# A Pharmacoepidemilogic approach to propofol delivery during esophagogastroduodenoscopy

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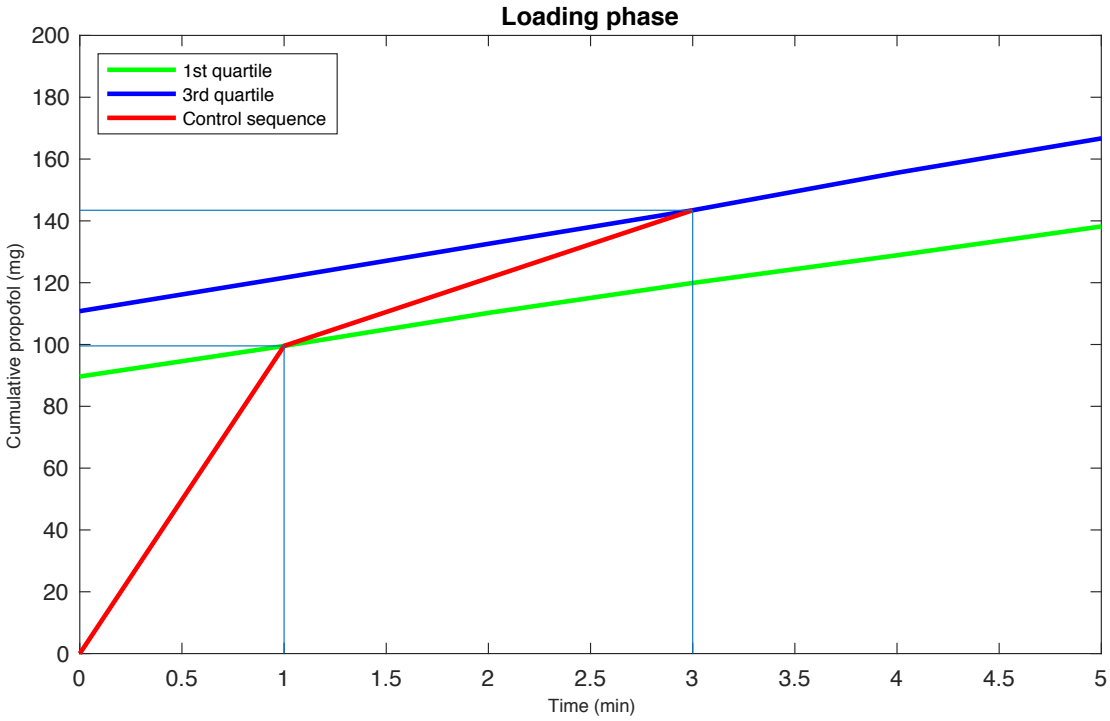
Background: Delivery of propofol for brief procedures such as esophagogastroduodenoscopy (EGD) is a commonly performed task which requires rapid assessment of patient sensitivity and adaptation of drug delivery to maintain appropriate sedation. While pharmacokinetic (PK) models may reduce the impact of covariates such as age or weight on drug effect, with a sufficiently large cohort a subcohort of patients of similar age and weight can be selected that will yield a lower error than that of a PK model. A control system that is based on such a pharmacoepidemilogic (PE) approach is described.

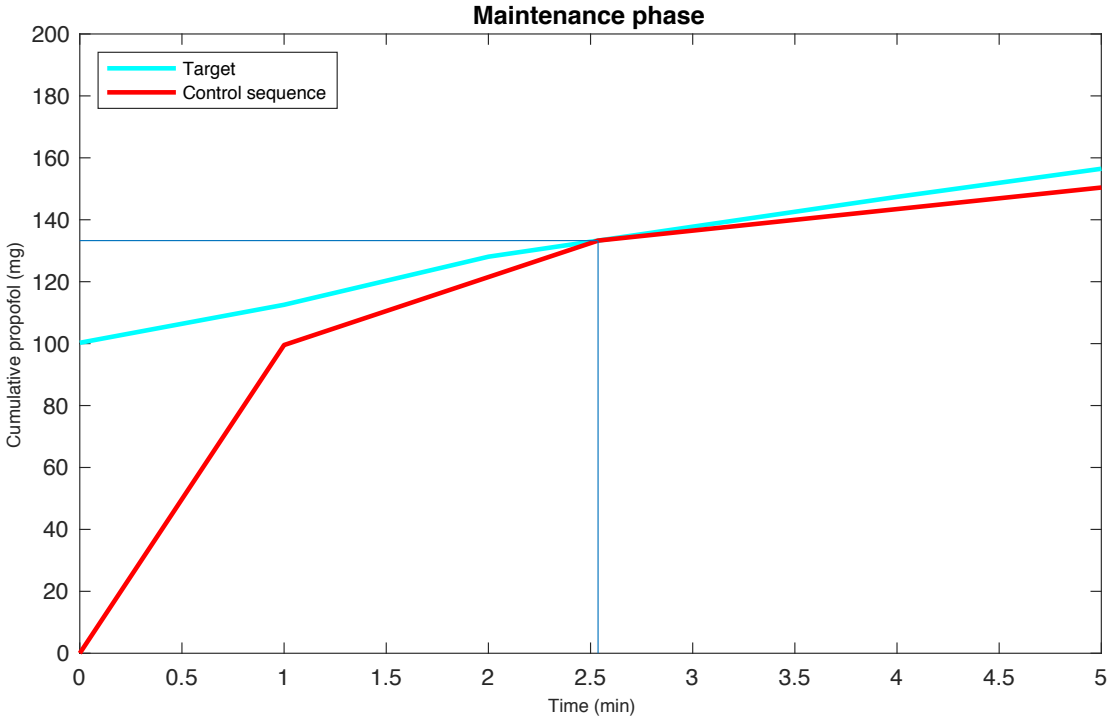
Methods: Data was extracted from the Penn Data Analytics database for all esophagogastroduodenoscopy cases from Jan 2016 to December 2017; cases with only bolus delivery were excluded, leaving 13,503 cases. Timed delivery entries were converted to continuously sampled infusion rates, and cumulative propofol administration determined at one-minute intervals. For any given patient, a subcohort of 100 patients is selected that most closely approximates the age and weight, and at each time interval the cumulative propofol ranked from lowest to highest. An infusion sequence (red) is determined that connects 3 points – 0 propofol at 0 minutes, the first quartile at 1 minute, and third quartile at 3 minutes. Note that the green and blue lines have non-zero y intercepts reflecting an initial bolus. This loading sequence is depicted in upper panel of the figure. The loading sequence is delivered until

adequate sedation is observed, the estimated ranking at that instant determined, and the control sequence updated to track the identified target, as depicted in the lower panel of the figure.

Results: Over the interquartile range of ages and weights, a subcohort of 100 patients can be formed with a maximum age range of 2 years and 2 kg.

Conclusions: PE control has several advantages over PK control. The control is based on actual observations during drug administration. As additional observations accrue, greater precision in covariates or additional covariates are possible. The observations can be specific to a particular locale. Implementation is simple, and can be performed with manual entry into a syringe pump. PE control will require clinical validation.


Loading phase
1st quartile
3rd quartile
Control sequence
Cumulative propofol (mg)
Time (min)
0
20
40
60
80
100
120
140
160
180
200
0
0.5
1
1.5
2
2.5
3
3.5
4
4.5
5


Maintenance phase
Target
Control sequence
Cumulative propofol (mg)
Time (min)
0
20
40
60
80
100
120
140
160
180
200
0
0.5
1
1.5
2
2.5
3
3.5
4
4.5
5