Journal of Scientific Innovation in Medicine

Warburton A, et al. Leveraging NADAC to Steer Drug Formularies in Resource-Limited Clinics. *Journal of Scientific Innovation in Medicine*. 2019; 2(1): 5. DOI: https://doi.org/10.29024/jsim.21

RESEARCH

Leveraging NADAC to Steer Drug Formularies in Resource-Limited Clinics

Andrew Warburton, Randal Serafini, Benjamin Shuham, Andrew Leader, Sharon Barazani, Joe-Ann Moser and Yasmin Meah

Icahn School of Medicine at Mount Sinai, US

Corresponding author: Andrew Warburton (andrew.warburton@icahn.mssm.edu)

Objectives: Free medical clinics provide healthcare to populations with limited options for insurance coverage and are thus key medical safety nets. Such clinics have limited operating budgets due in part to their lack of revenue streams through insurance reimbursements. Thus, pharmaceutical acquisitions can impose significant financial burdens in light of rising and volatile prices [1]. The goal of this study was to provide clinics with a real-time comparison of national retail pharmacy acquisition prices against clinic purchasing prices to determine potentially overpriced drugs.

Methods: Historical ledger data from the East Harlem Health Outreach Program (EHHOP) at Mount Sinai was used to determine the clinic's average price and volatility for specific drugs over time. Average prices were cross-referenced against the publicly available National Average Drug Acquisition Cost (NADAC) database, which outlines the average acquisition cost of drugs by retail pharmacies across the United States.

Results: This analysis demonstrated that 36% (16/45) of EHHOP drug price averages were significantly different than relative NADAC values, with 9% (4/45) more expensive and 27% (12/45) cheaper. Price volatility between EHHOP and NADAC acquisition prices varied. Assuming the NADAC benchmark for significantly more expensive EHHOP purchases resulted in potential savings of $4,424 (6% of budget) over the projected period.

Conclusions: Clinic drug acquisition price comparison to NADAC database prices serves as an effective benchmark for cost reduction. In order to implement change after expensive drug identification, we developed a decision-tree model that outlines several steps that can reduce drug expenditures. Using this process can potentially save financial resources for medical clinics.

Keywords: free clinics; NADAC; EHHOP; drug acquisition prices; decision model

Introduction

The complexity of healthcare in the United States has led to a large population of uninsured individuals, with at least 10% of the population in thirteen states uninsured in 2016 [2]. As a consequence of lack of insurance, individuals seek less medical attention, may experience poorer medical outcomes in the hospital environment, and are at higher risk for mortality [3–5]. For these reasons, the presence of free clinics in communities where lack of insurance is prevalent cannot be undervalued. These clinics come in several forms, including but not limited to student-run free clinics and volunteer physician clinics. Studies show that free clinics are a dependable resource for services such as physical examinations, blood screenings, vaccinations, and medication distribution [6–8]. Indeed, services provided by free clinics improve medical and financial outcomes for patients and lead to high patient satisfaction rates [9, 10].

In 2010, one study estimated the existence of over 1,000 free clinics in the United states, serving approximately 1.8 million individuals [11]. The mean operating budget of these clinics was $287,810, with almost 60% receiving no government funding [11]. Considering the high expenses surrounding medical care and the provision of pharmaceuticals, this data highlights the restrictive funding environment for free clinics [6]. Restrictive funding in free clinic settings thus necessitates the creation of cost-reduction protocols. While larger medical institutions have several cost-cutting options, such as reducing labor force, adjusting formularies, or changing large-scale operations, free clinics tend to have limited expenditure-reducing capabilities. Interestingly, while high drug prices can severely impact the expenditures of a medical institution, many do not have strict protocols in place to manage pharmaceutical spending. Those that do tend to find alternative suppliers, change prescriber habits, or develop stringent formularies [12].

For this study we looked at the East Harlem Health Outreach Partnership (EHHOP) Clinic at the Icahn School of Medicine at Mount Sinai. EHHOP is a physician-directed, student-run primary care clinic for uninsured adults of East Harlem. As a volunteer-run clinic supported through philanthropy and grants, EHHOP currently provides all patient services, including prescription medications and supplies, to over 280 patients annually, free of charge. Pharmacy-related costs constitute the majority of expenditures at EHHOP. In 2013, EHHOP pharmacy expenditures totaled nearly $27,000; in 2014, this nearly doubled to just over $51,000 despite a nominal change in the numbers of patients served. Review of the 2015 cost data revealed that pharmacy-related costs accounted for 63% ($51,579) of the clinic's total expenditures ($82,502). The increase in cost for various medications was a significant, but not exclusive, contributor to the doubling of expenditures [13]. There have been previous measures to reduce costs for a free clinic setting. One study described a formulary-based mobile application approach to reduce cost by comparing current drug prices, saving up to 30% on single-prescriptions [1]. However, limitations exist within this model ranging from prescriber compliance and bias to simple availability of the medication. Thus, although a provider-based savings program helps the clinic save money, a systemic approach to decrease upfront costs is needed within the small clinic setting.

