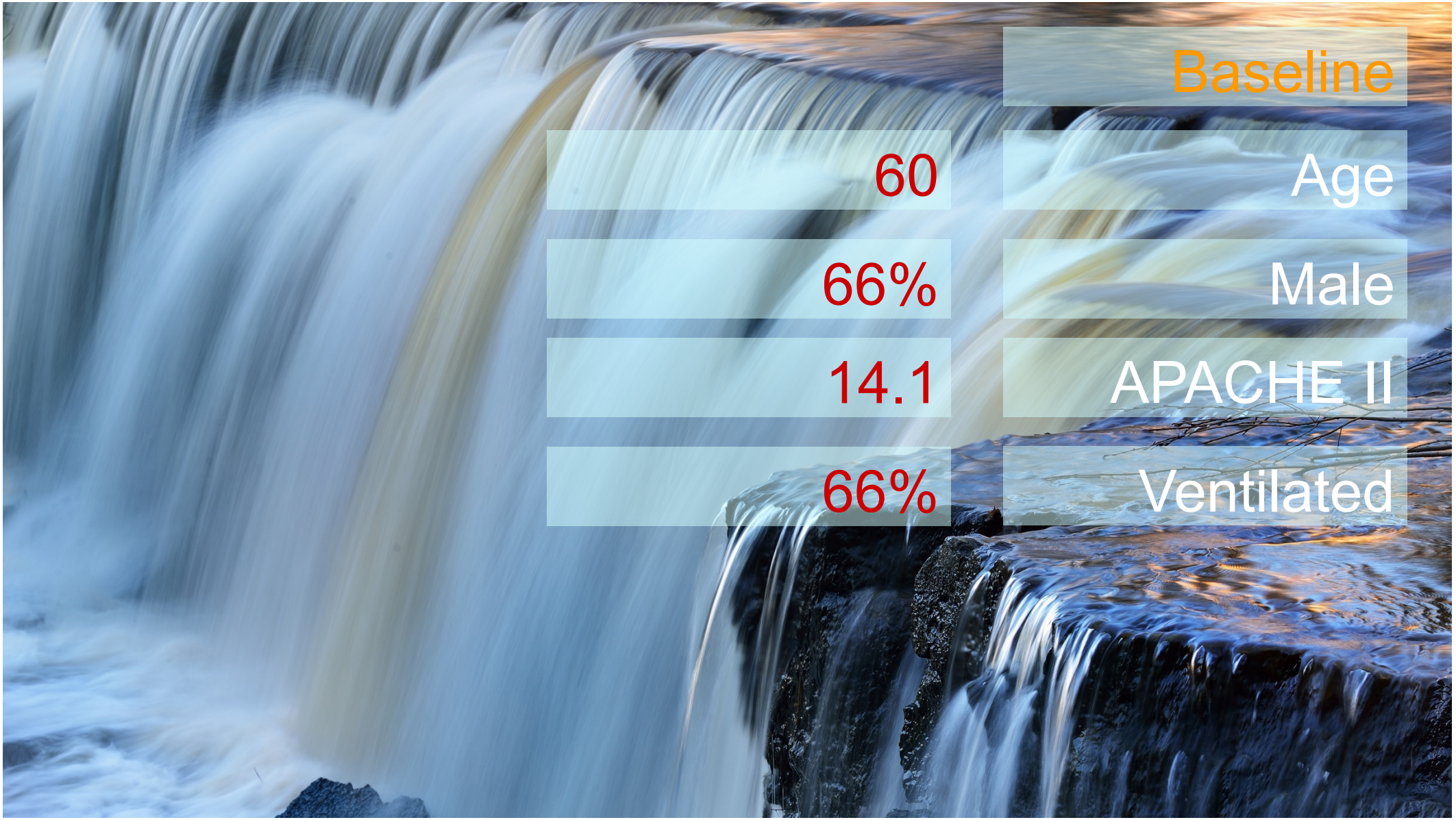

Acute Kidney Injury


Acute Kidney Injury
Power calculation


2278 Patients
4 Centres
1 Country


Plasmalyte
1162
Saline
1116


Baseline


Baseline
60
Age
66%
Male
14.1
APACHE II
66%
Ventilated


elective
surgical
few
Source
Comorbidities
Baseline

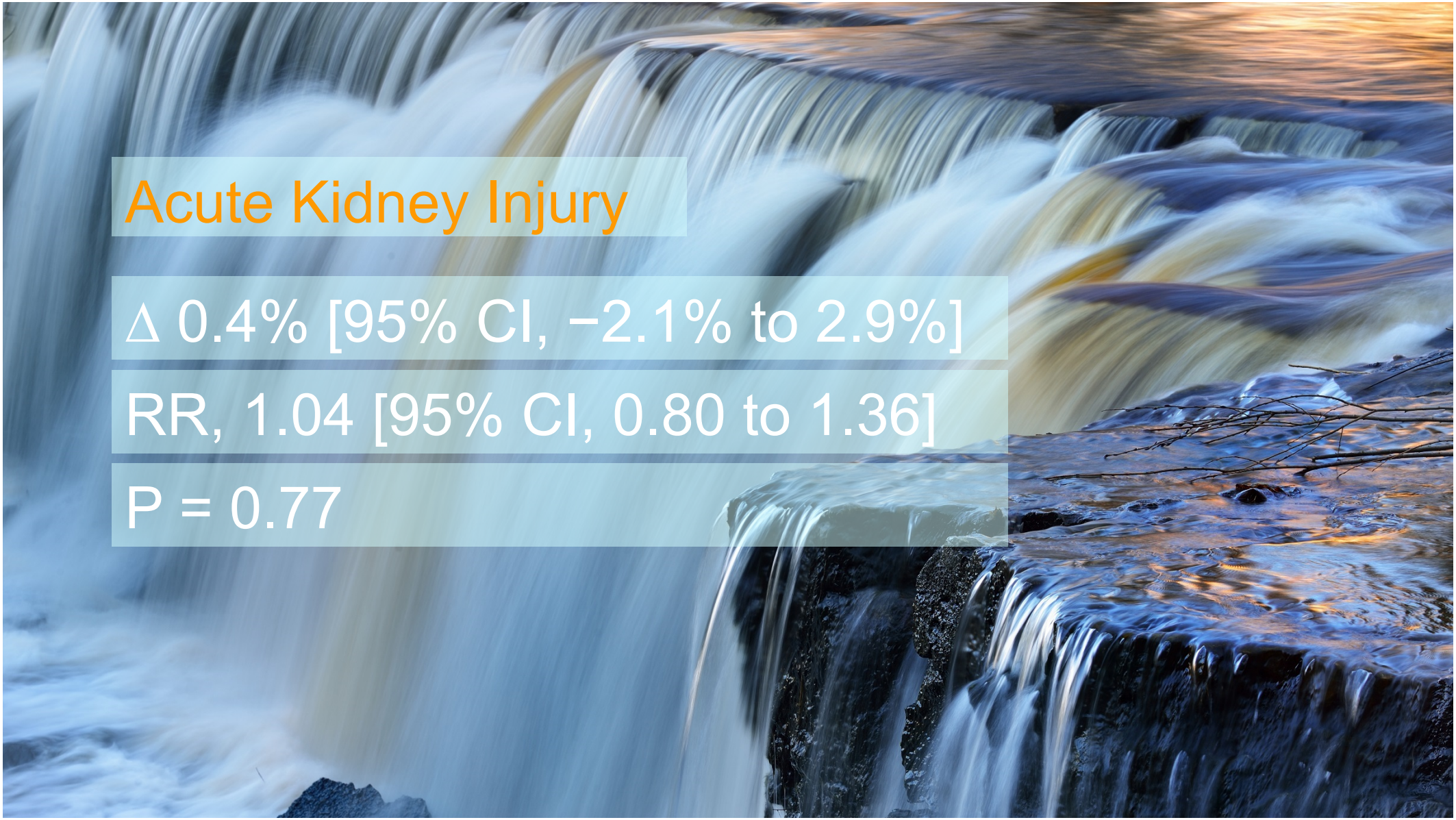

Dose
Plasmalyte
2000 ml
Saline
2000 ml


Plasmalyte
1200 ml
Saline
1000 ml


Plasmalyte
Plasmalyte
1200 ml
Saline
1000 ml


Acute Kidney Injury


Acute Kidney Injury
Plasmalyte
9.6%
Saline
9.2%


Acute Kidney Injury
Δ 0.4% [95% CI, −2.1% to 2.9%]
RR, 1.04 [95% CI, 0.80 to 1.36]
P = 0.77

