



## Clinical trial results: Comparing Restrictive vs. Liberal Oxygen Strategies for Trauma Patients: The TRAUMOX2 Trial

### Summary

EudraCT number	2021-000556-19
Trial protocol	DK
Global end of trial date	12 October 2024

### Results information

Result version number	v1 (current)
This version publication date	23 October 2025
First version publication date	23 October 2025

### Trial information

#### Trial identification

Sponsor protocol code	6011
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05146700
WHO universal trial number (UTN)	-

Notes:

### Sponsors

Sponsor organisation name	Rigshospitalet, Denmark
Sponsor organisation address	Inge Lehmanns Vej 6, Copenhagen, Denmark, 2100
Public contact	Jacob Steinmetz, Rigshospitalet, Denmark, Department of Anaesthesiology, Centre of Head and Orthopaedics, +45 35458434, jacob.steinmetz@regionh.dk
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Notes:

### Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 July 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 February 2024
Global end of trial reached?	Yes
Global end of trial date	12 October 2024
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The objective of this trial, TRAUMOX2, will be to compare the effect of a restrictive versus liberal oxygen strategy the first eight hours after trauma on the incidence of 30-day mortality and/or major respiratory complications (pneumonia and acute respiratory distress syndrome) within 30 days (combined endpoint).

Protection of trial subjects:

No additional protection besides standard care according to local practice.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 December 2021
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Scientific research
Long term follow-up duration	1 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 185
Country: Number of subjects enrolled	Denmark: 1226
Country: Number of subjects enrolled	Switzerland: 97
Worldwide total number of subjects	1508
EEA total number of subjects	1411

Notes:

### Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	1122

From 65 to 84 years	334
85 years and over	52

## Subject disposition

### Recruitment

Recruitment details:

Active recruitment from December 7, 2021, to September 12, 2023. 30-day follow-up ended October 12, 2023. 1-year follow-up ended October 12, 2024.

Recruitment across 5 major traumacenters and 15 prehospital bases in Denmark, The Netherlands, and Switzerland.

### Pre-assignment

Screening details:

Inclusion Criteria: Patients aged  $\geq 18$ ; Blunt or penetrating trauma; Direct transfer to one of the participating trauma centers; Trauma team activation; Expected hospital length of stay for 24 hours or longer

Exclusion Criteria: Patients with cardiac arrest prior to randomisation; Carbon monoxide intoxication; No/minor injuries after secondary surv

### Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Open-label. Primary outcome was assessor blinded.

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Restrictive oxygen

Arm description:

- Lowest oxygen delivery possible ( $\geq 21\%$ ) ensuring an SpO<sub>2</sub> target = 94% either using no supplemental oxygen, a nasal cannula, a non-rebreather mask or manual/mechanical ventilation (intubated trial participants)

and

- Only trial participants receiving an FiO<sub>2</sub> = 0.21 can saturate >94%

Pre-oxygenation as usual prior to intubation is permitted

Arm type	Experimental
Investigational medicinal product name	Oxygen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use, Nasal use

Dosage and administration details:

- Lowest oxygen delivery possible ( $\geq 21\%$ ) ensuring an SpO<sub>2</sub> target = 94% either using no supplemental oxygen, a nasal cannula, a non-rebreather mask or manual/mechanical ventilation (intubated trial participants)

and

- Only trial participants receiving an FiO<sub>2</sub> = 0.21 can saturate >94%

Pre-oxygenation as usual prior to intubation is permitted

<b>Arm title</b>	Liberal oxygen
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Arm description:

- 15 L O<sub>2</sub>/min flow for non-intubated trial participants in the pre-hospital phase, the trauma bay and during intrahospital transportation. In the operating room, intensive care unit, post-anesthesia care unit

and ward the flow can be reduced to  $\geq 12$  L O<sub>2</sub>/min if the arterial oxygen saturation is  $\geq 98\%$

or

- FiO<sub>2</sub> = 1.0 for intubated trial participants in the pre-hospital phase, the trauma bay and during intrahospital transportation. In the operating room, intensive care unit, post-anesthesia care unit and ward the FiO<sub>2</sub> can be reduced to  $\geq 0.6$  if the arterial oxygen saturation is  $\geq 98\%$