To address a lack of transparency in national trends of drug acquisition prices, the National Average Drug Acquisition Cost (NADAC) Database was created to systemically compile the prices paid by community retail pharmacies for Medicare-covered outpatient drugs. The average per unit cost of each drug was randomly sampled from pharmacies across all 50 states in the US on a monthly basis. No 340B pricing was included from this sampling, more accurately reflecting the private pharmaceutical supply chain. Cost observations greater than plus or minus two standard deviations from the mean were removed as outliers. Drugs were grouped by their active ingredient, strength, dosage form, and route of administration (grouping generic and brand-name drugs) to analyze pharmaceutically equivalent products. Periodic monthly price fluctuations observed were considered more likely due to changes in the profile of sampled pharmacies than changes in market prices for that drug [14].

Due to EHHOP's high drug expenditures as a proportion of its annual budget (51% of the $136,754 in expenditures for the 2017 calendar year), this study focused on identifying overpriced drugs and finding potential alternative suppliers. In order to accomplish this task, EHHOP drug acquisition costs were benchmarked against NADAC costs. The reason for this comparison is that EHHOP is a hospital-supplied free clinic associated with the Mount Sinai Health System's employee pharmacy, through which the EHHOP receives bulk-ordered medication at cost. Thus, we compared the pharmacy acquisition costs of Mount Sinai's employee pharmacy against the national average of retail pharmacy acquisition costs [15, 16].

After identifying highly-prescribed drugs acquired at a price significantly above the national average, we developed a decision tree model for finding cheaper alternative strategies for drug acquisition. Due to the overwhelming lack of literature in the broad context of the free medical clinic, the cost reduction model outlined in this study was designed to be applicable to free clinics of any form [17].

Methods

The aim of this study was to perform a comprehensive analysis of EHHOP drug purchasing techniques. The NADAC data was used as the control group [18]. Three aspects of drug purchasing at EHHOP were measured against the NADAC dataset (**Figure 1**):

1. Determining any significant price differences between average EHHOP purchasing prices and average NADAC listed prices.
2. Determining significant volatility within EHHOP pricing and measuring statistical correlation/covariance against NADAC volatility to see if EHHOP price changes were market-dependent or independent.
3. Determining potential savings for EHHOP if significantly more expensive drugs were purchased at average NADAC drug prices.

In order to begin analysis, ledger data was gathered on a monthly-basis for the EHHOP clinic from the beginning of January 2014 through the end of December 2017 (see Appendix). Each month was concatenated to create a yearly drug-purchasing profile (see Appendix). The same approach was used for the NADAC data.

The data was then imported into R version 3.4.4 and R Studio Version 1.1.383, where the total pricing data was condensed into a monthly analysis (see Appendix for R packages used). Data consolidation could be performed because the drug prices did not change inter-monthly, but were dynamic intra-monthly. The date ranges of each drug price were then distributed into sub-sets between the NADAC and EHHOP datasets to provide the most precise and fair comparisons between drug prices. This monthly price consolidation further allowed for improved statistical analysis and power.

Drugs were selected if they had been prescribed more than 30 times ($n > 30$) over the course of one year. This approach provided a list of the most-frequently-prescribed drugs for the patients and provider. Forty-six drugs were analyzed against NADAC in this process (Supplementary Table 2) and split into categories of drug type (Supplementary Table 1). Other drugs did not share similar NADAC names and/or did not have sufficient longitudinal data to build statistical power even though they did qualify as $n > 30$ [19]. These drugs were not included in the analysis.