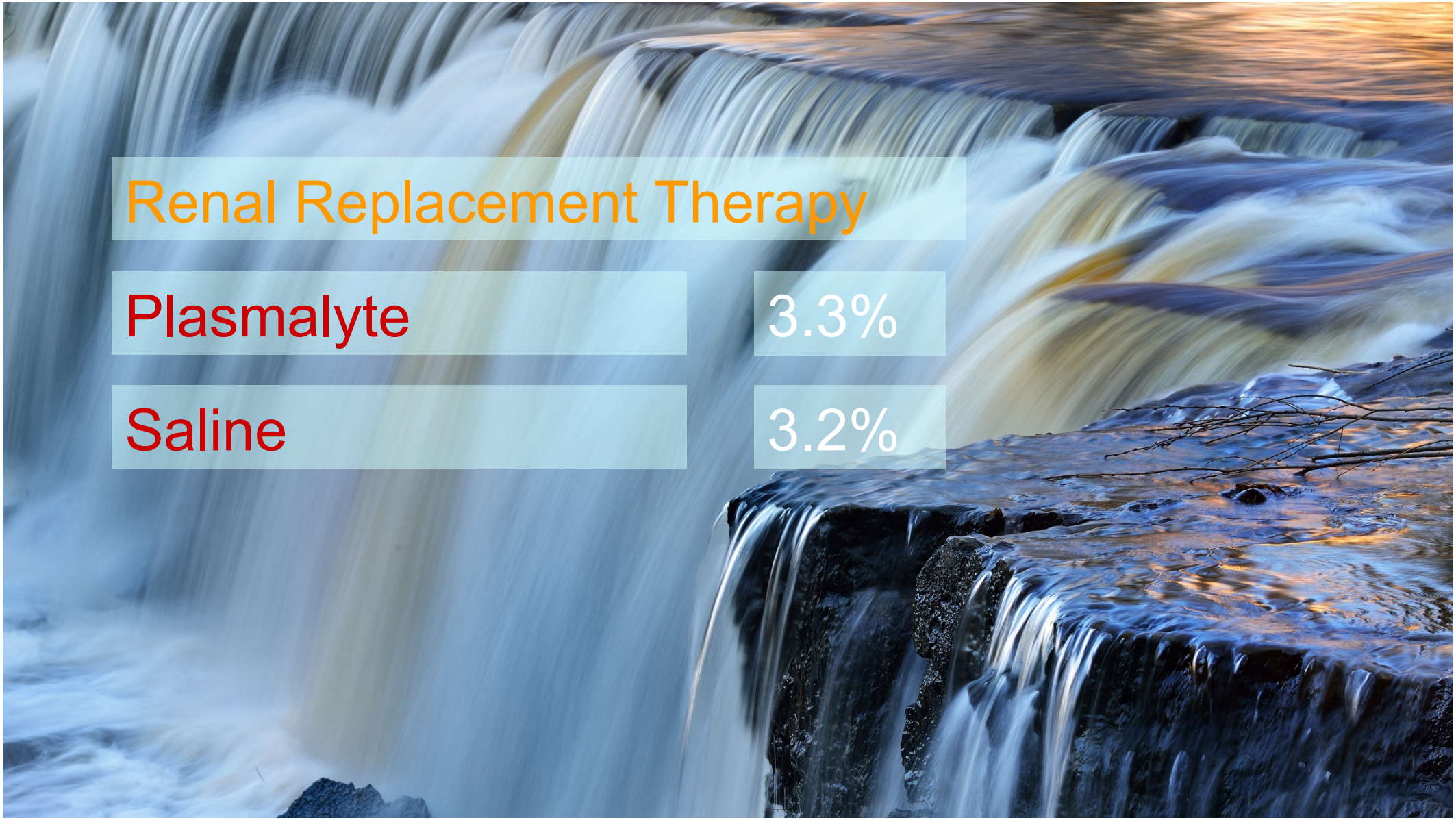
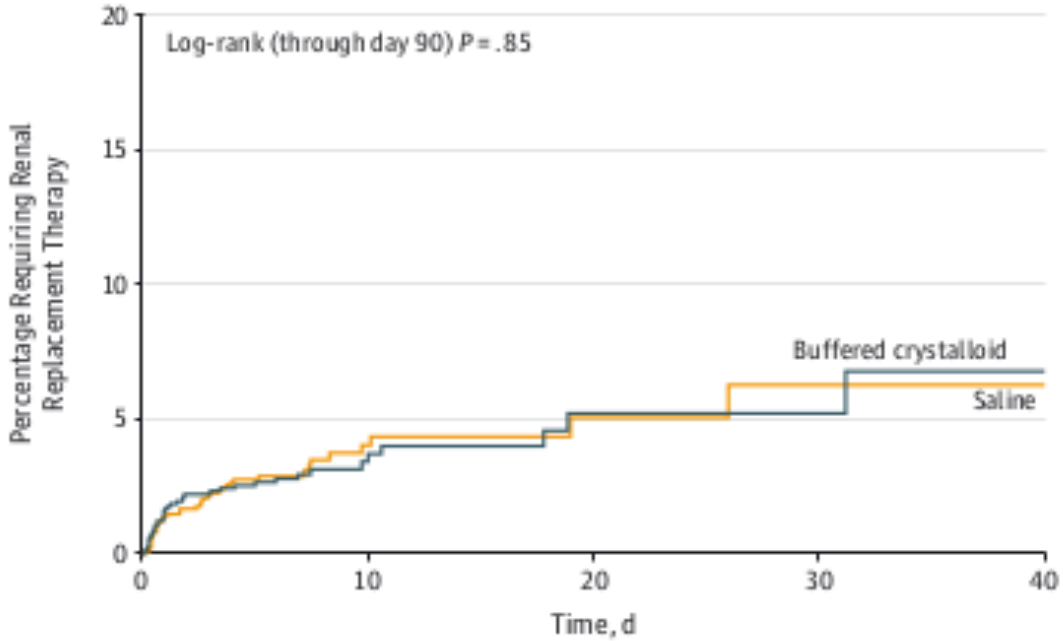

Renal Replacement Therapy
Plasmalyte
3.3%
Saline
3.2%

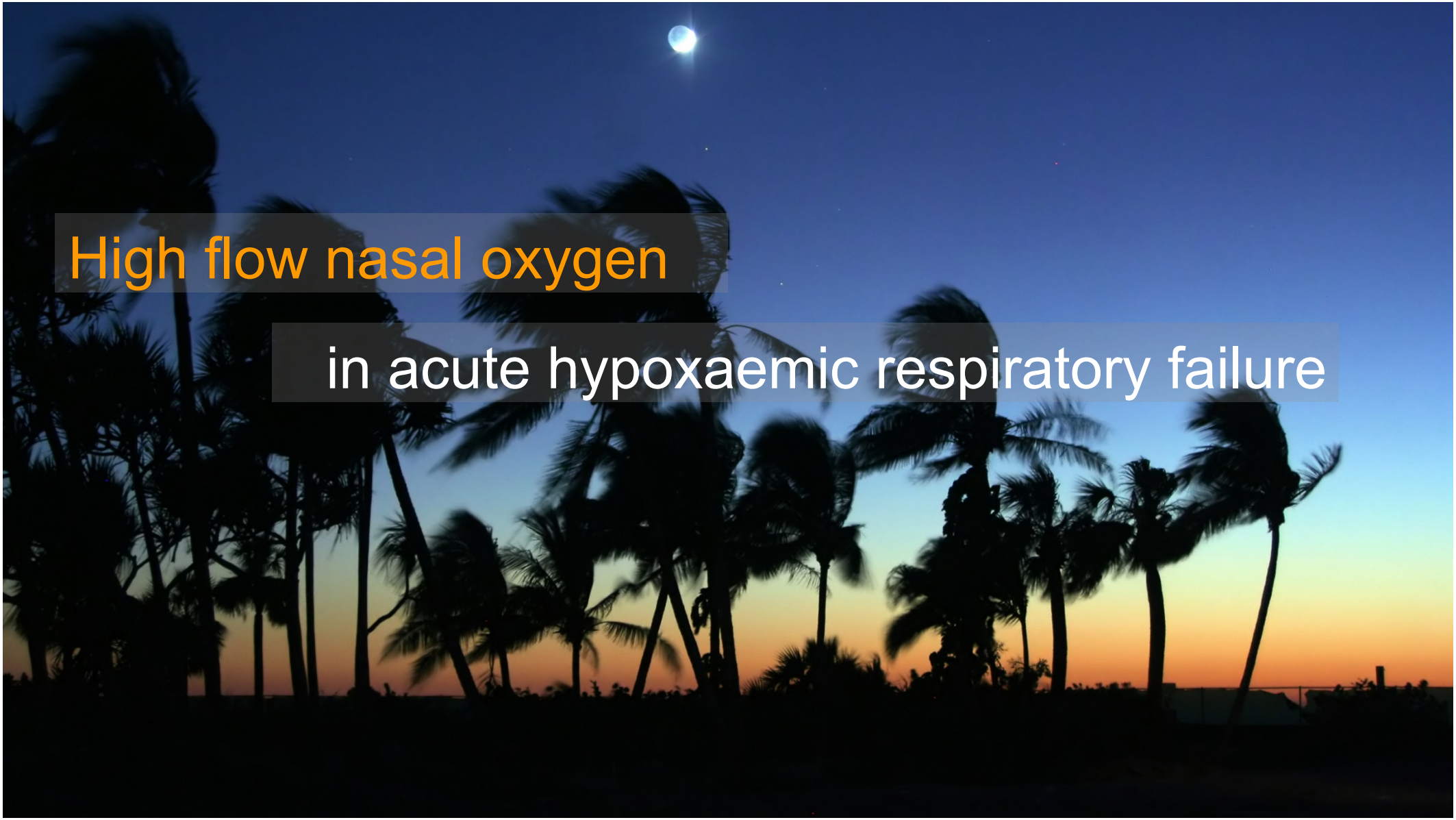
Figure 2. Cumulative Incidence of Patients Requiring Renal Replacement Therapy Until Day 90 After Enrollment in the SPLIT Trial

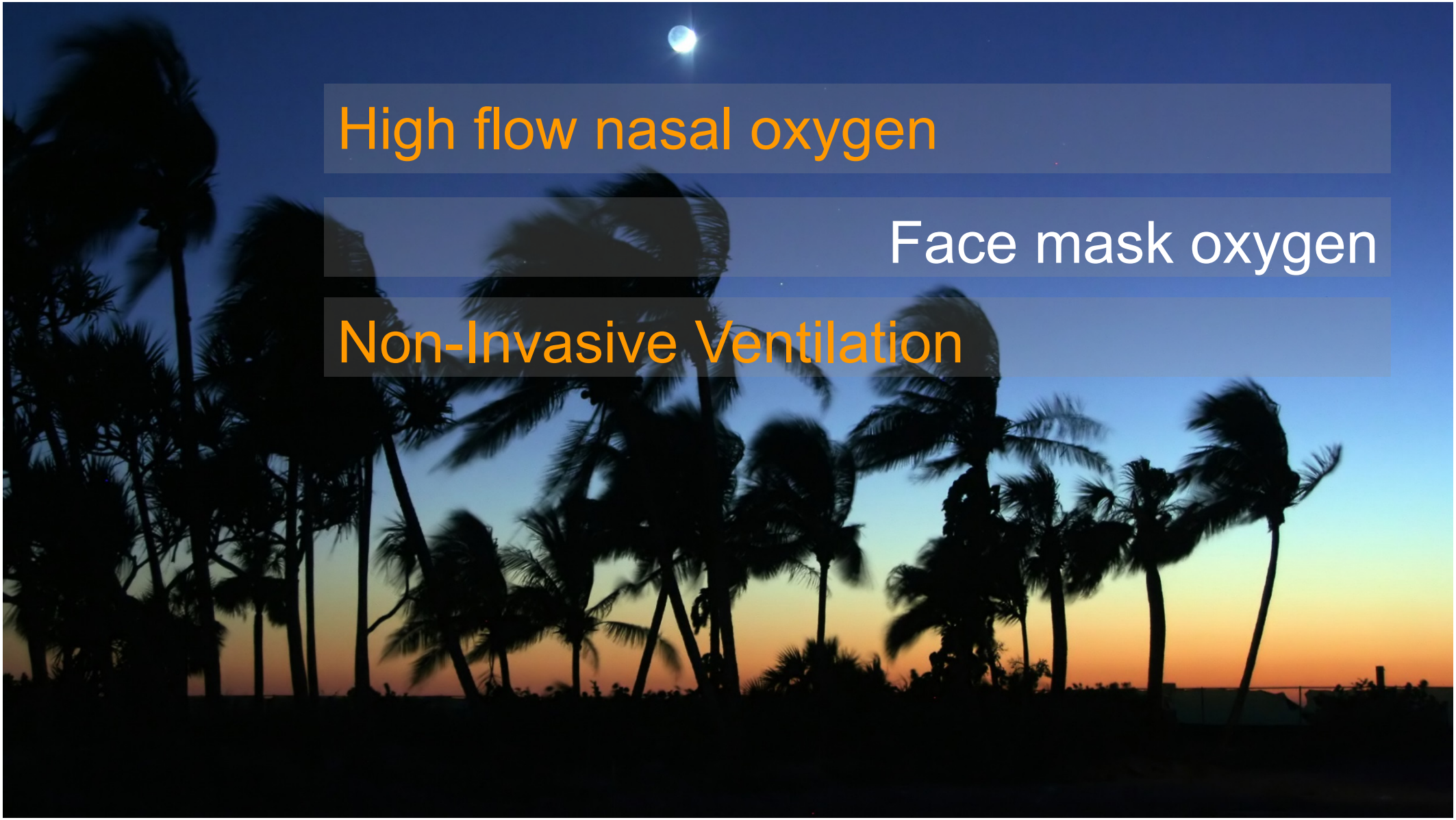


No. at risk					
Buffered crystalloid	1152	341	134	62	36
Saline	1110	310	124	64	28


