

ACC.24

Benzodiazepine-free Cardiac Anesthesia for Reduction of Postoperative Delirium (B-Free): A Multicentre, Cluster- Randomized, Crossover Trial

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**Population Health
Research Institute**
HEALTH THROUGH KNOWLEDGE



**AMERICAN
COLLEGE of
CARDIOLOGY**

Background

- Delirium = acute disorder of cognition
 - >15% of patients after cardiac surgery
- Serious problem for patients and systems:
 - prolongs hospital stay
 - cost per patient >\$10,229 USD
 - 30% develop PTSD
 - 32% increase in odds of in-hospital mortality



Background

- Benzodiazepines before and after cardiac surgery
 - associated with delirium
 - guidelines recommend avoidance
- Benzodiazepine use during cardiac surgery common
 - believed to prevent intraoperative awareness
 - given to 90%

No trial has examined effect of restricting intraoperative benzodiazepines



Study question

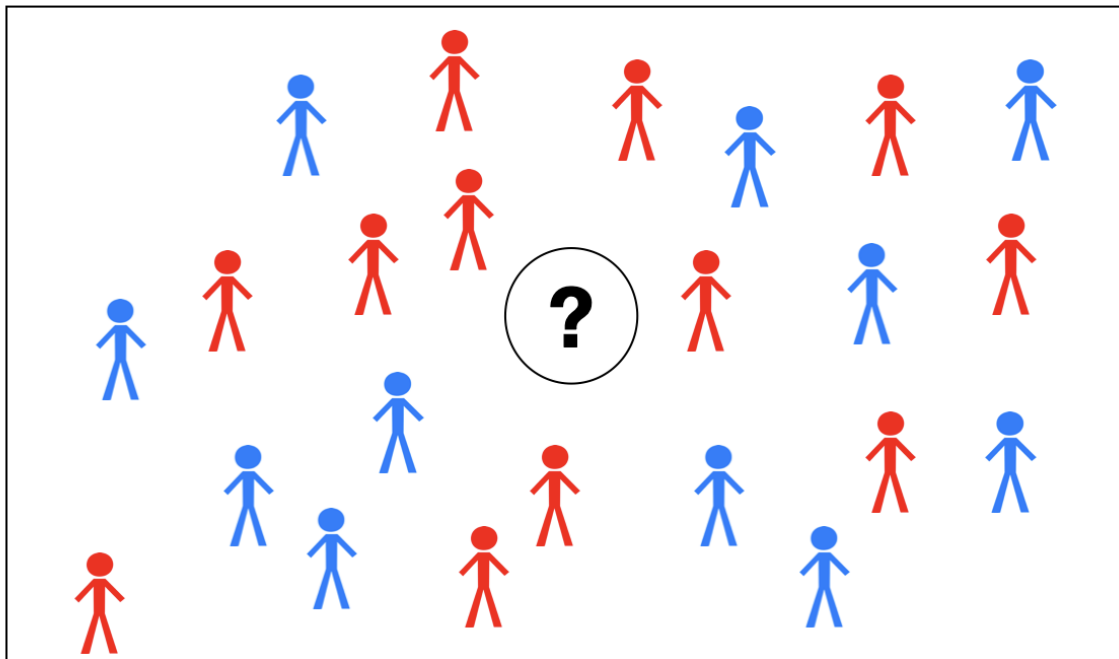
Does institutional policy of benzodiazepine-free cardiac anesthesia reduce incidence of delirium up to 72h after cardiac surgery?

Cluster Crossover trial design

- Selected because:
 - cardiac surgical care provided using standardized care pathways
 - anesthesiologists choose benzodiazepines (or not) based on preference
 - best way to test impact of restricting intraoperative benzodiazepines by randomly altering standard policy