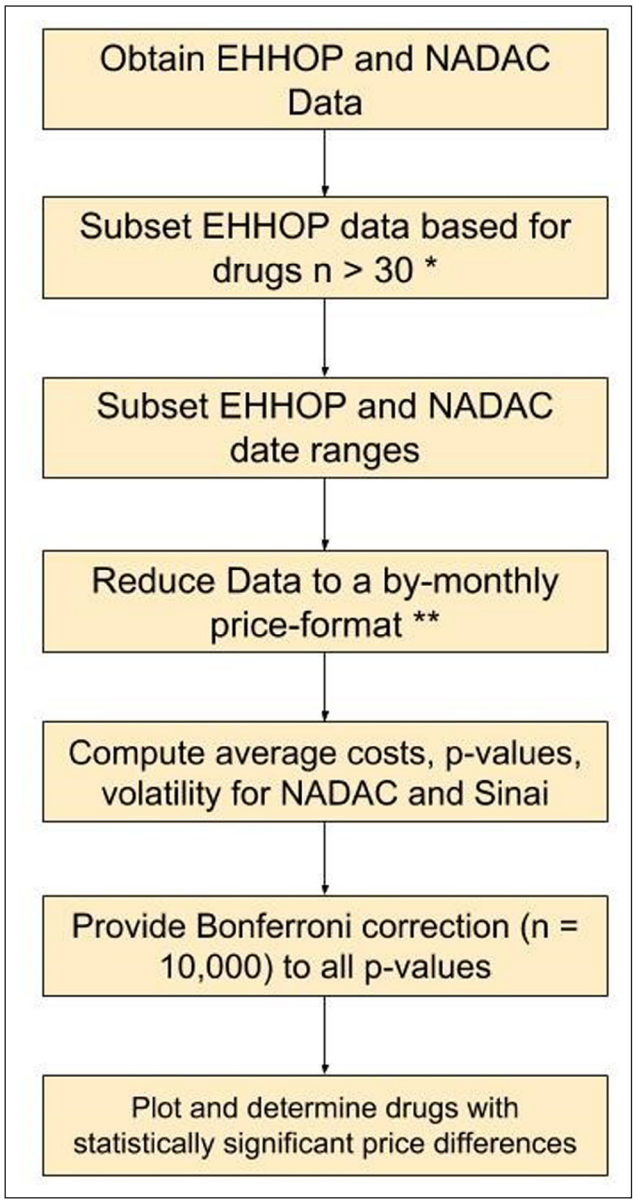

Figure 1: Computational methodology for processing and analyzing EHHOP and NADAC data.
* = Only analyzed drugs that were prescribed more than 30 times within a given year at EHHOP Clinic.
** = The monthly condensed format allowed for a direct comparison (paired t-tests, correlation, and covariance) to be applied to the NADAC and the EHHOP datasets. The fluctuation in drug prices does not change per month, so reducing the matrix to a monthly price-comparison eliminated false-discovery rates due to magnitudinal differences in measurement between the NADAC and EHHOP datasets.

Pricing differences were calculated by taking the average over the sub-set time-course between the NADAC and the EHHOP data. Unpaired t-tests (Student's t-test; significance $p < 0.01$), standard deviations, and the corresponding box plots were calculated using the consolidated monthly datasets. Correlations were calculated using a Pearson's product-moment correlation coefficient (r) with significant correlation ($r > 0.8$ or $r < –0.8$) [20]. Thus, any coefficient of determination greater than ($r^2 > 0.64$) was called significant.

In order to determine potential savings, the EHHOP drugs with a mean value significantly greater than the NADAC value were identified. The average drug prices for these drugs were then adjusted to the corresponding NADAC price and the difference in final EHHOP costs were determined over the timespan of 2014–2017 (Supplementary Table 2).

Results

In order to test the reliability of NADAC as a benchmark for attainable drug acquisition price reduction, we compared a hospital system-supplied free clinic's drug acquisition ledger to NADAC over the period of 2014–2017. Our analysis resulted in a variable distribution of EHHOP advantages over NADAC and vice versa with regards to both unit price aver-

ages and volatility. As seen in **Figure 2**, 36% (16/45) of EHHOP drug price averages were significantly different than the relative NADAC values, with 9% (4/45) significantly more expensive than NADAC and 27% (12/45) significantly cheaper than NADAC (Supplementary Table 2).