Methodologically excellent
Limitations few
Overall strong


FLORAL
I


High flow nasal oxygen
in acute hypoxaemic respiratory failure


High flow nasal oxygen
Face mask oxygen
Non-Invasive Ventilation

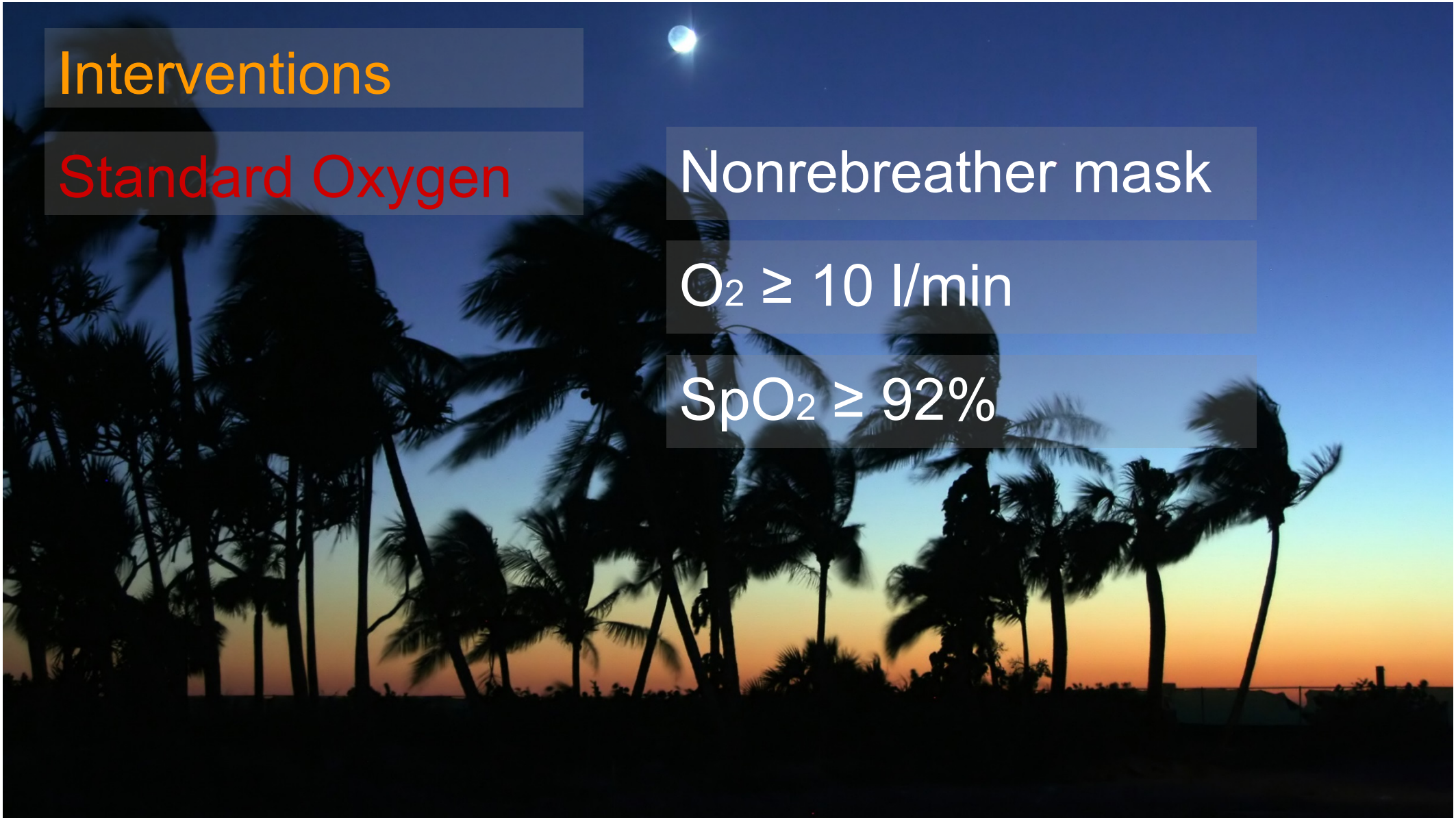

Inclusion
ICU Patient
Acute hypoxaemic respiratory failure


Exclusion
Hypercapnoea

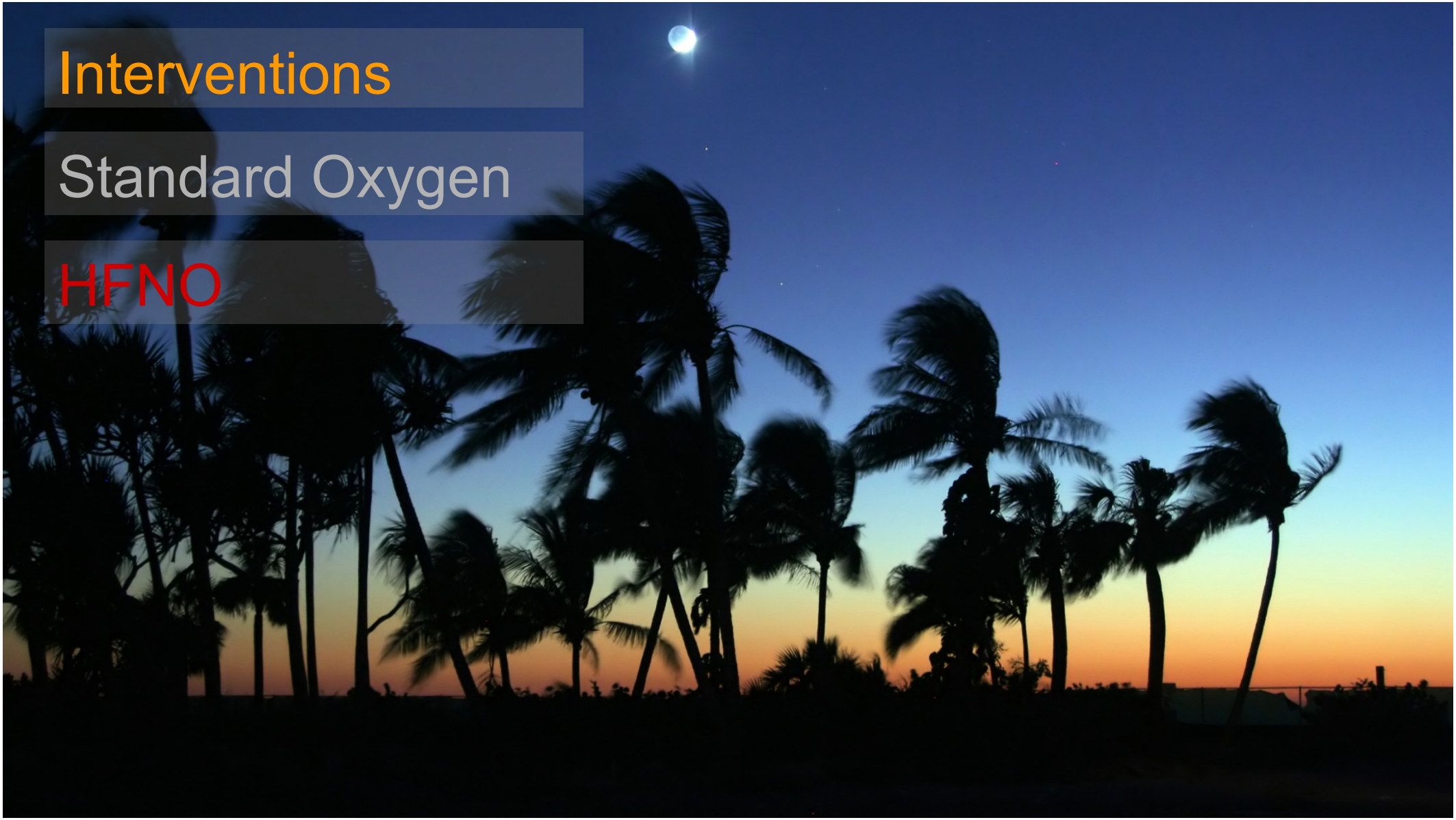

Design
Multicentre
Randomised
Controlled trial

