

Journal Club #2: December 9, 2025

TRAUMOX2 Trial: SUMMARY

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PRESENTERS

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STUDY CITATION

Arleth T, Baekgaard J, Siersma V, et al. Early Restrictive vs Liberal Oxygen for Trauma Patients: The TRAUMOX2 Randomized Clinical Trial. JAMA. 2025;333(6):479-489.

STUDY SNAPSHOT

Main Clinical Question: In adult trauma patients requiring full trauma team activation, does an early restrictive oxygen strategy (targeting SpO₂ 94%) compared to a liberal oxygen strategy (12-15 L/min or FiO₂ 0.6-1.0) for 8 hours reduce the incidence of death and/or major respiratory complications within 30 days?

Design: Pragmatic, international, multicenter, open-label RCT with blinded outcome assessment

Setting: 15 prehospital bases and 5 trauma centers (Denmark, Netherlands, Switzerland)

Patients: 1,508 adult trauma patients (blunt or penetrating) requiring full trauma team activation

Intervention: 8 hours of restrictive oxygen (SpO₂ target 94%) vs liberal oxygen (12-15 L/min or FiO₂ 0.6-1.0)

Follow-up: 30 days

Primary Outcome: Composite of death and/or major resp complications (pneumonia/ARDS)

KEY RESULTS

Primary Outcome: Death and/or Major Respiratory Complications

- **Restrictive group:** 118/733 (16.1%)
- **Liberal group:** 121/724 (16.7%)
- **Odds Ratio:** 1.01 (95% CI 0.75-1.37), p=0.94
- **Absolute difference:** 0.56% (95% CI -2.70 to 3.82)
- **Result: NO SIGNIFICANT DIFFERENCE**

Secondary Outcomes (30 days)

Outcome	Restrictive	Liberal	OR (95% CI)
Death	48/733 (6.5%)	40/724 (5.5%)	1.17 (0.76-1.82)
Major respiratory complications	77/733 (10.5%)	90/724 (12.4%)	0.87 (0.63-1.20)
Hypoxemic episodes (SpO ₂ <90%)	107/696 (15.4%)	62/695 (8.9%)	1.90 (1.36-2.65)*
Atelectasis	198/718 (27.6%)	245/707 (34.7%)	0.72 (0.57-0.91)*

*Statistically significant

Oxygenation Achieved

Measure	Restrictive	Liberal
PaO ₂ at 1 hour	85 mmHg (IQR 71-109)	280 mmHg (IQR 145-390)
PaO ₂ at 6 hours	86 mmHg (IQR 74-101)	230 mmHg (IQR 128-304)
Median O ₂ delivered (non-intubated)	0 L/min	12 L/min
Median FiO ₂ (intubated)	0.28	0.60

Note: Clear separation between groups achieved; interventions were successfully implemented

PATIENT CHARACTERISTICS

- **Median age:** 50 years
- **Male:** 73%
- **Median ISS:** 14 (moderate severity)
- **Intubated at randomization:** 24%
- **Prehospital enrollment:** 41%
- **Blunt trauma:** 89%
- **Head injury (AIS ≥3):** 29%
- **Pre-randomization oxygen exposure:** 47% received O₂ for median 30 minutes before enrollment

STUDY STRENGTHS

- ✓ Large sample size (1,508 patients) with adequate power
- ✓ Pragmatic design reflects real-world trauma care
- ✓ Prehospital enrollment (41%) captures early intervention period
- ✓ Blinded outcome assessment reduces detection bias
- ✓ Clear separation of oxygenation between groups
- ✓ Multiple countries and trauma systems enhance generalizability
- ✓ Pre-published protocol and statistical analysis plan

- ✓ Minimal loss to follow-up (96.6% primary outcome data)
- ✓ Subgroup analyses showed consistent results

STUDY LIMITATIONS

- ✗ Open-label design (providers knew allocation)
- ✗ High post-randomization exclusion rate (24%)
- ✗ Composite outcome with opposing trends (death ↑, respiratory complications ↓ in restrictive group)
- ✗ Short 8-hour intervention period
- ✗ Moderately injured population (median ISS 14; few in severe shock)
- ✗ 47% received supplemental oxygen before randomization
- ✗ Protocol violations more common in liberal group (13.7% vs 6.7%)
- ✗ No race/ethnicity data (relevant for pulse oximetry accuracy)
- ✗ High-resource European trauma systems may not generalize to all settings
- ✗ No long-term outcomes beyond 30 days

