

Supplementary File:

Supplementary Table S1. Generalized estimating equations (GEE) estimates of the intervention effect on repeated measures over the first 7 study days

Outcome	Model 1: β (95% CI)	P value	Model 2: β (95% CI)	P value
Heart Rate, beats per minute	11.33 (2.47, 20.18)	0.012*	5.17 (−0.17, 10.52)	0.058
Systolic Blood Pressure, mmHg	−1.31 (−7.27, 4.63)	0.664	−0.40 (−4.23, 3.43)	0.839
Diastolic Blood Pressure, mmHg	−3.31 (−8.28, 1.65)	0.191	−2.72 (−5.93, 0.49)	0.097
Glasgow Coma Scale	−0.16 (−1.35, 1.03)	0.790	0.65 (−0.16, 1.48)	0.118
qSOFA	−0.10 (−1.39, 1.19)	0.880	−0.15 (−1.11, 0.80)	0.747
Need For Ventilation†, OR (95% CI)	1.22 (0.64, 2.32)	0.544	1.57 (0.76, 3.29)	0.231

Model 1 includes group and the baseline value of each outcome. Model 2 includes group, the baseline value of each outcome, age, sex, weight, length of hospital stay, PCPC, PRISM III, cumulative fentanyl dose, and cumulative midazolam dose. Positive β indicates higher values in the intervention group compared with control. Accordingly, a positive β for heart rate means the control group's heart rate was lower by that amount on average.

Interpretation notes: Model 2 is the prespecified primary analysis and the basis for all conclusions in the Abstract, Results, and Discussion. It adjusts for baseline outcome and key prognostic covariates to improve precision and reduce residual confounding. Model 1 is provided only as a sensitivity check. If the two models differ, interpret and report Model 2.

† Estimated from logistic GEE; odds ratios are exponentiated coefficients.

**Statistically significant at $p < 0.05$.*

Supplementary Table S2. Hemodynamic trajectories over the first 7 study days by treatment group

Factor	Group	Day 1 (T1) mean ± SD	Day 2 (T2)	Day 3 (T3)	Day 4 (T4)	Day 5 (T5)	Day 6 (T6)	Day 7 (T7)	P value (time effect)	P value (time × group)	Within-group significant contrasts
Heart rate (beats per minute)	Control	115.46 ± 16.65	113.80 ± 22.03	106.73 ± 22.51	100.40 ± 22.0	101.44 ± 16.46	97.34 ± 15.66	101.45 ± 18.62	<0.001*	<0.001*	T1/T3*, T1/T4*, T1/T5*, T1/T6*, T1/T7*
	Intervention	105.50 ± 20.30	107.80 ± 18.32	102.40 ± 16.57	100.80 ± 23.69	109.75 ± 18.47	107.88 ± 15.61	104.16 ± 19.86	0.018*		T4/T5*
Systolic blood pressure (mm Hg)	Control	80.63 ± 11.25	81.50 ± 8.88	81.73 ± 9.62	81.60 ± 10.20	83.65 ± 10.31	80.60 ± 13.43	84.85 ± 9.77	0.173	0.012*	None
	Intervention	77.30 ± 8.31	80.63 ± 10.63	79.86 ± 10.83	82.30 ± 15.40	86.13 ± 13.09	82.84 ± 7.76	81.67 ± 10.78	0.008*		T1/T4*, T1/T5*, T1/T6*, T1/T7*
Diastolic blood pressure (mm Hg)	Control	43.60 ± 10.46	47.70 ± 13.23	45.97 ± 11.79	46.40 ± 9.26	49.68 ± 9.60	47.69 ± 9.43	52.35 ± 10.45	0.001*	0.001*	T1/T7*
	Intervention	42.20 ± 12.17	44.13 ± 7.85	44.46 ± 16.13	48.26 ± 11.51	48.72 ± 14.37	48.07 ± 12.71	45.58 ± 12.63	0.105		None

Values are mean ± SD at each time point. “P value (time effect)” tests change over time within each group; “P value (time × group)” tests whether time trends differ between groups for the factor. Estimates are from linear generalized estimating equation (GEE) models with exchangeable correlation and robust standard errors. Listed contrasts (e.g., T1/T4) are within-group comparisons with P < 0.05; exploratory, no multiplicity adjustment.