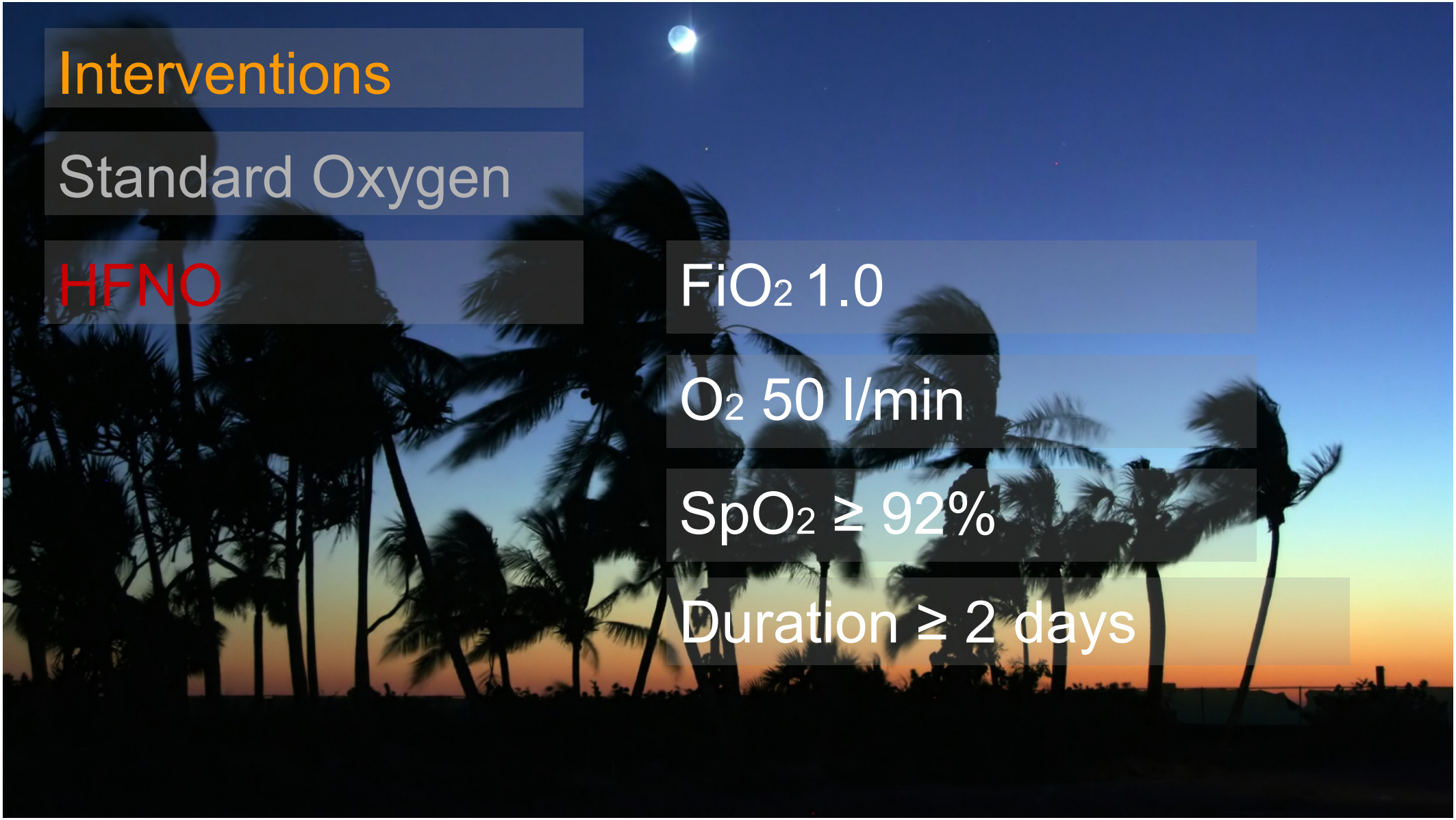
Interventions

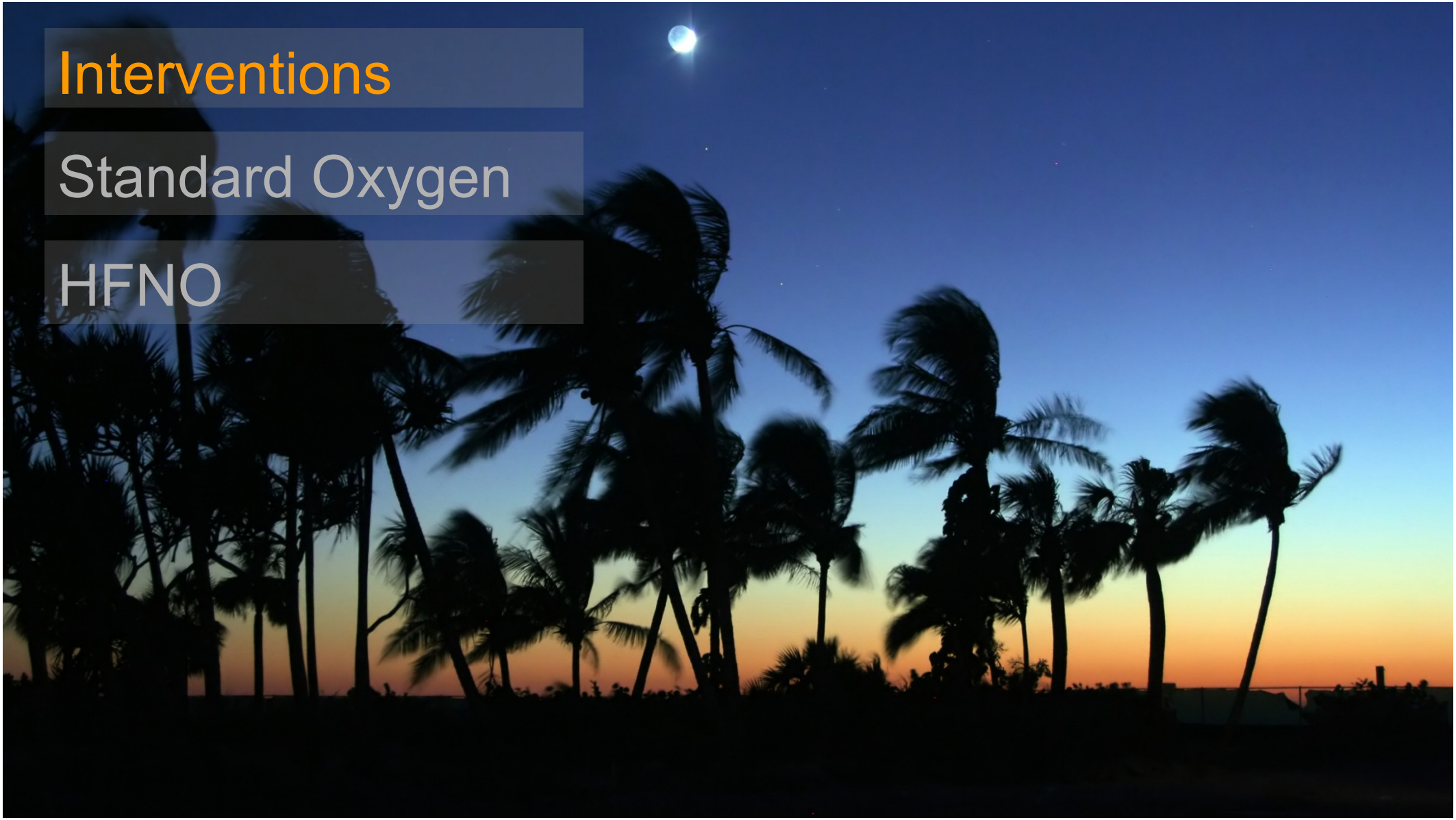

Interventions
Standard Oxygen


Interventions
Standard Oxygen
Nonrebreather mask
$O_2 \geq 10$ l/min
$SpO_2 \geq 92\%$

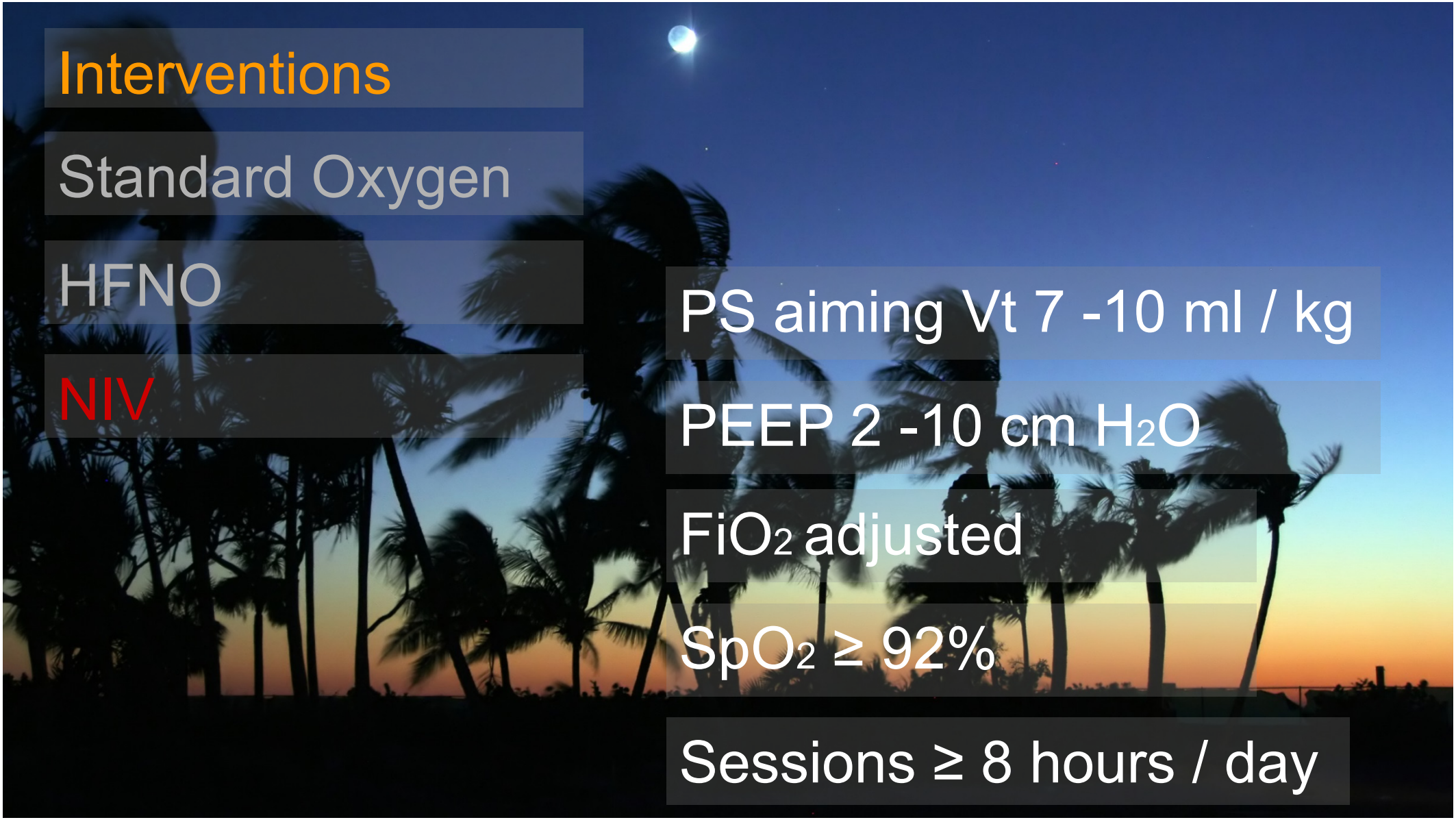

Interventions
Standard Oxygen


Interventions
Standard Oxygen
HFNO


Interventions
Standard Oxygen
HFNO
FiO2 1.0
O2 50 l/min
SpO2 ≥ 92%
Duration ≥ 2 days

