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Introduction

- The opioid crisis has been on an exponential growth curve, involving legitimate and illicit drug access (*Blood* 2017).
- Sickle cell disease (SCD) is a genetic disorder characterized by lifelong, painful vaso-occlusive events. Patients with SCD have justifiable reason to use opioids (*Blood* 2017).
- Prior studies have shown that opioid use in SCD patients accelerates during two age intervals, 12-17 and 18-45. The first wave of acceleration coincides with puberty, a time of intense physical, hormonal and neuromaturation growth (*Blood* 2017).
- Patients with SCD have disease-related obstacles in achieving developmental milestones, and therefore we hypothesize that these patients are at a higher risk of accelerated trajectories of opioid use.
- While only 5% of SCD patients account for the majority of sickle cell inpatient hospitalizations for painful episodes, we sought to develop visual and mathematical models of inpatient opioid consumption between the ages of 12-18, to see if patterns existed that would assist the clinician, the patient and the patient's family in forecasting the amount and duration of opioid use.
- We theorize that clear visualization of past patterns in acceleration and remittance of opioid consumption in real time could trigger clinical decision support for issues that may contribute to tolerance and addiction.

Methodology

- Cerner Health Facts' database captures and stores de-identified, longitudinal electronic health record data, and then aggregates and organizes the data into consumable data sets to facilitate analysis.
- Opioid amount and number of doses per year, along with gender, age and region of the country, were extracted from inpatient data out of Cerner Health Facts, using ICD 9 and 10 diagnosis codes on patients with SCD between the ages of 12-18.
- This study was approved by UMKC's IRB as non-human subjects research.
- Sample:** Opioid amount and number of doses were extracted on 451 individual patients across 862 patient encounters. The data from those with 5 or more encounters were used to form line charts in utilization per year. See figures 1, 2, 3, 4, 5, and 6. (The two vertical blue lines represent NHANES expected menarche in non Hispanic black women; the red line notes the average value). Simple linear regressions were conducted to examine the relationship between both age and dose, and age and amount. These individual patients were compared with age and gender.

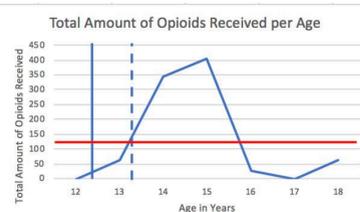


Figure 1: Female patient from western United States.

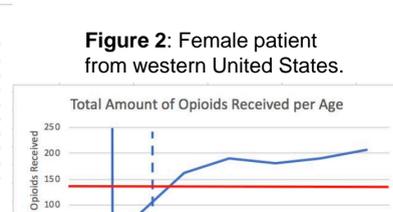


Figure 2: Female patient from western United States.

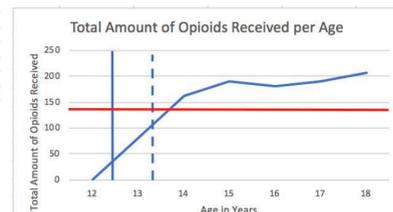


Figure 3: Female patient from southern United States.

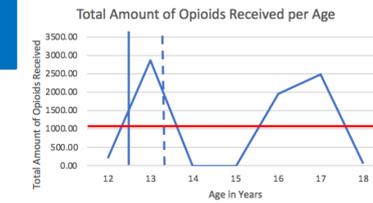
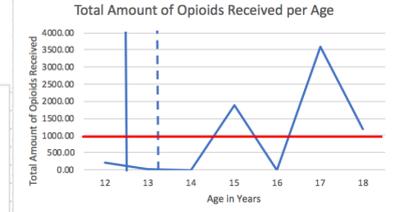


Figure 4: Female patient from northeastern United States.

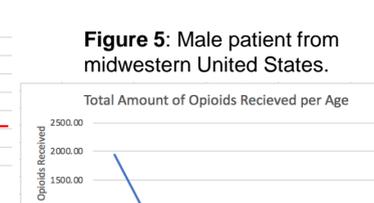


Figure 5: Male patient from midwestern United States.

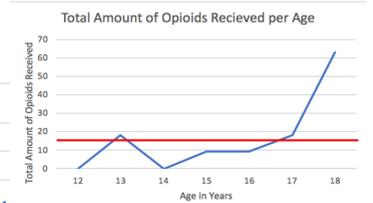
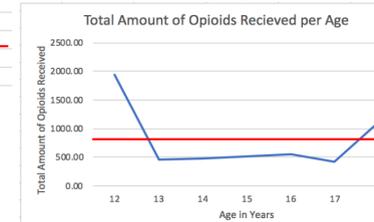


Figure 6: Male patient from western United States.