Arm type	Active comparator
Investigational medicinal product name	Oxygen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use, Nasal use

Dosage and administration details:

- 15 L O<sub>2</sub>/min flow for non-intubated trial participants in the pre-hospital phase, the trauma bay and during intrahospital transportation. In the operating room, intensive care unit, post-anesthesia care unit and ward the flow can be reduced to  $\geq 12$  L O<sub>2</sub>/min if the arterial oxygen saturation is  $\geq 98\%$

or

- FiO<sub>2</sub> = 1.0 for intubated trial participants in the pre-hospital phase, the trauma bay and during intrahospital transportation. In the operating room, intensive care unit, post-anesthesia care unit and ward the FiO<sub>2</sub> can be reduced to  $\geq 0.6$  if the arterial oxygen saturation is  $\geq 98\%$

<b>Number of subjects in period 1</b>	Restrictive oxygen	Liberal oxygen
Started	750	758
Completed	733	724
Not completed	17	34
Consent withdrawn by subject	15	-
Lost to follow-up	2	2
Consent withdrawn by subject	-	32

## Baseline characteristics

### Reporting groups

Reporting group title	Restrictive oxygen
Reporting group description:	
- Lowest oxygen delivery possible ( $\geq 21\%$ ) ensuring an SpO <sub>2</sub> target = 94% either using no supplemental oxygen, a nasal cannula, a non-rebreather mask or manual/mechanical ventilation (intubated trial participants)	

and

- Only trial participants receiving an FiO<sub>2</sub> = 0.21 can saturate  $>94\%$

Pre-oxygenation as usual prior to intubation is permitted

Reporting group title	Liberal oxygen
Reporting group description:	
- 15 L O <sub>2</sub> /min flow for non-intubated trial participants in the pre-hospital phase, the trauma bay and during intrahospital transportation. In the operating room, intensive care unit, post-anesthesia care unit and ward the flow can be reduced to $\geq 12$ L O <sub>2</sub> /min if the arterial oxygen saturation is $\geq 98\%$	

or

- FiO<sub>2</sub> = 1.0 for intubated trial participants in the pre-hospital phase, the trauma bay and during intrahospital transportation. In the operating room, intensive care unit, post-anesthesia care unit and ward the FiO<sub>2</sub> can be reduced to  $\geq 0.6$  if the arterial oxygen saturation is  $\geq 98\%$

Reporting group values	Restrictive oxygen	Liberal oxygen	Total
Number of subjects	750	758	1508
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Not recorded	1	1	2
Adults (18 years or older)	749	757	1506
Age continuous Units: years			
median	48	51	-
inter-quartile range (Q1-Q3)	29 to 64	33 to 66	-
Gender categorical Units: Subjects			
Female	208	201	409
Male	540	555	1095
Unknown	2	2	4

Predominant type of injury Units: Subjects			
Blunt	667	678	1345
Penetrating	82	79	161
N/A	1	1	2
Site of inclusion Units: Subjects			
In-hospital	442	451	893
Prehospital	308	307	615
Injury Severity Scale score Units: Points			
median	14	14	
inter-quartile range (Q1-Q3)	9 to 22	9 to 22	-

## End points

### End points reporting groups

Reporting group title	Restrictive oxygen
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Reporting group description:

- Lowest oxygen delivery possible ( $\geq 21\%$ ) ensuring an SpO<sub>2</sub> target = 94% either using no supplemental oxygen, a nasal cannula, a non-rebreather mask or manual/mechanical ventilation (intubated trial participants)

and

- Only trial participants receiving an FiO<sub>2</sub> = 0.21 can saturate >94%

Pre-oxygenation as usual prior to intubation is permitted

Reporting group title	Liberal oxygen
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Reporting group description:

- 15 L O<sub>2</sub>/min flow for non-intubated trial participants in the pre-hospital phase, the trauma bay and during intrahospital transportation. In the operating room, intensive care unit, post-anesthesia care unit and ward the flow can be reduced to  $\geq 12$  L O<sub>2</sub>/min if the arterial oxygen saturation is  $\geq 98\%$

or

- FiO<sub>2</sub> = 1.0 for intubated trial participants in the pre-hospital phase, the trauma bay and during intrahospital transportation. In the operating room, intensive care unit, post-anesthesia care unit and ward the FiO<sub>2</sub> can be reduced to  $\geq 0.6$  if the arterial oxygen saturation is  $\geq 98\%$

### Primary: Death and/or major respiratory complications

End point title	Death and/or major respiratory complications
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End point description:

End point type	Primary
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End point timeframe:

30-day outcome.

End point values	Restrictive oxygen	Liberal oxygen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	733	724		
Units: Subjects	118	121		

### Statistical analyses

Statistical analysis title	Death and/or major respiratory complications
Comparison groups	Restrictive oxygen v Liberal oxygen



Number of subjects included in analysis	1457
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	1.37

## Secondary: Death

End point title	Death
End point description:	
End point type	Secondary
End point timeframe:	
30-day	

End point values	Restrictive oxygen	Liberal oxygen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	733	724		
Units: Subjects	63	53		

## Statistical analyses

<b>Statistical analysis title</b>	Death
Comparison groups	Restrictive oxygen v Liberal oxygen
Number of subjects included in analysis	1457
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.92

## Secondary: Major respiratory complications

End point title	Major respiratory complications
End point description:	
End point type	Secondary
End point timeframe:	
30-day outcome	

End point values	Restrictive oxygen	Liberal oxygen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	733	724		
Units: Subjects	65	78		

### Statistical analyses

<b>Statistical analysis title</b>	Major respiratory complications
Comparison groups	Restrictive oxygen v Liberal oxygen
Number of subjects included in analysis	1457
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	1.19

### Secondary: Hypoxemic episode(s)

End point title	Hypoxemic episode(s)
End point description:	
End point type	Secondary
End point timeframe:	
During 8-hour intervention.	

End point values	Restrictive oxygen	Liberal oxygen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	737	737		
Units: Episodes	44	28		

## Statistical analyses

Statistical analysis title	Hypoxemic episodes
Comparison groups	Restrictive oxygen v Liberal oxygen
Number of subjects included in analysis	1474
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.02
upper limit	2.7

## Secondary: ICU readmission

End point title	ICU readmission
End point description:	
End point type	Secondary
End point timeframe:	
During the initial hospital admission (not at hospital readmission).	

End point values	Restrictive oxygen	Liberal oxygen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	368	352		
Units: Admissions	17	18		

## Statistical analyses

Statistical analysis title	ICU readmission
Comparison groups	Restrictive oxygen v Liberal oxygen

Number of subjects included in analysis	720
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.26
upper limit	1.37

## Secondary: Sepsis

End point title	Sepsis
End point description:	
End point type	Secondary
End point timeframe:	
During the initial hospital admission (not at hospital readmission).	

End point values	Restrictive oxygen	Liberal oxygen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	736	727		
Units: Incidence	19	31		

## Statistical analyses

<b>Statistical analysis title</b>	Sepsis during hospital admission
Comparison groups	Restrictive oxygen v Liberal oxygen
Number of subjects included in analysis	1463
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	1.02

## Secondary: Surgical site infection

End point title	Surgical site infection
End point description:	
End point type	Secondary
End point timeframe:	
Within 30 days after enrollment.	

End point values	Restrictive oxygen	Liberal oxygen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	736	724		
Units: Incidence	23	32		

### Statistical analyses

<b>Statistical analysis title</b>	Surgical site infections
Comparison groups	Restrictive oxygen v Liberal oxygen
Number of subjects included in analysis	1460
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.25
upper limit	0.99

### Secondary: Pneumonia post discharge

End point title	Pneumonia post discharge
End point description:	
End point type	Secondary
End point timeframe:	
Within 30 days after enrollment.	