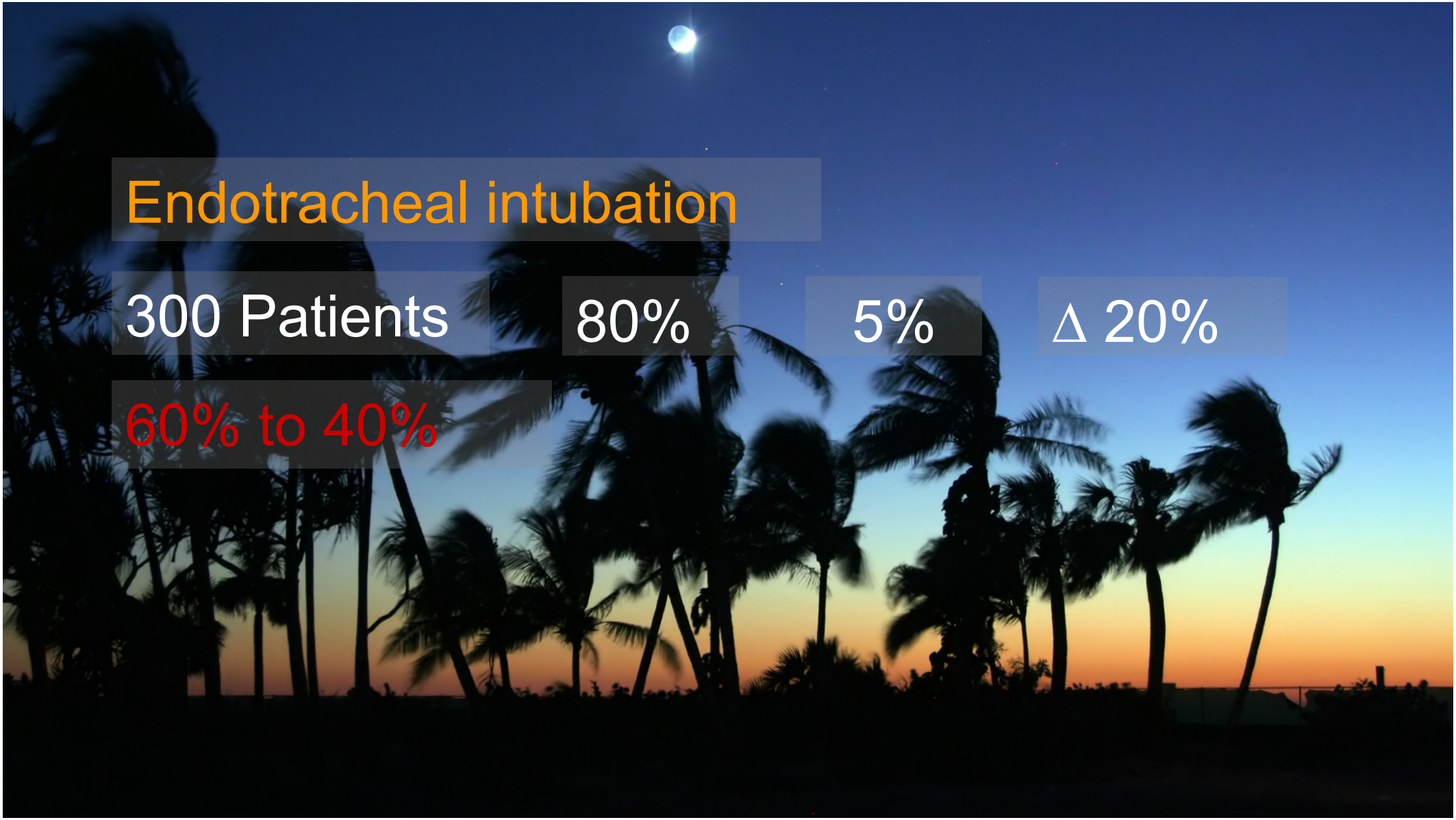

Interventions
Standard Oxygen
HFNO

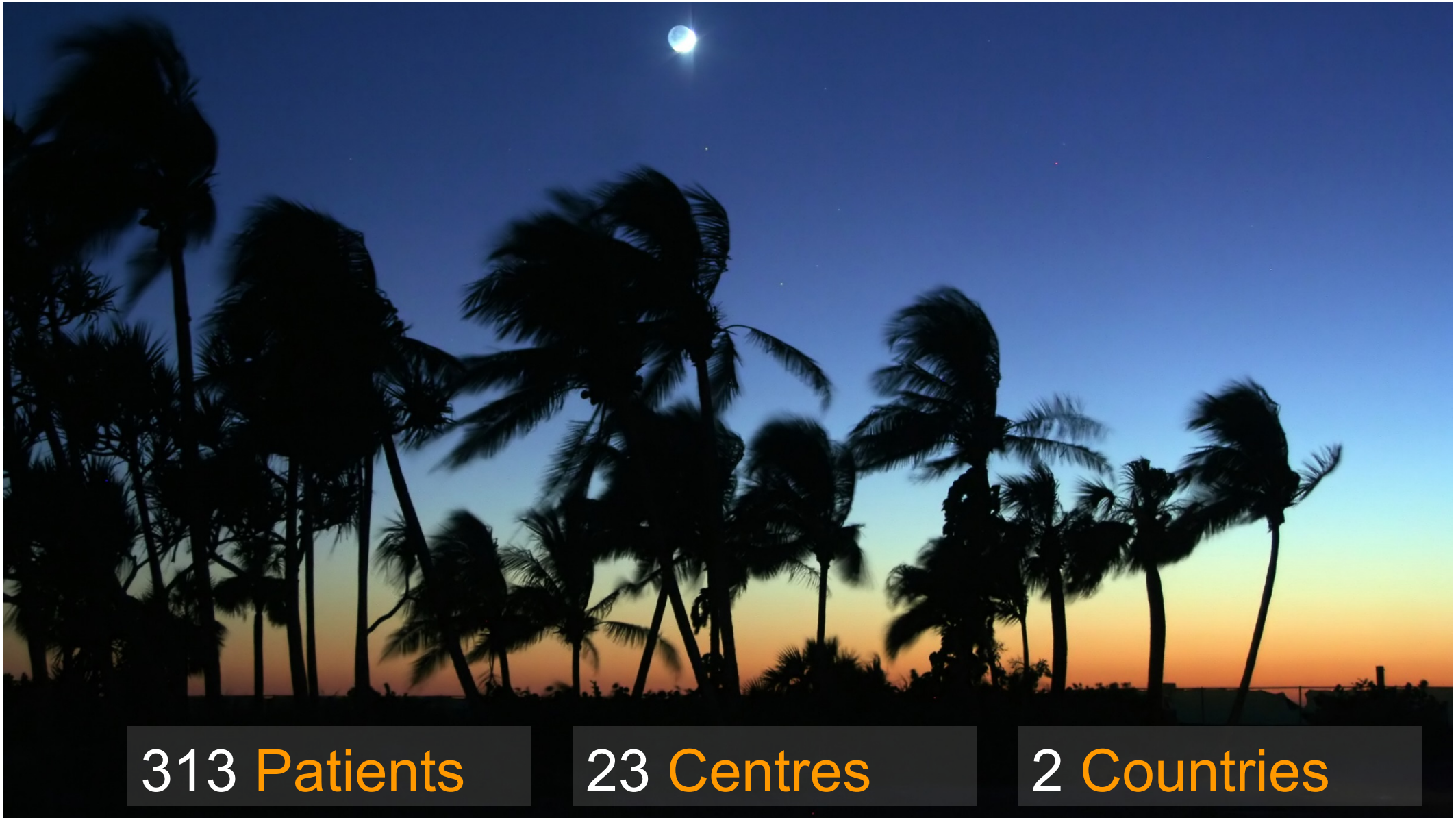

Interventions
Standard Oxygen
HFNO
NIV


Interventions
Standard Oxygen
HFNO
NIV
PS aiming Vt 7 -10 ml / kg
PEEP 2 -10 cm H_2O
FiO_2 adjusted
SpO_2 ≥ 92%
Sessions ≥ 8 hours / day

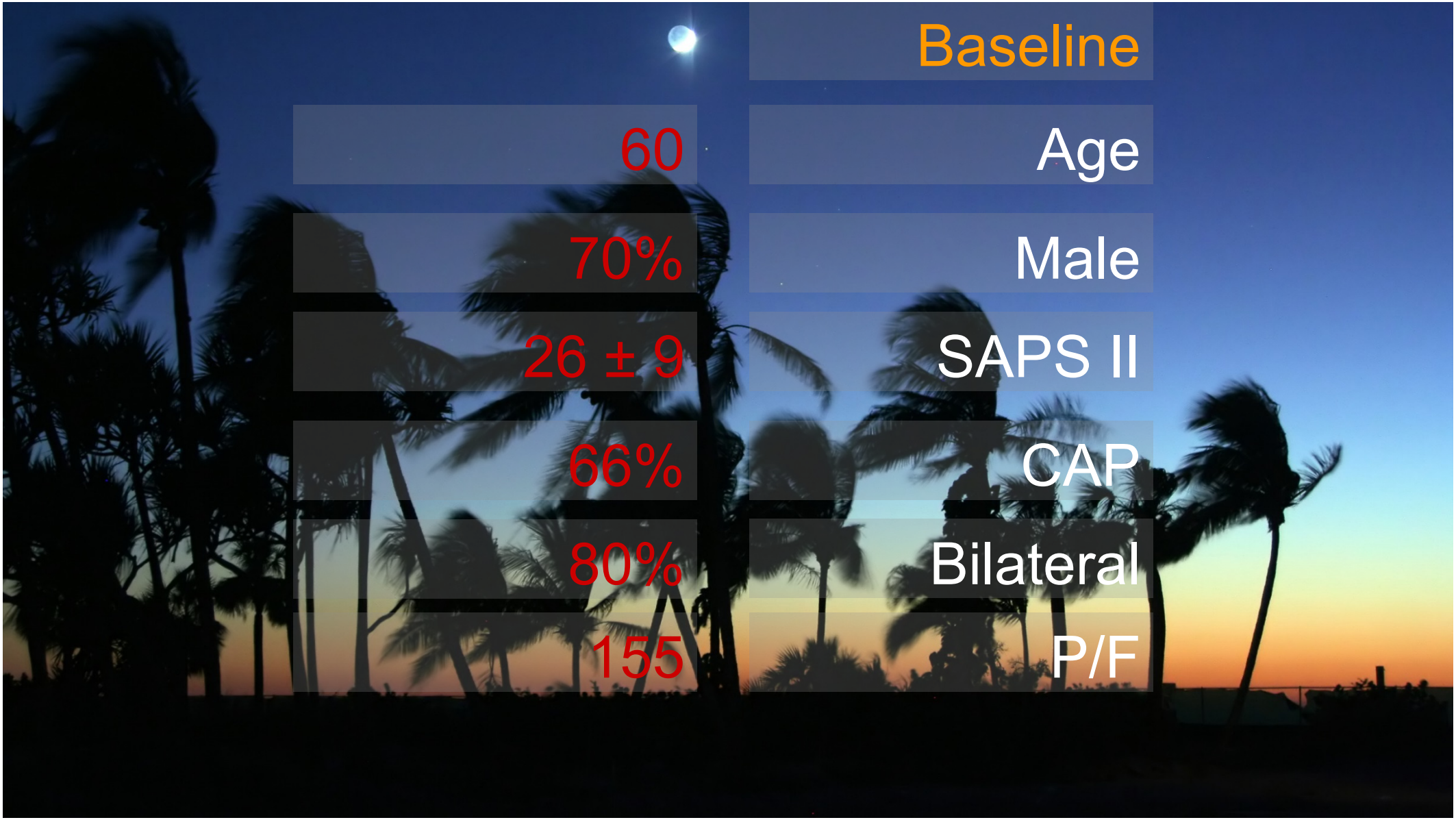

Endpoints
Haemodynamic instability
Neurological deterioration
Ongoing respiratory failure


