Analysis of grouped opioid use on ICU outcomes using MIMIC IV and RXNorm API

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**Initial Data Analysis**

The present study focuses on the use of opioids and their prescription in Intensive Care Unit (ICU) settings and this impact on patient health including mortality. The data were abstracted from the Medical Information Mart for Intensive Care (MIMIC)-IV1 dataset. MIMIC-IV consists of over 65,000 patients admitted to the ICU and over 200,000 patients admitted to the emergency department from the Beth Israel Deaconess Medical Center in Boston, Massachusetts in the United States. Data in MIMIC-IV has been de-identified and is available for research use following receiving credentials and approval. The present study utilized data from the most recent readily available version of MIMIC, MIMIC-IV 3.1 from October 2024.

Linkage with the MIMIC-IV dataset focused on extraction of NDC code groupings from the MIMIC data and the RXNorm getNDC API. Following literature review2, a list of relevant opioid medications for study was accumulated including buprenorphine, fentanyl, hydrocodone, meperidine, methadone, morphine, oxycodone, oxymorphone, and tramadol. This list of opioids was queried into the RXNorm getDrugs API, and returned a list of RXNorm Concept Unique Identifiers, or RXCUIs. This list of RXCUIs was then used with the getNDCs API to obtain an ontology mapping table with 3 columns comprising the name of the opioid, all its RXCUIS, and all its NDC codes. The NDC codes were then linked with the MIMIC-IV data to obtain the group of opioid usage in the ICU setting. Extraction of NDC codes was performed using Python.3

Following acquisition of MIMIC-IV and NDC code data, all necessary tables were uploaded to a PostgreSQL database using pgAdmin4. The data uploaded process consisted of 4 tables from MIMIC-IV (admissions, patients, icustays, and diagnoses\_icu) and the NDC code mapping table. Patients were screened for their inclusion criteria of having been prescribed an opioid medication in an ICU setting, with the linkage from the prescriptions table to the icustays table ensuring that these prescriptions were indeed coming from an ICU stay. The NDC codes table was used to provide the information on which opioid group this prescription was from. Patient demographics including gender and age were extracted from the patients table in MIMIC-IV, and baseline comorbidities were extracted from the diagnoses\_icd table. These baseline comorbidities were also extracted from the literature review2, and consisted of COPD, Chronic obstructive pulmonary disease; CAD, coronary artery disease; CHF, congestive heart failure; ESRD, end stage renal disease; ESLD, end stage liver disease, stroke, depression and diabetes. The baseline comorbidities were included as binary variables to indicate incidence of the condition. There were two outcomes for the study; 30 day mortality and 1 year mortality. Both 30-day mortality and 1-year mortality were also included as binary variables, and they were calculated from the reference date of the out time of the patient’s first ICU visit where they received an opioid medication. These outcomes were also extracted following literature review.2 Patient mortality was extracted using the date of death column from the patients data table. MIMIC-IV acquires patient mortality information from a combination of hospital records and state records to ensure accuracy. Patient covariates, exposure to opioids, and outcomes (30 day and 1 year mortality) were combined following data cleaning using SQL queries in pgAdmin4 to create a final analytical dataset. Following the data processing pipeline the data was imported into Python for analysis.

A total of 40,470 were included in the final analytical dataset. Of these, the most common prescriptions were for oxycodone and fentanyl with 21,616 and 7,833 individuals prescribed, respectively. The proportion of individuals who observe 30 mortality stratified is shown below. Morphine and fentanyl have the highest proportion of 30 day mortality.

* A graph of a number of drugs

  Description automatically generated with medium confidence

Proportion of mortality at 1 year stratified by type of opioid users is shown below. Again morphine and fentanyl have the highest unadjusted proportion of mortality. Note that the proportions are higher in each category for mortality at 1 year, as this metric is calculated by any incidence of mortality in the year since ICU visit. Thus, anyone with mortality in 30 days will have mortality in 1 year.

* A graph of a number of patients

  Description automatically generated with medium confidence
* The table and plots display the total number of patients for each opioid type and the total numbers of their mortality events. We can see that the largest proportion of patients take oxycodone, followed by fentanyl and morphine.

|  |  |
| --- | --- |
| * **Opioid Drug Group** | * **Number of Patients** |
| * oxycodone | * 21,616 |
| * fentanyl | * 7,833 |
| * morphine | * 7,066 |
| * tramadol | * 1,738 |
| * meperidine | * 1,197 |
| * methadone | * 759 |
| * buprenorphine | * 231 |
| * hydrocodone | * 30 |

Methadone, buprenorphine, and hydrocodone had relatively fewer numbers of patients, with hydrocodone having only 30 patients included in the final data.

* A graph of a patient

  Description automatically generated with medium confidence

For patient comorbidities, analysis was conducted by first analyzing the proportion of patients with each comorbidity and then by constructing a heatmap to analyze the correlation between each comorbidity in the patient population. The comorbidities CHF, congestive heart failure; ESRD, end stage renal disease; ESLD, end stage liver disease all did not have any incidence in the dataset and were excluded. Further analysis is necessary to determine why this occurred and will be conducted during the next phase.

A graph of blue bars

Description automatically generated with medium confidence

Diabetes and COPD were the most common patient comorbidities, with nearly one third of patients having diabetes. Correlations from the heatmap between patient comorbidities were all relatively low. The highest correlation was between individuals with diabetes and individuals with obesity.

A screenshot of a graph

Description automatically generated

Continuous variables included Age and Length of Stay in days for the ICU visit. Density plots of these variables are shown below. We can see that the anchor age is centered around older people and that individuals stays in the ICU are typically less than 25 days.

**A graph of a graph

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Overall, the initial data analysis proved to be a success. Data was successfully acquired from MIMIC-IV and linked to NDC codes extracted from the RXNorm API. All data tables were successfully uploaded to the PostgreSQL database and date cleaning pipelines were performed using SQL commands. Finally, relevant metrics and plots for the analytical dataset were extracted in Python. The data dictionary of relevant variables was compiled and complete data quality checks were conducted to ensure feasibility for the next phase of analysis. Both of these tables are available in Excel format along with the entire code and results of this project at . Moving forward, the next phase of the project will consist of the model fitting and machine learning analysis phase, in order to further elucidate the effect of different groups of opioid medications on patient mortality in an ICU setting from this dataset.

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**References**

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