<b>End point values</b>	Restrictive oxygen	Liberal oxygen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	640	620		
Units: Events	27	24		

## Statistical analyses

<b>Statistical analysis title</b>	Pneumonia post-discharge
Comparison groups	Restrictive oxygen v Liberal oxygen
Number of subjects included in analysis	1260
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	1.85

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

To monitor events, a TRAUMOX2 investigator assessed the trial participant's medical record:

- Once within the first 24 hours after inclusion
- Every third day until discharge (maximum of 30 days)

Adverse event reporting additional description:

The local investigators at each centre is responsible for recording the different types of events. All events were assessed for correlation between an event and trial medicine using this event policy:

- 1: Unrelated
- 2: Possible related
- 3: Probably related
- 4: Related

Assessment type	Systematic
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### Dictionary used

Dictionary name	None
Dictionary version	0

### Reporting groups

Reporting group title	Restrictive oxygen
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Reporting group description:

- Lowest oxygen delivery possible ( $\geq 21\%$ ) ensuring an SpO<sub>2</sub> target = 94% either using no supplemental oxygen, a nasal cannula, a non-rebreather mask or manual/mechanical ventilation (intubated trial participants)

and

- Only trial participants receiving an FiO<sub>2</sub> = 0.21 can saturate >94%

Pre-oxygenation as usual prior to intubation is permitted

Reporting group title	Liberal oxygen
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Reporting group description:

- 15 L O<sub>2</sub>/min flow for non-intubated trial participants in the pre-hospital phase, the trauma bay and during intrahospital transportation. In the operating room, intensive care unit, post-anesthesia care unit and ward the flow can be reduced to  $\geq 12$  L O<sub>2</sub>/min if the arterial oxygen saturation is  $\geq 98\%$

or

- FiO<sub>2</sub> = 1.0 for intubated trial participants in the pre-hospital phase, the trauma bay and during intrahospital transportation. In the operating room, intensive care unit, post-anesthesia care unit and ward the FiO<sub>2</sub> can be reduced to  $\geq 0.6$  if the arterial oxygen saturation is  $\geq 98\%$

Serious adverse events	Restrictive oxygen	Liberal oxygen	
Total subjects affected by serious adverse events			
subjects affected / exposed	100 / 750 (13.33%)	104 / 758 (13.72%)	
number of deaths (all causes)	63	53	
number of deaths resulting from adverse events	0	0	
General disorders and administration site conditions			
Death			

subjects affected / exposed	63 / 750 (8.40%)	53 / 758 (6.99%)	
occurrences causally related to treatment / all	0 / 63	0 / 53	
deaths causally related to treatment / all	0 / 0	0 / 0	
Was life-threatening			
subjects affected / exposed	8 / 750 (1.07%)	13 / 758 (1.72%)	
occurrences causally related to treatment / all	0 / 8	0 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Involved or prolonged hospital length of stay			
subjects affected / exposed	29 / 750 (3.87%)	37 / 758 (4.88%)	
occurrences causally related to treatment / all	0 / 29	0 / 37	
deaths causally related to treatment / all	0 / 0	0 / 0	
Resulted in a congenital anomaly or birth defect			
subjects affected / exposed	0 / 750 (0.00%)	1 / 758 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

<b>Non-serious adverse events</b>	Restrictive oxygen	Liberal oxygen	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	223 / 750 (29.73%)	283 / 758 (37.34%)	
Respiratory, thoracic and mediastinal disorders			
Atelectasis	Additional description: Only atelectases assessed by a radiologist were recorded		
subjects affected / exposed	207 / 750 (27.60%)	263 / 758 (34.70%)	
occurrences (all)	207	263	
Irritability of airway mucosa	Additional description: Recorded only if registered by the health care staff in the medical record		
subjects affected / exposed	16 / 750 (2.13%)	20 / 758 (2.64%)	
occurrences (all)	16	20	



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

None
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Notes:

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/39657224>