APPLICABILITY TO MANITOBA PRACTICE

Generalizable Elements:

- Oxygen physiology and trauma pathophysiology universal across populations
- Similar trauma systems and ATLS guidelines used in Manitoba (minus physician in pre-hospital environment)
- Mixture of urban and prehospital care reflects Manitoba context
- Pragmatic design mirrors real-world clinical practice

Manitoba-Specific Considerations:

Urban Winnipeg Trauma Center:

- **Recommendation:** Implement restrictive oxygen strategy (target SpO₂ 94%)
- Similar patient populations and resources to study sites
- Easy to monitor with continuous pulse oximetry

Rural/Remote Manitoba:

- Longer transport times (multi-hour vs study median ~60 min)
- Cold exposure affects oxygen-hemoglobin dissociation curve
- Limited monitoring capabilities in some settings
- May require individualized approach for hypothermic patients
- Study did not include Indigenous populations
- Pulse oximetry accuracy concerns in darker skin tones

Air Ambulance:

- Prolonged transport times
- Altitude physiology considerations
- May warrant slightly more conservative (liberal) initial approach

BOTTOM LINE FOR PRACTICE

Current Concerns:

ATLS guidelines recommend supplemental oxygen for all severely injured trauma patients, but provide no specific targets. This often leads to routine high-flow oxygen administration and hyperoxemia ($\text{PaO}_2 > 200$ mmHg), which may cause harm without proven benefit.

What This Study Shows:

Targeting normoxia ($\text{SpO}_2 \sim 94\%$) is **SAFE** and **FEASIBLE** but does not significantly reduce death or respiratory complications compared to liberal oxygen. However, liberal oxygen does NOT improve outcomes and may increase atelectasis.

DEM journal club discussion concluded that this study will not change our current practice but may provide some reassurance regarding a more restrictive oxygen delivery strategy in rural/northern communities when oxygen supplies are scarce.

Special Considerations:

- **Severe TBI:**
 - May consider higher SpO_2 targets ($>95\%$) per Brain Trauma Foundation guidelines
- **Preoxygenation:**
 - Brief $\text{FiO}_2 1.0$ for airway procedures is appropriate
- **Carbon monoxide exposure:**
 - Requires high-flow oxygen regardless
- **Hypothermia:**
 - Left shift of oxy-hgb dissociation curve - may get falsely normal O_2 sats with tissue hypoxia. Higher O_2 while rewarming before switching to restrictive O_2 strategy

EBM Lesson

Intention-to-Treat (ITT) - Analyzes all participants in the groups they were originally randomized to, regardless of whether they completed the study, received the intervention, or deviated from protocol. This preserves randomization benefits and reflects real-world effectiveness, but may dilute treatment effects if there's significant non-compliance.

Modified Intention-to-Treat (mITT) - A pragmatic middle ground that includes all randomized participants who received at least some intervention or met minimal inclusion criteria (like having at least one post-baseline assessment). The specific modifications should be pre-specified and justified. This approach is commonly used in trials where analyzing participants with zero exposure makes little clinical sense, though it introduces some risk of bias.

Per-Protocol (PP) - Includes only participants who completed the study according to protocol - they received the full intervention as intended, had adequate follow-up, and had no major protocol violations. This estimates treatment efficacy under ideal conditions but loses the protection of randomization and is vulnerable to selection bias, since reasons for non-adherence may be related to treatment effects or outcomes.

Clinical Interpretation - ITT is generally considered the gold standard for regulatory and superiority trials because it's most conservative and maintains randomization. However, examining both ITT and PP analyses together provides complementary information - if results differ substantially, it suggests adherence or protocol violations affected outcomes. For non-inferiority trials, PP analysis is often the primary analysis since ITT can paradoxically favor finding non-inferiority.

KEY TAKE-HOME MESSAGES

- **Targeting SpO₂ 94% in trauma is SAFE** – No increase in adverse outcomes despite more hypoxemic episodes
- **Liberal oxygen does NOT improve outcomes** – High-flow oxygen for all patients is unnecessary
- **Hyperoxemia may cause harm** – Significantly higher atelectasis rates with liberal strategy
- **Individualize your approach** – Clinical judgment trumps rigid protocols