Endotracheal intubation

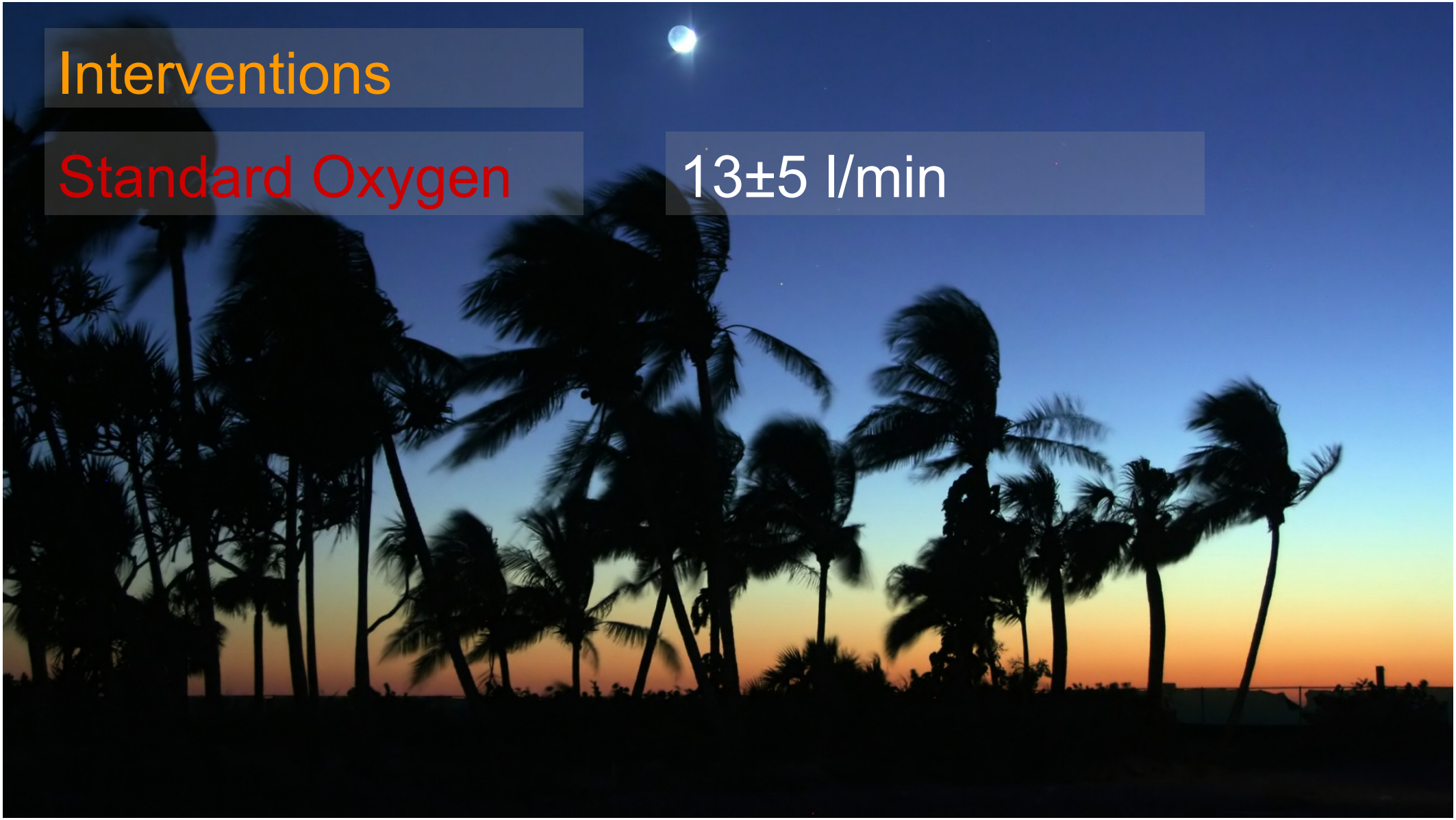

Endotracheal intubation
300 Patients
80%
5%
Δ 20%
60% to 40%

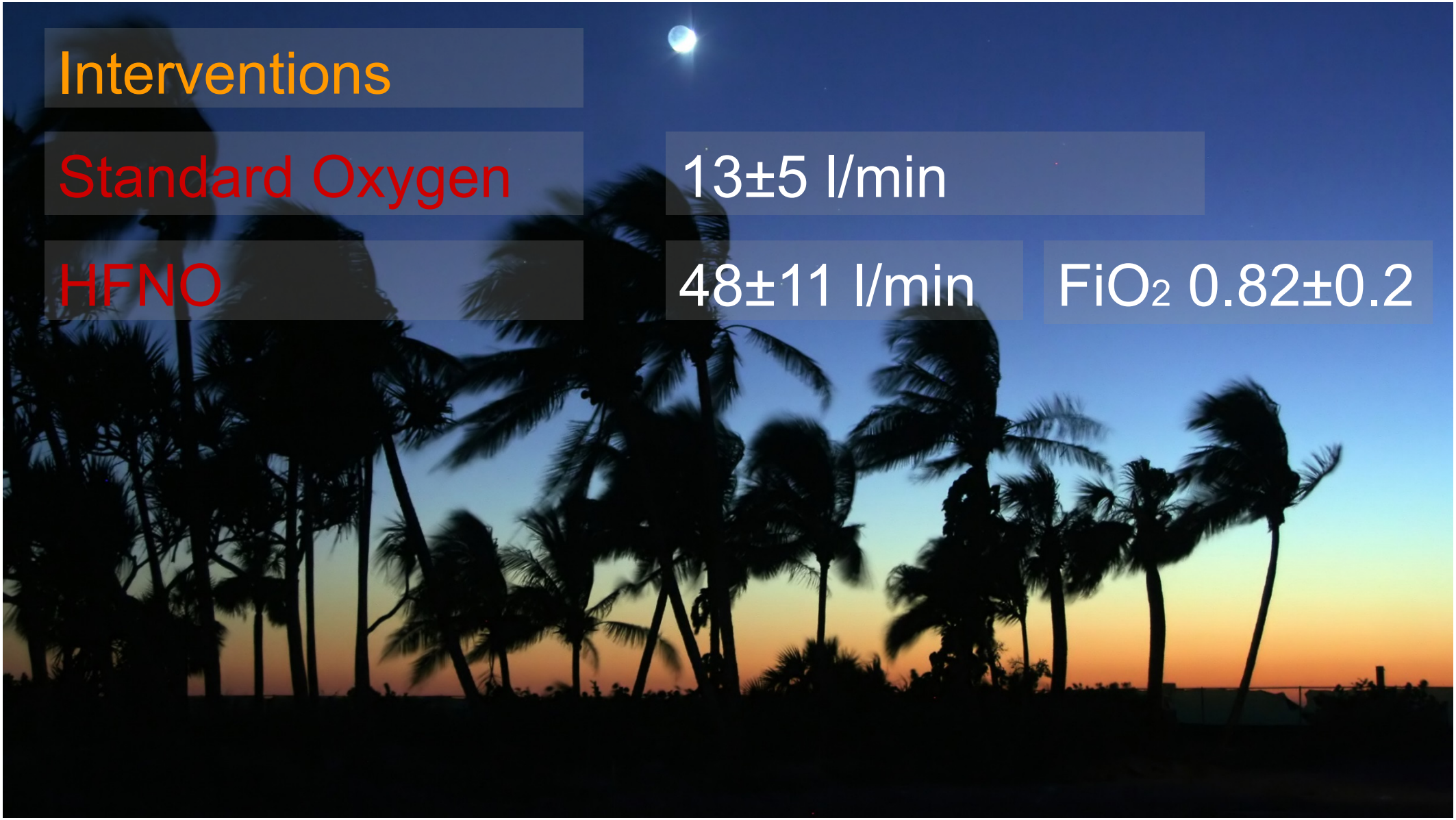

313 Patients
23 Centres
2 Countries

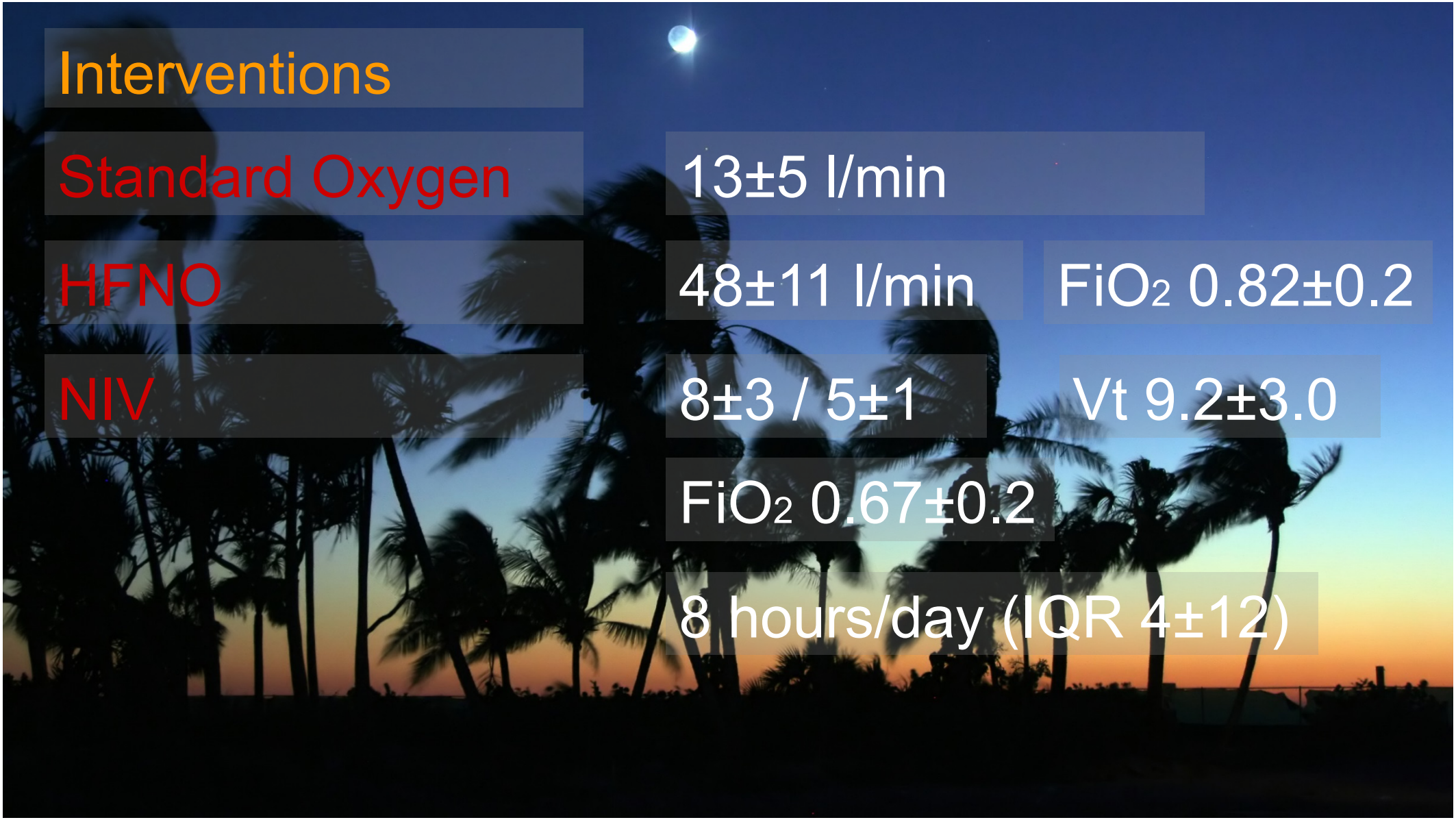

Standard O_2
94
HFNO
106
NIV
110

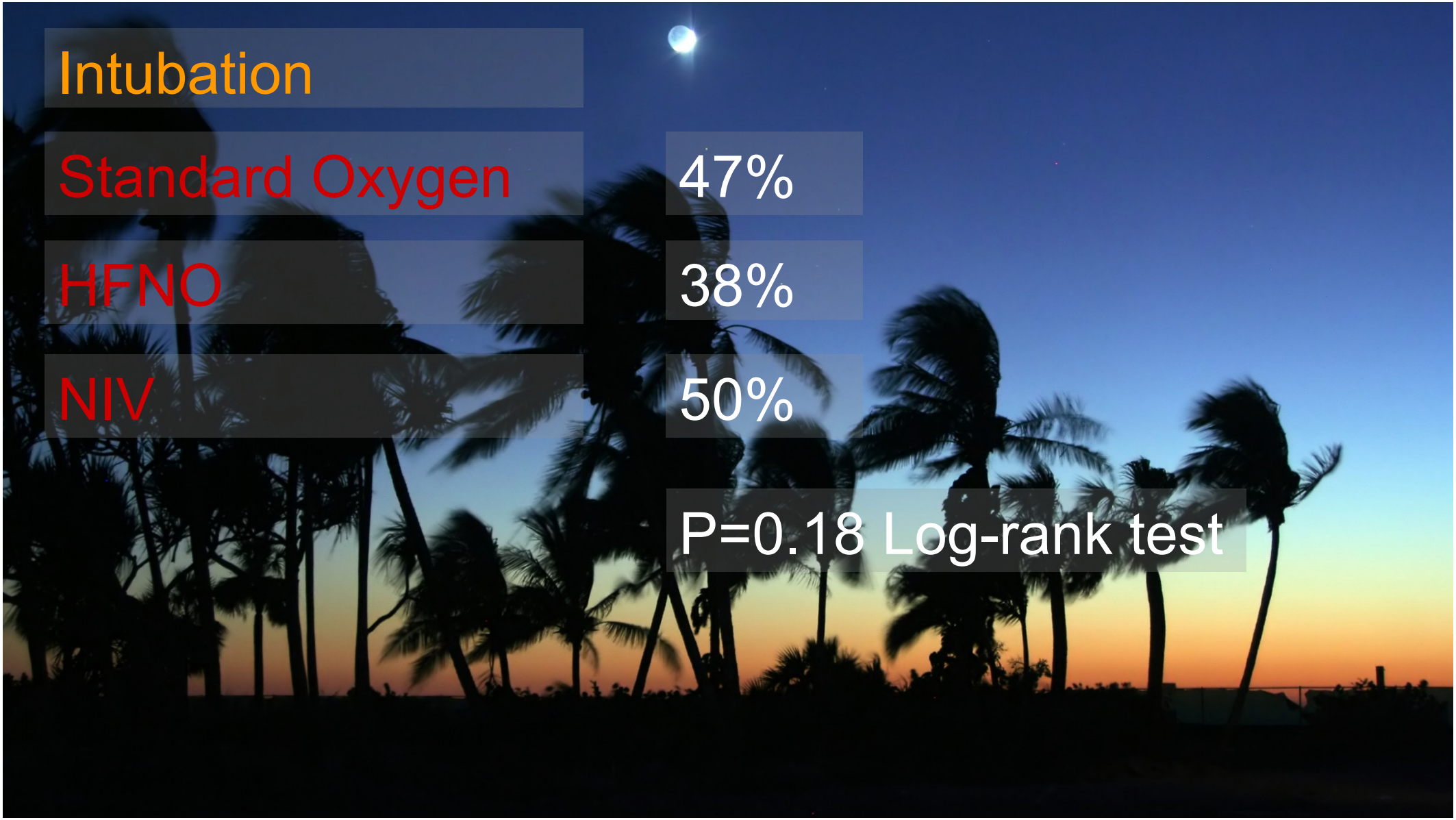

Baseline
60
Age
70%
Male