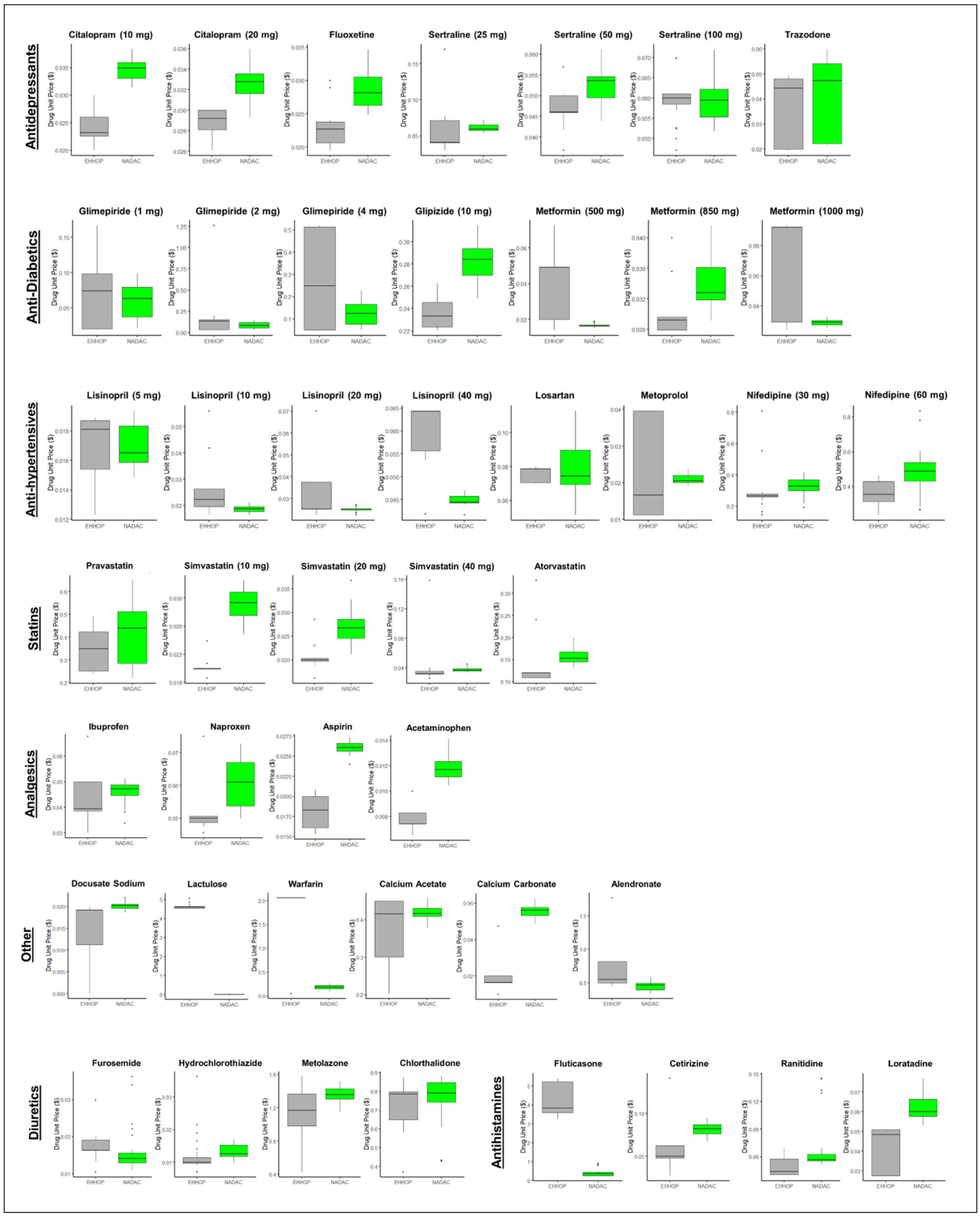

Figure 2: Drug bar graphs showing EHHOP vs NADAC for 45 drugs falling under eight categories: Analgesics, Antidepressants, Antihistamines, Diuretics, Anti-Diabetics, Anti-hypertensives, Statins, and Other. Four drugs were statistically more expensive at EHHOP compared to NADAC [Lactulose (500 mL), Fluticasone (50 mcg), Metformin (500 mg), Metformin (1000 mg)]. Twelve drugs were statistically lower than NADAC [Acetaminophen (325 mg), Aspirin (81 mg), Citalopram (10 mg), Calcium carbonate (1250 mg), Loratadine (10 mg), Simvastatin (10 mg), Simvastatin (20 mg), Glipizide (10 mg), Citalopram (20 mg), Cetirizine (10 mg), Sertraline (50 mg), Fluoxetine (20 mg)].