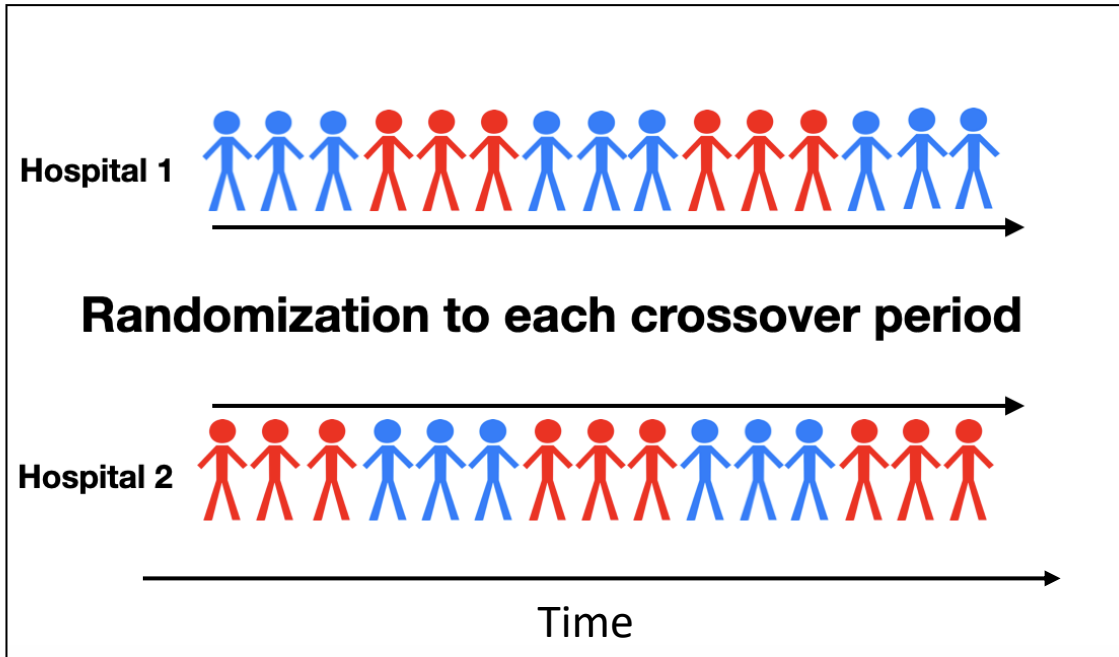
Current Practice

Haphazard



Cluster Crossover Trial

Random,
Structured



Liberal



Restrictive

Study intervention arms

**Restricted benzodiazepine
policy**

No routine administration
of benzodiazepines

**Liberal benzodiazepine
policy**

≥ 0.03 mg/kg Midazolam
equivalent



Outcomes

- Primary outcome: delirium up to 72h after CV surgery
 - assessed by nurses in routine care
- Safety outcome: intraoperative awareness
- Post hoc outcome:
 - number of positive delirium assessments



Analysis

- Primary outcome: logistic mixed model
- All models:
 - fixed effects term for period
 - random effects to account for within-period ICC
 - adjusted for age, sex, emergency surgery, hx ETOH, and hx of home BZD use
 - Primary analysis: ITT



Results

- 20 hospitals in Canada and US
- 19,768 patients
 - 9,827 restricted policy; 9,941 liberal policy
- Adherence to policy: **92.0%**
 - **91% restrictive, 93% liberal**



Baseline characteristics

- Mean (SD) age: 65 (12) years
- Female patients: 27%
- Hx of home benzodiazepine use: 7%
- Hx of heavy ETOH: 5%



Surgical characteristics

- Surgical procedures
 - isolated CABG: 49%
 - isolated valve: 17%
 - other: 34%
- Emergency surgery: 8%
- Mean (SD) CPB time 116 (58) mins



Perioperative benzodiazepines

- Preoperative (within 24h): 16%
- Intraoperative
 - Restricted periods: 9%
 - Liberal periods: 93%
 - Mean (SD) dose when given (overall): 4.1 (2.5) mg
- Postoperative: 11%



Primary analysis population

Outcome	Restricted benzodiazepine policy (N=9827)	Liberal benzodiazepine policy (N=9941)	Adjusted OR (95% CI)	P value
Delirium up to 72h after cardiac surgery – no. (%)	1373 (14.0)	1485 (14.9)	0.92 (0.84 - 1.01)	0.07