26 ± 9
SAPS II
66%
CAP
80%
Bilateral
155
P/F

Interventions

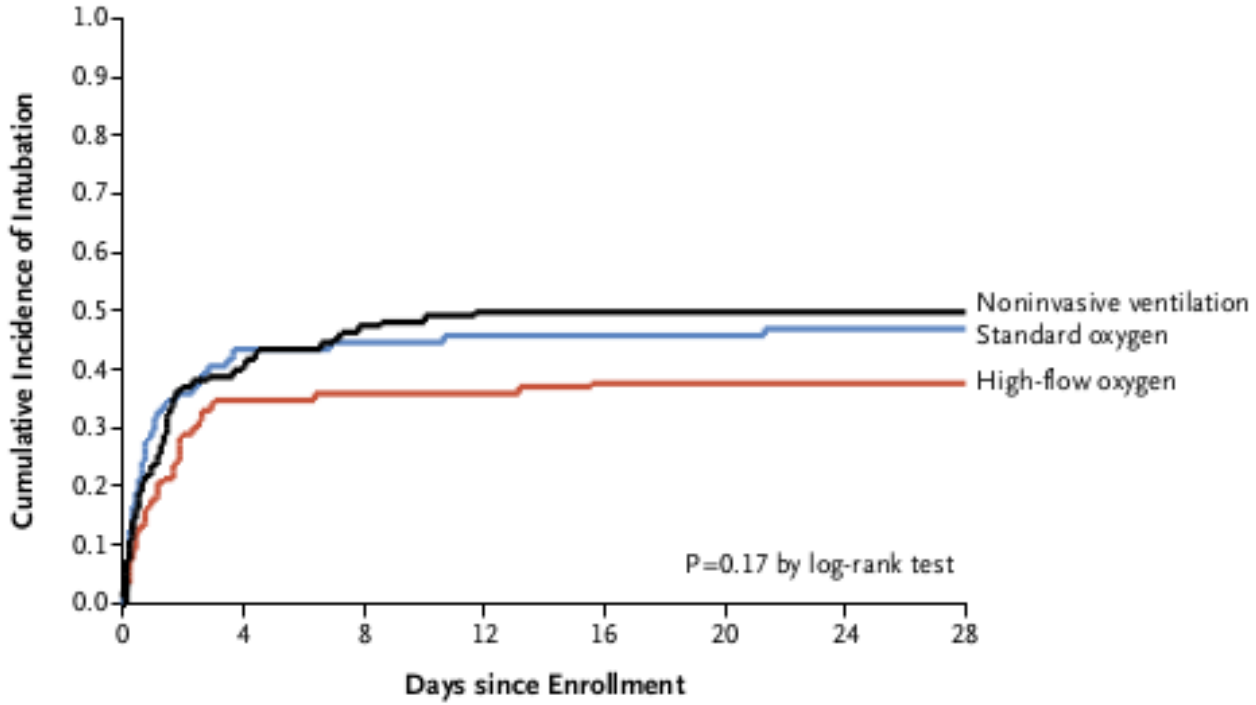

Interventions
Standard Oxygen
13±5 l/min


Interventions
Standard Oxygen
13±5 l/min
HFNO
48±11 l/min
FiO2 0.82±0.2


Interventions
Standard Oxygen
13±5 l/min
HFNO
48±11 l/min
FiO2 0.82±0.2
NIV
8±3 / 5±1
Vt 9.2±3.0
FiO2 0.67±0.2
8 hours/day (IQR 4±12)

