Using Medical Dosing Across PEDSnet to Respond to Chemotherapy Sterile Injectable Drug Shortages in Pediatric Oncology

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Research Category: Clinical Applications - Clinical Characterization

Background

Within the past decade, a number of critical drug shortages have occurred in the United States[1]. In pediatric oncology, this problem was brought to the forefront in October 2019 when Pfizer Pharmaceuticals, the only remaining supplier of vincristine, experienced delays in manufacturing this critical chemotherapy agent, which is a backbone of childhood cancer therapy[2]. Other shortages have involved bleomycin, nelarabine, and crisantaspase. In order to inform planning for drug reserves, we aim to estimate the annual use of commonly used pediatric paranteral chemotherapeutics through evaluation of hospital pharmacy purchasing data, medication administration data, and deterministic prescribed dose modeling. The goal of this pilot project is to assess the effectiveness of a pediatric clinical data network as a representative sample for estimating chemotherapy usage, and to take preliminary steps in capturing medical dosing data for common chemotherapy sterile injectables across the network.

Methods

PEDSnet is a clinical data research network comprising data for over 6 million children in the United States from seven different children's hospital systems. EHR data is structured in the OMOP common data model v5.0, with adaptions and extensions optimized for pediatric research[3]. For this analysis, drug exposure data from six PEDSnet institutions for 25 common paranteral chemotherapy medications were analyzed between January 1, 2017 and December 31, 2018. Intermediate mapping from ancestor ingredients to descendant drug formulations was constructed via concept_ancestor. Several checks were then completed for each site to evaluate the quality of the network data:

1. Mean drug exposure per patient mean by year (initial quality control analysis from the beginning of PEDSnet data collection to most recent PEDSnet data)
2. Total drug exposure count/total person count (2017-2018)
3. Specific checks for vincristine, daunorubicin, doxorubicin, and ifosfamide (over the course of a patient's treatment from 2017-2018), as agents representing a broad range of treatment plans
    a. Median dose basis (effective_drug_dose) compared to expected dose bases (based on treatment protocols)
    b. Total number of drug exposures per person

To consolidate differences in units for the expected dose bases check, all effective drug doses were converted to milligrams per square meter (body surface area (BSA)) where anthropometric data is available, using the Mosteller method for BSA computation (Figure 1).

Figure 1. Effective Drug Dose Conversions (median height and weight taken for cases of more than one of each measurement in the same visit occurrence)

Results

The pilot spanned a cohort of over 3521 patients (Figure 2). Of these patients 98% had height and weight records at site A, 88% at site B, 99% at site C, 95% at site D, 88% at site E, and 85% at site F necessary for mg/m^2 conversions. Eleven drugs were present in all 6 sites, 9 drugs were present in all 5, three drugs

were present in 4, one drug was present in all 3 sites, and one drug was present in one site. Across all sites, leukemia and sarcoma were the most treated conditions, and methotrexate and vincristine were the most used chemotherapeutics. After converting effective drug doses to mg/m^2, 77% of the 22 median exposures for specific checks of vincristine, daunorubicin, doxorubicin, and ifofamide were within 5mg/m^2 from the expected dose basis and when comparing the total number of drug exposures per person, the distribution across sites was most similar for doxorubicin (Figure 4, 5). The distribution curves in the total number of exposures per person was variable (Figure 3).

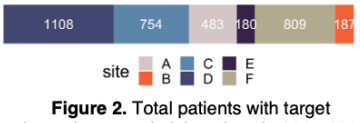

Figure 2. Total patients with target chemotherapy administrations in 2017-2018

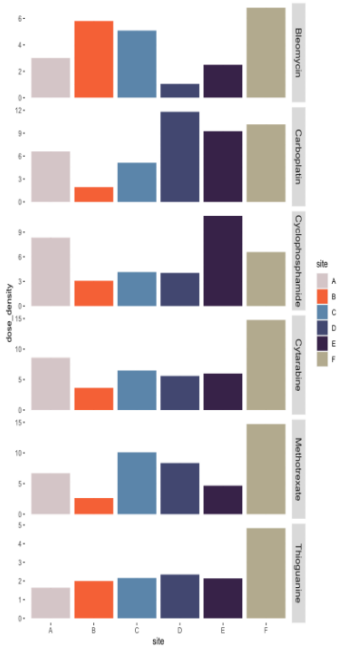

Figure 3. Distribution of total drug exposures/total patients per drug (not all drugs included

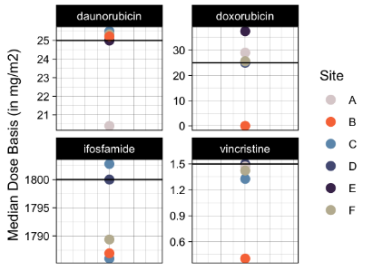

Figure 4. Comparing sites against expected dose basis

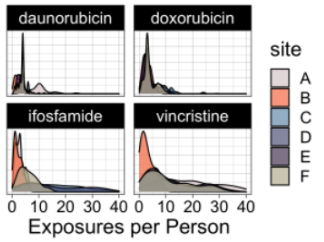

Figure 5. Total drug exposures per person by site

Discussion/Conclusion

Through our analysis of chemotherapy administration, we believe that PEDSnet data standardized to the OMOP CDM can be used as an effective tool to evaluate the usage of sterile injectables in the pediatric hospital setting. The use-specific data quality checks allow us to reach out to sites of origin about anomalies in order to improve drug data capture. We can then move forward in calculating total drug administration values for each chemotherapy drug within the two-year time frame across the six children's hospitals.

References

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