** P < 0.05 (nominal, exploratory).*

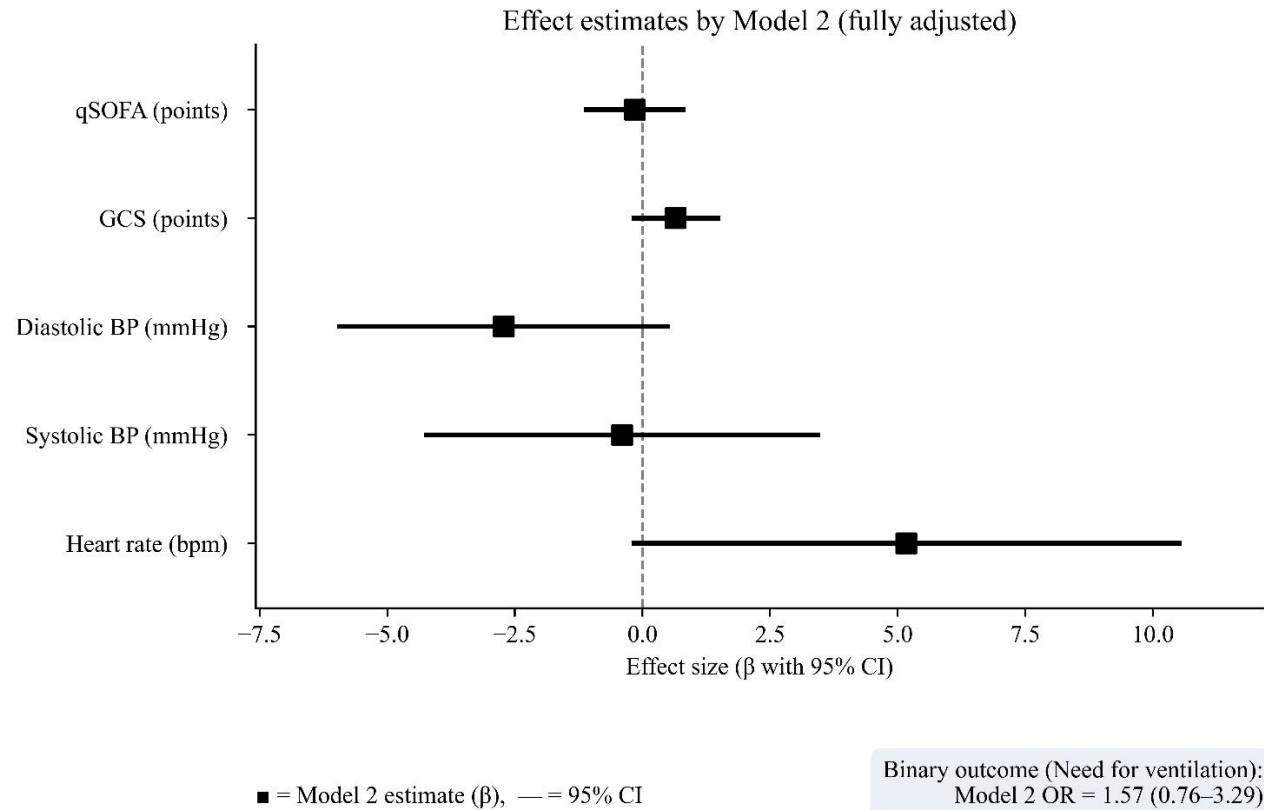
Supplementary Table S3. Clinical assessment trajectories (GCS and qSOFA) and proportion requiring mechanical ventilation over the first 7 study days by treatment group

Factor	Group	Day 1 (T1)	Day 2 (T2)	Day 3 (T3)	Day 4 (T4)	Day 5 (T5)	Day 6 (T6)	Day 7 (T7)	P value (time effect)	P value (time × group)	Within-group significant contrasts
GCS, median (IQR)	Control	4 (4–4)	4 (4–5)	4 (4–5)	4 (4–5)	5 (4–6)	5 (4–8)	4.5 (4–9)	0.032*	<0.001*	T1/T4*, T1/T5*, T1/T6*, T1/T7*
	Intervention	5 (4–6)	5 (4–6)	5 (4–6)	5 (4–8)	6 (5–9)	6 (4–10)	6 (5–10)	0.005*		T1/T4*, T1/T5*, T1/T6*, T1/T7*
qSOFA, median (IQR)	Control	11 (9–12)	11 (9–12)	11 (9–13)	11 (9–13)	11 (8–12)	9.5 (5–12)	8.5 (5–12)	<0.001*	<0.001*	T1/T3*, T1/T5*, T1/T6*, T1/T7*
	Intervention	11 (10–13)	11 (9–13)	11 (10–12)	10.5 (8–12)	10.5 (8–12)	10 (7–11)	9 (5–12)	0.070		—
Need for ventilation, n (%)^a	Control	29 (96.67)	26 (86.67)	29 (96.67)	29 (96.67)	22 (73.33)	17 (56.67)	13 (43.33)	<0.001*	<0.001*	T1/T5*, T1/T6*, T1/T7*
	Intervention	30 (100)	28 (93.33)	26 (86.67)	23 (76.67)	19 (63.33)	18 (60.0)	15 (50.0)	<0.001*		T1/T2*, T1/T3*, T1/T4*, T1/T5*, T1/T6*, T1/T7*

Values are median (IQR) or n (%). “P value (time effect)” tests change over time within each group; “P value (time × group)” tests whether trajectories differ between groups. Models use generalized estimating equations (GEE) with exchangeable correlation and robust standard errors. Listed contrasts are within-group comparisons with $P < 0.05$ (exploratory, no multiplicity adjustment). GCS = Glasgow Coma Scale; qSOFA = quick Sequential Organ Failure Assessment.

^a Logistic GEE was used for the ventilation outcome.

Supplementary Figure S1. Forest plot of fully adjusted GEE effect estimates (Model 2).



Note: Effect estimates from the prespecified fully adjusted generalized estimating equation (GEE; Model 2) comparing adjunct low-dose dexmedetomidine with standard midazolam–fentanyl sedation over study days 1–7. Squares show β coefficients and horizontal lines their 95% CIs; the dashed vertical line marks no effect ($\beta = 0$). Positive β indicates higher values in the dexmedetomidine arm relative to control. The binary endpoint (“need for ventilation”) is summarized as an odds ratio (OR 1.57, 95% CI 0.76–3.29) and displayed outside the axes. Model 2 adjusts for baseline value of the outcome, age, sex, weight, PRISM III, PCPC, cumulative fentanyl and midazolam doses (days 1–7), and length of hospital stay; exchangeable working correlation with robust standard errors. Abbreviations: BP, blood pressure; GCS, Glasgow Coma Scale; qSOFA, quick Sequential Organ Failure Assessment.