Because the main goal of this analysis was to identify unnecessary drug expenditures, the next step was to determine whether NADAC benchmarking allowed for the identification of a particular drug dosage that was less expensive and volatile than NADAC. Average drug prices for EHHOP and NADAC from 2014–2017, statistical differences, and correlation (covariance strength) can be seen in Supplementary Table 2. There were twelve drugs with significantly lower prices compared to NADAC [Acetaminophen (325 mg), Aspirin (81 mg), Citalopram (10 mg), Calcium carbonate (1250 mg), Loratadine (10 mg), Simvastatin (10 mg), Simvastatin (20 mg), Glipizide (10 mg), Citalopram (20 mg), Cetirizine (10 mg), Sertraline (50 mg), Fluoxetine (20 mg)] and four with significantly higher costs compared to NADAC [Lactulose (500 mL), Fluticasone (50 mcg), Metformin (500 mg), Metformin (1000 mg)] (Supplementary Table 2).

Correlations were run for all the aforementioned drugs. Four drugs were significantly, positively correlated with NADAC: Metformin (850 mg) (r = 0.83), Chlorthalidone (25 mg) (r = 0.80), Trazodone (50 mg) (r = 0.90), and Pravastatin (40 mg) (r = 0.91).

Discussion

This study resulted in three important findings: four drugs had significantly greater average prices purchased by the EHHOP clinic compared to NADAC, only four drugs had significant correlation (co-variance) with NADAC fluctuations, and high volatility in drug acquisition prices existed across drug classes. Drugs which demonstrated significantly greater average prices when compared to NADAC did not fall into one category. Drugs which demonstrated significantly lower average prices when compared to NADAC were reflected in the "Statins" and "Other" category. The ability for EHHOP to both outperform and underperform against NADAC across drug classes suggests this benchmarking system is realistic for a small clinic application.

Metformin was a significant outlier in drug price and volatility. Metformin (850 mg) was significantly cheaper and less volatile, which was not the situation with Metformin (500 mg) or Metformin (1000 mg) (**Figure 2** – Anti-Diabetics). Metformin (500 mg) and Metformin (1000 mg) had significantly greater volatility than NADAC, as opposed to Metformin (850 mg) (**Figure 3**; (Metformin Standard Deviation = EHHOP vs. NADAC) 500 mg SD = 0.015 vs. 0.001; 850 mg SD = 0.005 vs. 0.004; 1000 mg SD = 0.032 vs. 0.003). Correlation between Metformin (850 mg) and NADAC showed significant covariance (r = 0.83), suggesting that the Metformin price fluctuations seen in the EHHOP data had a strong positive correlation with the fluctuations in price in the NADAC data. The Metformin (500 mg) and Metformin (1000 mg) did not have significant correlation coefficients (r = –0.34 and r = –0.73). Given this data, it can be stipulated that the Metformin (500 mg) and Metformin (1000 mg) were not correlating well with the NADAC and other factors were dictating their price changes. The EHHOP data also elucidated the prescribing habits for different Metformin doses. Even though Metformin (500 mg) was prescribed over 16 times more frequently than Metformin (850 mg) (851 vs 51 prescriptions respectively) and over 8 times more frequently compared to metformin (1000 mg) (851 vs 102 prescriptions respectively), Metformin (500 mg) demonstrated the most volatile pricing. At larger pharmacies such as CVS, however, equally higher demand exists for the 850 mg and 1000 mg dosages [21]. Thus, differences between EHHOP and NADAC prices may be related to opposing dosage preferences. Ultimately, the reason for Metformin (500 mg) and Metformin (1000 mg) price fluctuation is currently unknown. According to a study by the National Organization for Research at the University of Chicago (NORC), which surveyed 712 US community hospitals, price increases for inpatient drugs appeared random and unpredictable while leading to difficulties managing overall hospital costs. The results of this NORC study mirror the high variability of certain drugs acquired by Mount Sinai for EHHOP; however, the bulk-ordered prescriptions with significant buyer power showed that it is possible to mitigate the effects of random drug fluctuations [22].