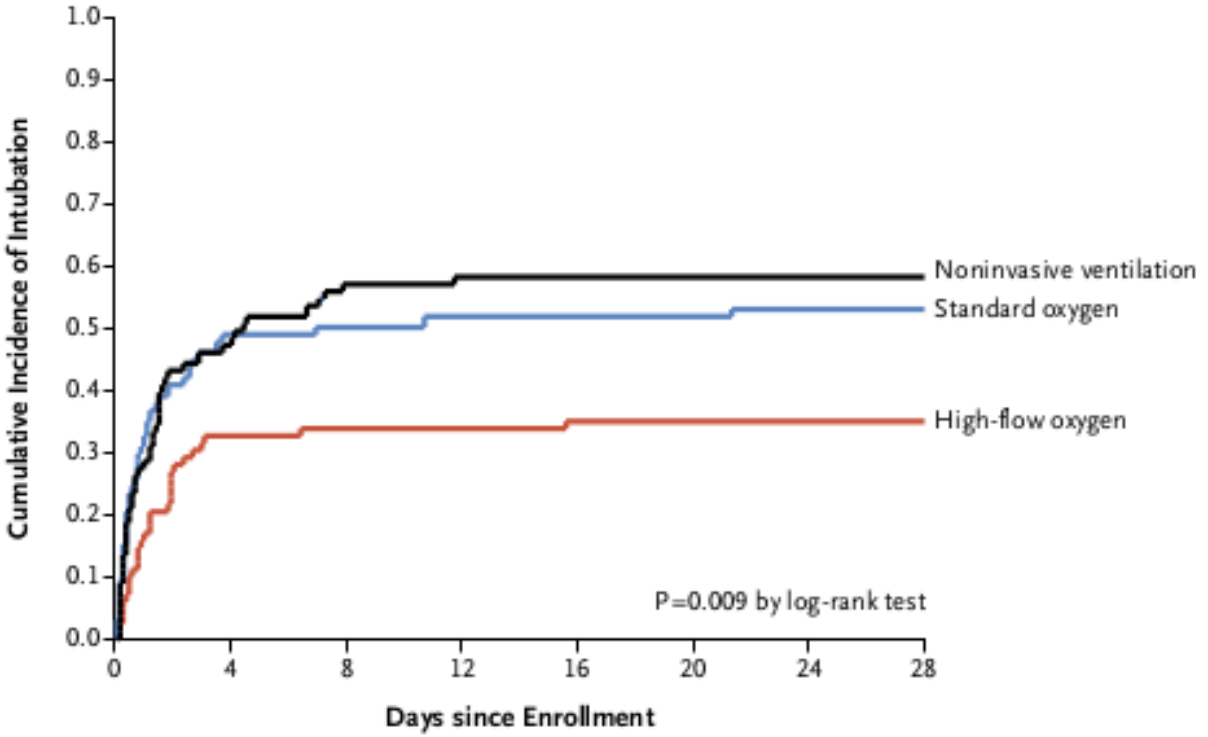

Intubation
Standard Oxygen
47%
HFNO
38%
NIV
50%
P=0.18 Log-rank test

A Overall Population

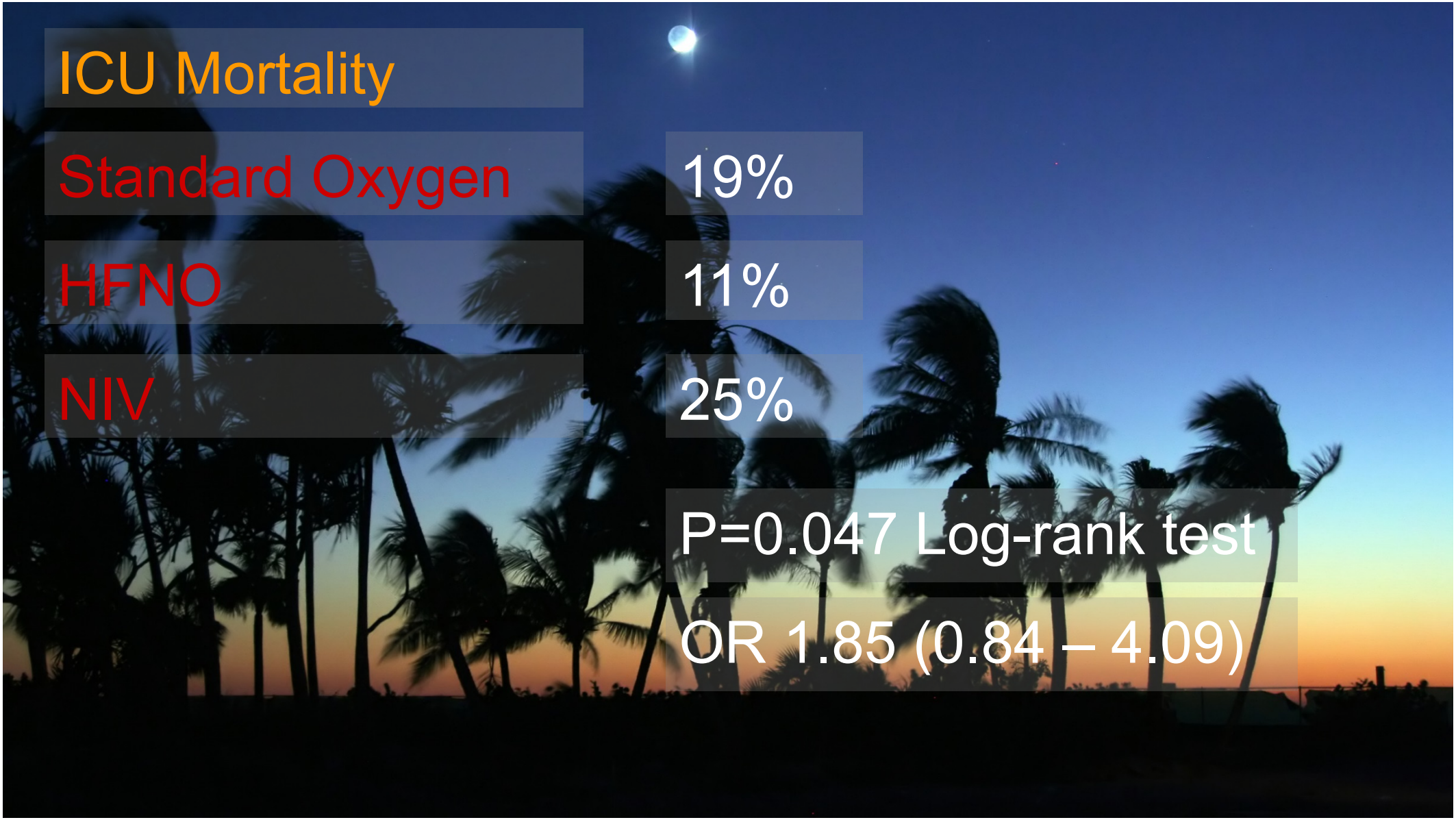


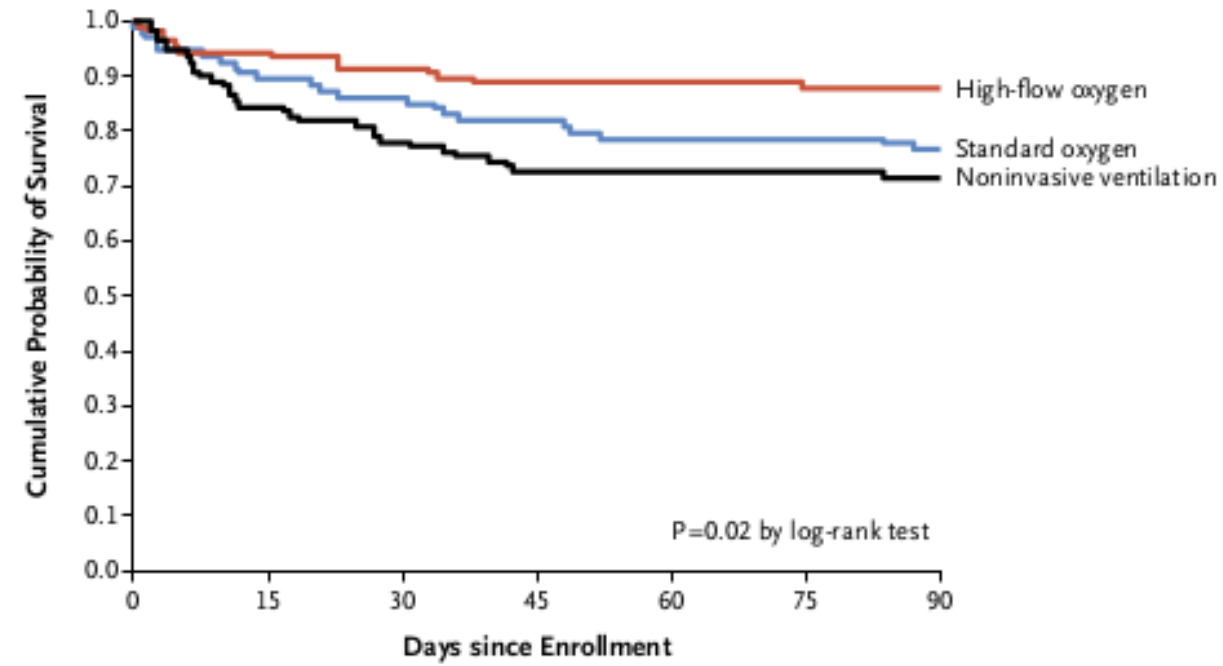
No. at Risk								
High-flow oxygen	106	68	67	67	65	65	65	65
Standard oxygen	94	52	50	49	49	49	48	48
Noninvasive ventilation	110	64	57	53	53	53	53	52

B Patients with a Pao_2:FIO_2 ≤200 mm Hg



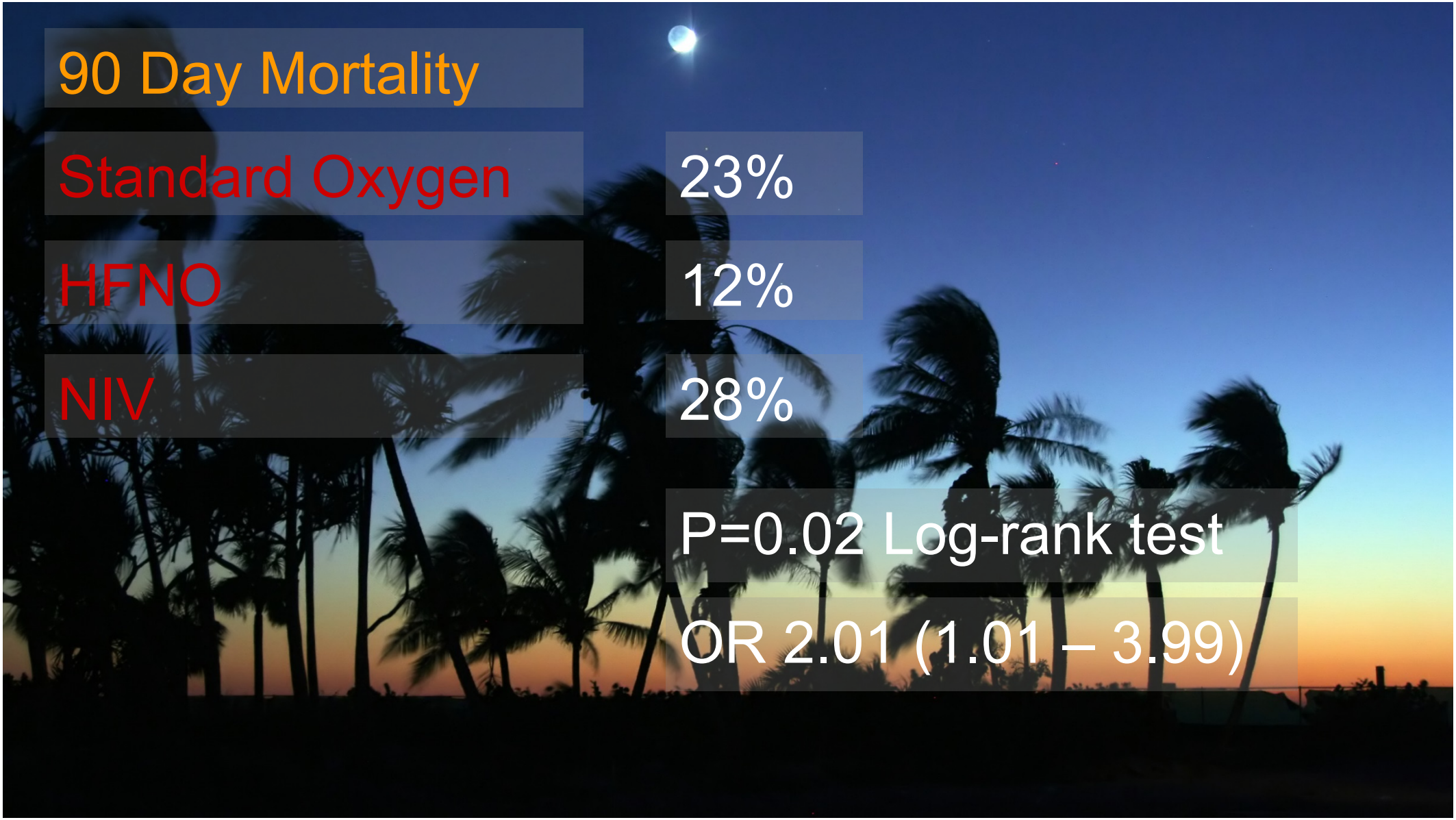
No. at Risk								
High-flow oxygen	83	55	54	54	53	53	53	53
Standard oxygen	74	37	35	34	34	34	33	33
Noninvasive ventilation	81	41	34	32	32	32	32	32


ICU Mortality
Standard Oxygen
19%
HFNO
11%
NIV
25%
P=0.047 Log-rank test
OR 1.85 (0.84 – 4.09)



No. at Risk							
High-flow oxygen	106	100	97	94	94	93	93
Standard oxygen	94	84	81	77	74	73	72
Noninvasive ventilation	110	93	86	80	79	78	77

Figure 3. Kaplan–Meier Plot of the Probability of Survival from Randomization to Day 90.


90 Day Mortality
Standard Oxygen
23%
HFNO
12%
NIV
28%
P=0.02 Log-rank test
OR 2.01 (1.01 – 3.99)


HFNO
More comfortable
Better in P/F < 200


Methodologically Good
Limitations Some
Overall Impressive


Critical Care Reviews
Meeting 2016
Titanic Centre, Belfast


Critical Care Reviews Meeting 2017
Titanic Centre, Belfast
Friday January 27th
H & W
John Myburgh
Paul Marik
Mervyn Singer
Anthony Gordon
Danny McAuley