# A Retrospective Cohort Study of a Very Cool Intervention on Patients Outcomes

SAP Version: MM/DD/YYYY

**Administrative Details**

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## **Amendment History**

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| **Version** | **Date** | **Item / Section** | **Details** |
| V1 | YYYY-MM-DD | SAP/all sections | Initial SAP V1 |
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**Introduction**

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**The proposed project is aimed to** XXXXXXXX XXXXXXXX XXXXXXXX XXXXXXXX XXXXXXXX XXXXXXXX XXXXXXXX XXXXXXXX XXXXXXXX XXXXXXXX XXXXXXXX XXXXXXXX XXXXXXXX XXXXXXXX XXXXXXXX.

## **Study Design**

### **Data Sources**

This retrospective cohort study will include all eligible patients determined by a list of pre-defined inclusion and the exclusion criteria. Electronic Health Records (EHR) data from all eligible patients will be extracted from the Mass General Brigham (MGB) institutional Enterprise Data Warehouse (EDW) system and analytical platform. For this particular project, we will design systematic data queries to maximize our capacity in identifying all eligible patients from the EPIC EHR system, utilizing different matching and dictionary-based searching algorithm on EPIC operational, clinical and financial databases.

### **Detailed Inclusion and Exclusion Criteria**

### This retrospective cohort study will include all patients who previously presented to MGH for a surgical procedure requiring general anesthesia between April 2016 and March 2020.

|  |  |
| --- | --- |
| **Inclusion Criteria** | **Exclusion Criteria** |
| * Male and female patients 18 years old and older. * Date of surgery: April 2016 – March 2020. * Non cardiac surgery. * Receiving general anesthesia. | * Male and female patients younger than 18 years old. * Scheduled surgeries that were not performed. * Cardiac surgery. * Not receiving general anesthesia |

### **Data Flow Diagram**

We will describe our data management process in reaching to the final analytical sample using a data flow diagram recommended by the STROBE guideline, highlighting records that have been removed from the final analysis, such as duplicate values and values needed to be excluded.

**Hypothesis and Objectives**

Background theories:

It is commonly assumed that XXXXXXX. And such relationship is XXXXXX.

Primary hypothesis:

The exposure is associated with the outcome.

Secondary hypothesis:

1. The exposure is associated with A
2. The exposure is associated with B
3. The exposure is associated with C
4. There was an interaction effect between exposure, outcome and D…
5. More…

### **Exposure:**

The exposure is defined as a XX variable of XXXX…

### **Outcomes**

* Primary outcome: XXXX
* Secondary outcome 1: XXXX
* Secondary outcome 2: XXXX
* Secondary outcome 3: XXXX

### **Biases and Confounders**

A direct acyclic graph (DAG) of potential relationships between the studied variables is presented in the attached **Figure supplement**. The DAG is created using the [Dagitty](http://www.dagitty.net/) web-tool.

Detailed lists of blocks of covariates/confounders are:

Preoperative variables:

* Demographic characteristics (such as age and gender)
* Comorbidities (such as obesity [BMI], smoking, asthma, COPD, OSA, hypertension, diabetes, cardiovascular, cerebrovascular and peripheral neurologic disease)
* Treatments (such as inhaled agents, steroids, beta-blockers, aspirin)

Intraoperative variables:

* Intraoperative management:

1. Pharmacology (such as type of inhaled anesthetic, type of opioid used);
2. Ventilator settings (such as VT, PEEEP, FiO2, RR)

* Intraoperative physiology:

1. Respiratory mechanics (Compliance, peak airway pressure);
2. Gas exchange (such as SpO2, ETCO2, PaO2 [if available], PaCO2 [if available]);
3. Hemodynamics (such as MAP, HR);
4. Temperature;
5. Renal function (urine output).

### **Statistical Analysis Plan**

Given the retrospective nature of this study, we will collect data on all patients meeting eligibility criteria who are captured in the EPIC database to yield maximal statistical power to detect differences in outcomes, especially when stratified by type of surgery. We will cap our search date at December 2019. We estimate that approximately 90,000 distinct patient admissions will meet our eligibility parameters. This amount of records is necessary as it represents all surgical cases in the EPIC database that fit our inclusion/exclusion criteria (all surgical cases that required general anesthesia). Limiting the sample size to only a subset of surgical cases would reduce the generalizability of our results and perhaps bias our conclusions (depending on how we limit our sample), preventing us from answering our research question. In addition, collecting data on all surgical cases in our database will provide enough power to identify differences between subpopulations of surgical cases (based of type of surgery), which will have much smaller sample sizes and, in some cases, a smaller incidence of complete postoperative data.

**Power Analysis**

Utilizing a two independent-sample t-test with two-sided alpha = 0.025, our available study sample N = 90000 would yield a power ≥ 0.99 to detect an effect size as small as 0.06 point mean difference in primary outcome of pain scores, assuming its Standard Deviation = 2. This minimal detectable effect size, defined as statistically significant is very small and not clinically meaningful; thus instead, we propose to use a clinical significance threshold of half a point-difference (0.5) in pain scores as the limits of clinical significance.

**Descriptive statistics**

Descriptive statistics will be summarized and reported using appropriate functions such as mean/standard deviation or median/25th and 75th percentiles for continuous variables; and frequencies/percentages for categorical outcomes. Standard Mean Differences (SMDs) will be reported, and SMD > 0.1 is set as the criterion for statistical significance.

**Primary analysis**

The primary analysis will be performed using survival models (e.g., mixed Cox regression models, etc.) based on the nature of primary outcome as time-to-event data. Both univariate and multivariable models will be constructed and compared for inferences. To overcome biases (e.g., s), confounding variable sets will be determined using DAG as demonstrated, and they will be incorporated into the multivariable model depending on data structures (e.g., adjustments, derived weighting scores). Hazard ratios (both crude and adjusted) along with their 95% confidence intervals (95% CIs) will be reported.

**Secondary analysis**

Secondary analyses will be performed on secondary outcomes defined in aforementioned “outcomes” section. Generalized linear models with appropriate link functions (e.g., normal, logit) will be utilized for inferences. Both univariate and multivariable models will be constructed. Model parameter estimates along with their corresponding 95% confidence intervals will be reported, respectively.

**Missing data**

Missing data due to censorship for time-to-event outcomes will be handled by survival models. Missingness in demographics and confounding variables will be addressed using appropriate analytical methods (e.g., list-wise deletion, single-imputation with EM algorithm) depending on the data distribution and missing patterns.

**Interaction analysis**

**Subgroup analysis**

## **References:**