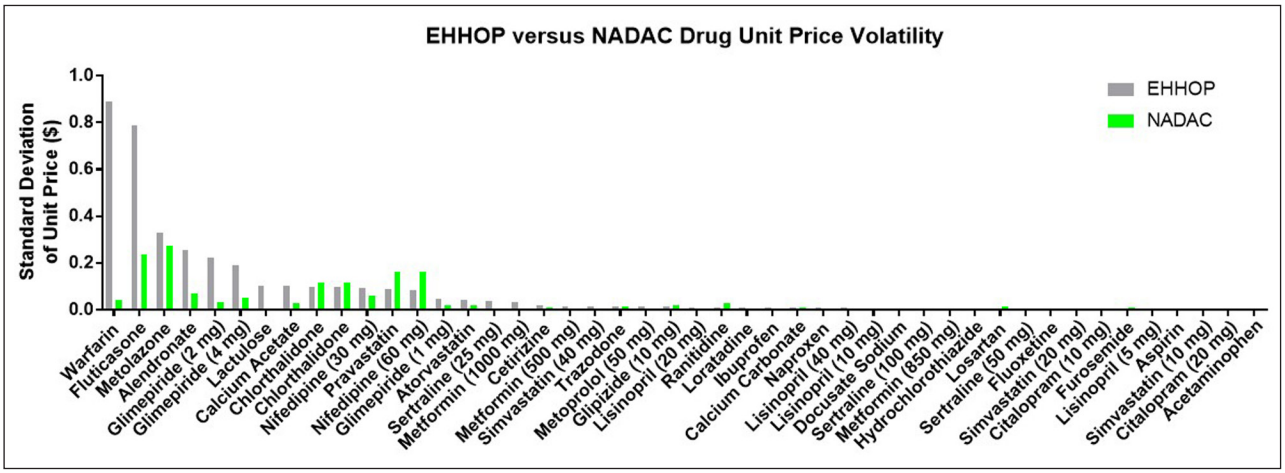

Figure 3: Comparison of standard deviation of monthly drug unit prices led to the finding that EHHOP has several drugs that are more volatile that NADAC, such as Warfarin (7.5 mg) and Fluticasone (50 mcg). However, EHHOP acquisition volatility did outperform NADAC with certain drugs, such as Pravastatin (40 mg).

Interestingly, nearly all the drugs (three out of four) with an average price significantly greater than NADAC were negatively correlated with the direction of NADAC price fluctuations: Metformin (1000 mg) ($p = 0.004$, $r = -0.74$), Metformin (500 mg) ($p = 9.24E{-}07$, $r = -0.35$), and Fluticasone (50 mcg) ($p = 1.15E{-}15$, $r = -0.19$). This negative correlation against NADAC could be due to a number of factors, such as a lack of purchasing power or institutional prescribing habits. Other drugs with negative correlations (Calcium acetate (667 mg), Alendronate (70 mg), Metoprolol (50 mg)) did not demonstrate a significant difference in price (all p values = 1.000).

A large impediment to cost reductions in the medical setting today is lack of physician education regarding pharmaceutical pricing. For example, one review found that only 31% of the physicians, trainees, or medical students analyzed across twenty-four studies were accurate within 20–25% of the true cost of medications when surveyed about prescription prices [23]. Interestingly, doctors overestimated the cost of inexpensive drugs and underestimated the cost of expensive drugs [23, 24]. For this reason, institutions such as the University of Michigan developed an inpatient pharmacy cost tracker to better analyze drug use and expense data, which could result in better prescribing practices and reduced hospital expenditures [25]. Alternatively, some clinics and hospital systems employ pharmacy benefit management companies (PMC) to streamline and improve their purchasing techniques. However, one of the principle concerns with using a PMC in a clinic is cost-effectiveness for small to medium hospitals. The model proposed in this study will be freely available for clinics to use without needing to employ a PMC while gaining insight into how their drug purchases compare nationally [26].

While larger institutions may have protocols in place, such as constantly improving electronic prescribing with formulary decision support, this often may not be the case for smaller clinics, such as free clinics [27]. As a result of this lack of resources and structure, it is necessary to employ a standardized approach for identifying unnecessary drug expenditures and finding alternative acquisition routes when these drugs are identified [28]. Here, we propose the use of publicly available NADAC data to perform such an analysis at no cost, thus reducing the financial burden on small clinics. However, finding alternative drug purchasing routes can be difficult. Thus, we propose a drug-dependent decision model that walks the clinic prescriber through cost saving measures (**Figure 4**).