Figures 1-6: Examples of 6 unique SCD patients with greater than 5 hospital admissions for pain crisis. Each individual patient had cumulative dose of opioids administered per year graphed at each age between the ages of 12-18. By graphing opioid consumption across a set age range, opioid trajectory can be identified and addressed accordingly.

Summary/Conclusion

- Attempts to manage opioid consumption in chronic disease will require comprehensive interventions that can be mobilized at or around the time sharp changes in opioid consumption occur.
- Interventions should be oriented to the age of the patient and the specifics of the disease. This can be done by linking dose and duration with structured data such as age, gender and concomitant medical events.
- Transitions in care between the outpatient and inpatient settings can lead to a lack of consistency in opioid dosing patterns. Practitioners could utilize visualization tools that isolate trends, recognize previous prescribing patterns and highlight deviations in consumption between crisis and baseline that forecast tolerance and addiction.
- Regarding the current state of opioids in this country, there is likely to be a significant payout from opioid makers and distributors. However, past payouts, such as the Master tobacco settlement of 1998, were not structured to provide support services for those most affected. Clinical input from those who take care of patients with chronic diseases requiring long-term opioid intake, such as SCD, should assist healthcare policy planners in the division of funds when new healthcare policy is written regarding the use of opioids.

Limitations

- This is a database study from Cerner Health Facts, and thus limited by the information collected and provided in the databank.
- Sickle cell is a not one single disease, however information on patient's sickle cell genotypes and comorbidities were not available in the database used.
- Opioid medications administered during inpatient hospitalizations were not equated using morphine equivalents. Therefore, number of doses administered was used in data analysis rather than amount administered.

References

- Ballas SK, et al. Opioid Utilization Patterns in United States Patients with Sickle Cell Disease. *Blood* 2017; 130: 130.
- Ogunsile FJ, et al. Physician Prescribing Practices in Sickle Cell Disease. *Blood* 2017; 130: 3540.
- Squeglia LM, et al. The influence of substance use on adolescent brain development. *Clin EEG Neurosci* 2009; 40(1): 31-8.
- Zhou K & Zhu Y. The paraventricular thalamic nucleus: A key hub of neural circuits underlying drug addiction. *Pharmacol Res* 2019;142: 70-76.

Results

Opioid Dose Analysis: Solution for Fixed Effects

Effect	Estimate	Standard Error	DF	t Value	Pr > t
Intercept	-0.9930	3.8247	34	-0.26	0.7967
Year	6.8098	2.0883	34	3.26	0.0025

Age	N	Mean	Standard Deviation	Minimum	Maximum
12	36	8.2	14.6	0	53
13	36	14.6	26.1	0	116
14	36	16.7	21.2	0	89
15	36	23.4	25.6	0	124
16	36	26.8	49.8	0	284
17	36	43.7	62.6	0	333
18	36	46.9	84.3	0	401

Table 1: Dose Analysis. Of the 451 individual patient encounters, 36 patients with SCD were identified as high utilizers with greater than 5 hospital encounters. Linear regressions were conducted to further examine the relationship between age and dose. As seen on this table, there is a steady increase in the mean dose administered across these 36 patients as age increases.

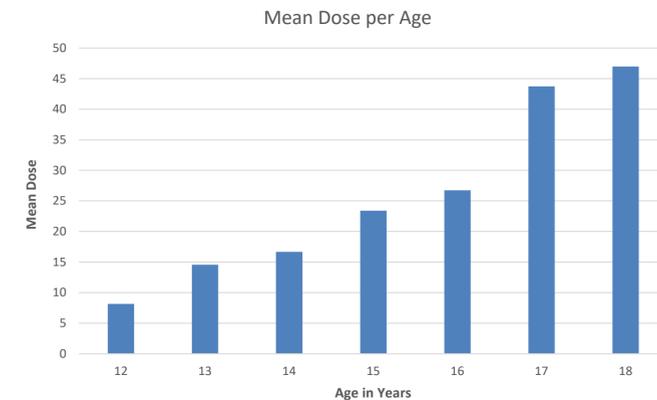


Figure 7: Graphical Representation of Mean Dose per Age. When analyzing mean dose consumed per year, there is a 6.8096 increase in average number of doses consumed per one year increase in age, with $p < 0.0025$. Of note, this increase in opioid dose per one year increase in age applies only to sickle cell patients who received inpatient administration of opioids.