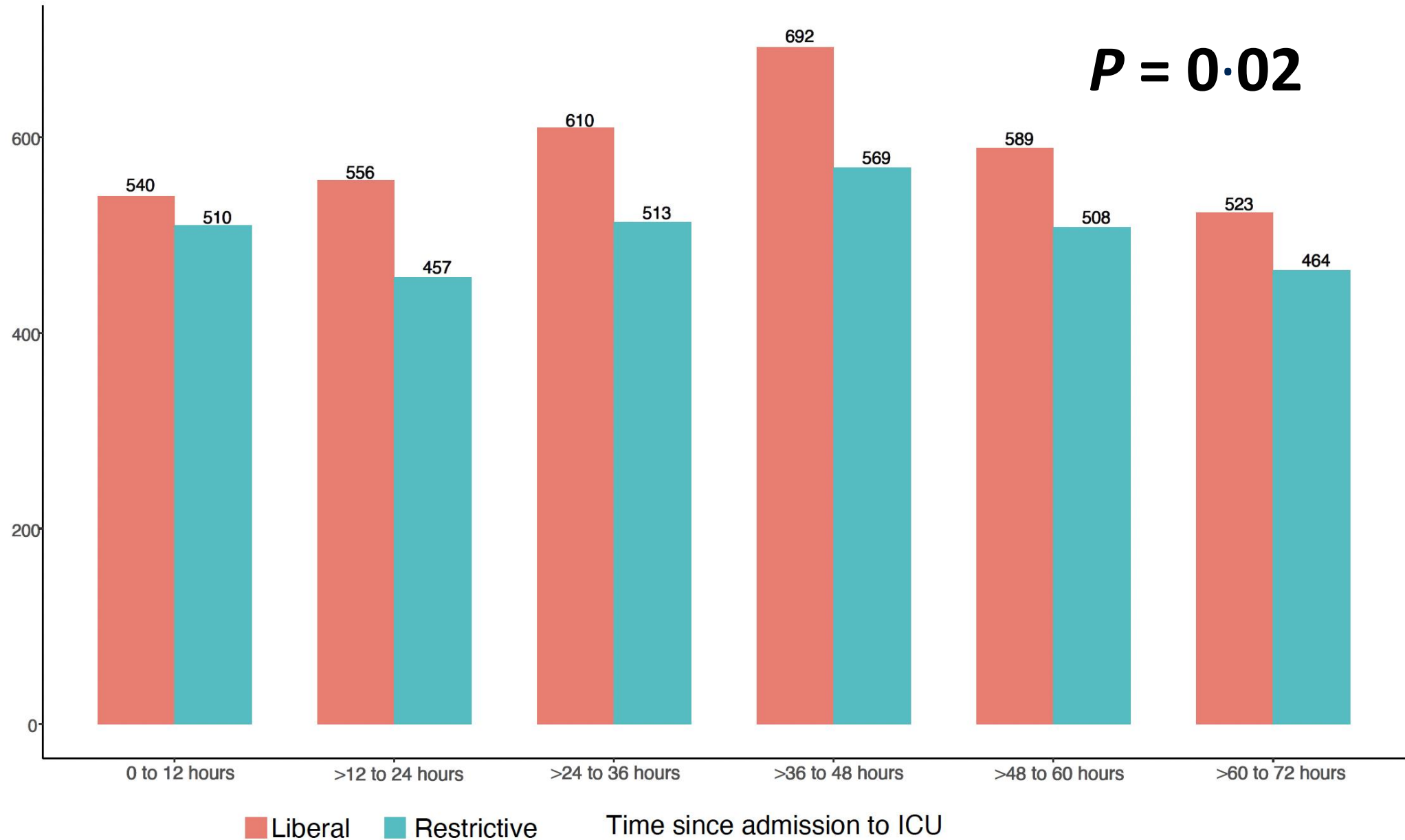


Intraoperative awareness and # positive delirium assessments

Outcome	Restricted benzodiazepine policy (N=9827)	Liberal benzodiazepine policy (N=9941)	Adjusted RR (95% CI)	P value
Intraoperative awareness – no. (%)	0	0	n/a	n/a
Delirium assessments positive for delirium per 72 hours – crude mean (\pm SD)	0.3 (1.0)	0.4 (2.2)	0.87 (0.78, 0.98)	0.02



Number of positive delirium assessments



Excluding restrictive arm patients who received BZD within 24h before surgery

Outcome	Restricted benzodiazepine policy (N=8391)	Liberal benzodiazepine policy (N=9941)	Adjusted OR (95% CI)	P value
Delirium up to 72h after cardiac surgery – no. (%)	1149 (13.7)	1485 (14.9)	0.88 (0.81 - 0.97)	0.01



Patients managed according to intraoperative policy

Outcome	Restricted benzodiazepine policy (N=9827)	Liberal benzodiazepine policy (N=9941)	Adjusted OR (95% CI)	P value
Delirium up to 72h after cardiac surgery – no. (%)	1219 (13.7)	1372 (14.8)	0.90 (0.82 - 0.99)	0.02
Removing patients who received BZD within 24h from restrictive arm				
Delirium up to 72h after cardiac surgery – no. (%)	1024 (13.4)	1372 (14.8)	0.87 (0.79 - 0.96)	0.005



Conclusions

- By ITT, restricted BZD policy did not reduce postoperative delirium
- No evidence of adverse events
 - no cases of intraoperative awareness reported
- On-policy analysis: ~10% reduction in delirium with BZD restriction
- Greater effect size the more that BZD exposure eliminated
- **Restricting benzodiazepines during cardiac surgery should be considered**



Implications

- ~500,000 cardiac surgeries performed in US annually
 - 90% of patients receive intraoperative BZD
 - ~75,000 will develop postoperative delirium
- Institutional costs of 1 case of delirium: \$10,229
- Restricting intraoperative BZD in all patients may on an annual basis in the US alone:
 - eliminate 5,000 cases of delirium
 - save institutions \$51,145,000