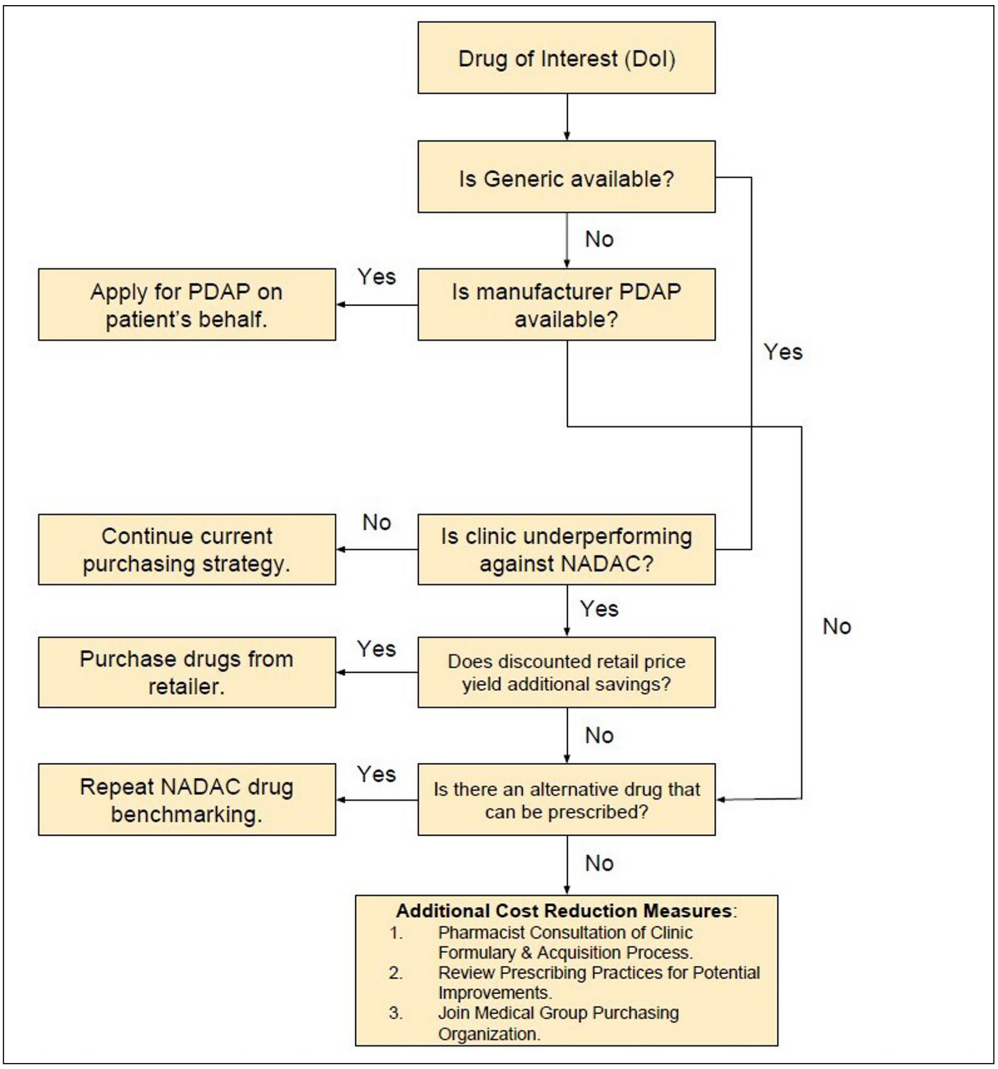

Figure 4: This drug-dependent decision model provides several alternative acquisition routes and cost reduction measures, including patient drug assistance programs (PDAP), discount retailers, and clinic efficiency strategies.

In this model (**Figure 4**), step one involves differentiating between brand name and generic drugs prescribed in the clinic. If a generic version of a prescribed brand name drug exists, the clinic should consider transitioning to said generic. If that is not a viable option, the clinic can consider alternative drug acquisition routes, such as patient drug assistance programs (PDAPs), through which clinics can apply for the provision of free or discounted pharmaceuticals from manufacturers. If the PDAP route is not available, the clinic can consider substituting this particular drug with another compound within the same drug class (provided this adds no risk to the patient), preferably a generic medication. Alternatively, if the clinic currently prescribes a generic, it can then perform a historical price comparison to NADAC. If the drug is significantly more expensive, the clinic can determine whether discounted retail prices (after retrieving coupons from sources such as GoodRx.com) provide adequate savings. If this is not the case, the clinic can try to select an alternative drug in the same class that could outperform NADAC based on the clinic's drug acquisition strategy. Finally, the clinic can take any of the three following routes for further expense reductions: recruit a pharmacist for consultation of clinic drug purchasing practices, adjust physician prescribing practices, or attempt to join a medical purchasing group organization [23, 29, 30].

Ultimately, this model aims to improve purchasing decisions at a higher level to help physicians prescribe appropriate medications at fair prices. This model combined with price comparisons of current medication prices will save clinics money and increase access to prescription drugs. Incorporating this code and methodology into a pre-existing formulary could provide healthcare providers real-time data before they prescribe any medications. Patients could have lower copayments and physicians could actively and intelligently prescribe lower-cost prescriptions to their patients. At a more administrative scale, this model could provide fair price points for highly-prescribed medications and could be used as an educational tool to promote cost-effective prescription habits. We believe this strategy is generalizable to health-system affiliated small clinics and will further serve as a method of identifying potentially unsustainably high drug prices for non-health system affiliated small clinics.

Possible limitations may arise due to the small size of certain healthcare providers. If a private clinic with no significant purchasing power used this methodology, they may not be able to achieve the same benefits a larger hospital system/healthcare network could due to lack of purchasing power against manufacturers or wholesalers. These clinics should test the decision-tree model over a timeline similar to that used in this study in order to decide whether this model proves to be financially viable. It may be found that obtaining prescriptions from multiple vendors for a small clinic is not as cost-effective or efficient as simply having a principal provider.

Future studies should look at the possible geographic variations in wholesale prices (i.e. pharmaceutical prices may significantly differ within Manhattan, New York compared to Fargo, North Dakota). It may be observed that localized geographic pricing studies are more representative rather than comparing EHHOP prices against the NADAC. While association with a large medical system could provide some form of purchasing power, it is possible that potential socioeconomic and demographic differences between a hospital system and its surrounding community might result in smaller-sized purchases of drugs used primarily by an associated free clinic. This, in turn, could negate any financial advantages of purchasing drugs through the employee pharmacy.

Conclusions

This study resulted in three important findings: four drugs had significantly greater average prices purchased by the EHHOP clinic compared to NADAC, only four drugs had significant correlation (co-variance) with NADAC fluctuations, and high volatility in price for drugs existed across drug classes.

The methodology of this study can be applied to clinics and hospital systems throughout the United States. A decision tree (**Figure 4**) can be used to help clinic/hospital/pharmacy administrators compare their ledger data against the national average and leverage buying power to conserve finances. This study can also be implemented in physician educational programs to augment the knowledge-base of pharmaceutical prices within the physician population.

Data Accessibility Statement

R scripts for analysis available on GitHub, as well as a sample of EHHOP ledger data and NADAC data for reproducibility.

List of abbreviations

EHHOP: East Harlem Health Outreach Program
NADAC: National Average Drug Acquisition Cost
NORC: National Organization for Research at the University of Chicago
PMC: Pharmacy Benefit Management Company
PDAP: Patient Drug Assistance Program

Additional Files

The additional files for this article can be found as follows:

- **Appendix.** R packages used. DOI: https://doi.org/10.29024/jsim.21.s1
  plyr_1.8.4
  Tools_3.4.4

scales_1.0.0
reshape2_1.4.3
ggplot2_3.0.0
dplyr_0.7.6
zoo_1.8-3

- **Supplementary Tables.** Tables 1 and 2 describe how drug categories were assigned from the EHHOP ledger and which of those drugs had a significantly different price compared to the NADAC. DOI: https://doi.org/10.29024/jsim.21.s2

Ethics and Consent

Not applicable as data was fully de-identified. All data was gathered and analyzed with the permission of the EHHOP clinic. The EHHOP clinic has consented to the publication of this study.

Acknowledgements

We would like to thank the EHHOP technology team for compiling and providing the drug acquisition ledger data. We would like to acknowledge Mount Sinai for its drug acquisition transparency and provision of drugs at cost to EHHOP.

Competing Interests

The authors have no competing interests to declare.

Author Contributions

AJW performed data analysis in R, conceptualized project, and contributed to writing the paper. RAS conceptualized the project and contributed to writing the paper. BS, SB, JAM, and AL provided the EHHOP ledger data and assisted in final conceptualization of project. YSM provided oversight and mentorship for this project.

Andrew Warburton and Randal Serafini authors contributed equally to this manuscript.

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How to cite this article: Warburton A, Serafini R, Shuham B, Leader A, Barazani S, Moser J-A and Meah Y. Leveraging NADAC to Steer Drug Formularies in Resource-Limited Clinics. *Journal of Scientific Innovation in Medicine.* 2019; 2(1): 5. DOI: https://doi.org/10.29024/jsim.21

Submitted: 20 June 2019 **Accepted:** 13 August 2019 **Published:** 30 August 2019