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The Impact of Enhancing Quality of Provider Practices for Older Adults in the Emergency Department (EQUiPPED) on Potentially Inappropriate Medications (PIMs)

By

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Degree to be awarded: Master of Public Health

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B.Sc.
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Abstract

The Impact of Enhancing Quality of Provider Practices for Older Adults in the Emergency Department (EQUiPPED) on Potentially Inappropriate Medications (PIMs)
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Background: The elderly play an important role in health care. One of the biggest issues of the health care for the elderly is medical prescriptions. Some medications perform well in the general population while they would cause side effects that outweigh the benefits in the elderly, which are called potentially inappropriate medications (PIMs). PIMs were prescribed very often in the emergency department (ED), where the pace is fast and chaotic. The program "Enhancing Quality of Provider Practices for Older Adults in the Emergency Department (EQUiPPED)" was created with the hope to reduce the use of PIMs. The previous study found it effective in VA settings. We implemented EQUiPPED and analyzed its performance on reducing PIMs count/rate in the first non-VA setting in this paper.

Methods: The intervention include provider education, EHR-based clinical decision tools and provider feedback. The intervention was divided into three periods: Pre-Intervention, Post- Intervention and Intervention (five months). Both weekly- and monthly-based PIMs rates were calculated, and the changing trends were analyzed. Bonferroni adjusted proportion test and exact ratio test were conducted to find the unadjusted effect of EQUiPPED on PIMs rate. Several regression models for count outcomes were fitted and compared. A regression-based test was used to determine the adjusted effect on the final model.

Results: The EQUiPPED program successfully was implemented. The Bonferroni adjusted proportion test indicated significant differences between both Pre-Intervention vs Post-Intervention and Intervention vs Post-Intervention (P-value both < 0.001). The exact rate ratio test gave us similar outcome: with an estimated ratio of 2.51(95% confidence interval 2.30 – 2.73, P-value < 0.001). Negative binomial model was selected given the outcome of Vuong test, dispersion parameter, AIC and BIC. Two models with covariates selected using different criteria were finally fitted. The adjusted effects of EQUiPPED period showed no signs of effectiveness (P-value = 0.40 and 0.44 respectively for these two models)

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Contents:

1. Introduction:

In health care, the elderly play an important role because they are a vulnerable and growing population. The personal health care expenditure by older people (defined as persons aged 65 years old or greater) is 33.9 percent ($744 billion out of $2,193 billion)[1] of all the personal health care costs in 2010. Moreover, people aged 55 and over account for over half of total health spending[2]. The rate of emergency department (ED) visits for people aged 65+ is 56,803 per 100,000 population in 2015, accounting for approximately 32% of all the visits[3]. Within the Veterans Health Administration, this percentage was predicted to increase to 40%[4] in 2015. Promoting health care service for the elderly is thus an effective way to improving the overall health care quality.

Additionally, the world's population is also increasingly aging, making the health care for the older population extremely urgent. The last one and a half decades witnessed a growing number of older people: 6.9% of people worldwide (419 million) aged 65+ in 2000[10] while this percentage rose to 8.5% ($617 million) in 2015[5]. In the United States, this trend is even greater with 15.2% ($49.2 million) in 2015[6] compared to 12.4% ($35.0 million) in 2000[7]. With continuously increasing life expectancy, the older population continues to grow. The projected older population in 2050 is nearly 17% (1.6 billion) around the world[5] and about 22% (83.7 million) in the US[8], which almost doubled the number in 2015. Thus, as a result, more efficient healthcare systems and processes are necessary for senior citizens.

Older patients often have different clinical manifestations than younger adults as apparent in clinical symptoms and signs, co-morbidities, more complications, etc. making the treatment of them more complicated and difficult. One of the biggest areas of concern is medical prescriptions. In the Emergency Department (ED), these differences can be magnified due to the fast-paced, chaotic environment of this health care setting. Given physiological changes like reduced kidney function, altered pharmacokinetics and pharmacodynamics and degenerated cognitive function of the elderly, older patients are at increased risks of adverse drug reactions (ADRs) due to medication[9]. Medications found to cause side effects that outweigh the benefits in the older patients are called potentially inappropriate medications (PIMs). These medications compose the Beers criteria[10]. The Beers criteria were developed by Dr. Beers, originally published in 1991[11] and most recently revised in 2015[12]. The Beers criteria PIMs, hereafter called PIMs, continue to be prescribed as treatment for many patients, despite the safety risk to this patient population. PIMs have been found to be associated with poor health outcomes and ADRs, including confusion, falls, and mortality[11-13]. Thus, the avoidance of PIMs improves prescribing practice and will lead to higher quality care for older adults.

The program "Enhancing Quality of Provider Practices for Older Adults in the Emergency Department (EQUiPPED)" was created with the hope to reduce the use of PIMs. EQUiPPED is a multicomponent quality improvement (QI) program combining provider education, electronic health record (EHR)-based clinical decision support tools, individual provider feedback and program evaluation with peer benchmarking.

EQUiPPED was first piloted in eight Veterans Affairs (VA's) EDs, aiming to decrease the use of PIMs[14].

Results of this pilot study reported significant reduction in PIM prescriptions[14] in VA settings. Four VA sites implemented EQUiPPED was studied: At site 1, the PIM rates reduced from 11.9% before the intervention to 5.1% after the intervention; At site 2, it reduced from 8.2% to 4.5%; At site 3, it reduced from 8.9% to 6.1%; At site 4, it reduced from 7.4% to 5.7%. Additionally, Dr. Stevens and his team fitted four Poisson regression models at each site with PIMs rate as the dependent variable, EQUiPPED period (before or after the program implementation) as the only independent covariate and the number of prescriptions adjusted as offset. All four coefficients of EQUiPPED period showed statistically significant outcome. In this study, we would analyze the prescription data at Grady Memorial Hospital, the first site to implement this program outside of the VA system, to further study the impact of EQUiPPED on PIMs rate.

2. Methods:

2.1. Setting and Interventions:

Grady Memorial Hospital is a county funded hospital with residency training programs such as emergency medicine located in Atlanta, GA. The site implemented EQUiPPED interventions including provider education, electronic health record (EHR)-based clinical decision support tools and individual provider feedback and program evaluation with peer benchmarking. The provider education was implemented from August 1st, 2016 to March 31st, 2017. The provider feedback started from August 1st, 2016 ended in September 30th, 2018. The EHR-based tools were implemented from August 1st, 2016 and are still in use. The Provider survey was conducted at the end of the implementation period to collect demographic information as well as opinion of provider's clinical environment and knowledge of PIMs.

2.2. Provider education:

A presentation entitled "Principles of Prescribing for Older Adults" was provided by the EQUiPPED team to staff providers and ED residents. Clinical pharmacists were offered support to complete training and certification in geriatric pharmacotherapy. Reminder cards with a list of top PIMs were placed at provider computer workstations.

2.2.1. EHR-based clinical decision support tools:

EPIC™ electronic health record is one of the top 5 popular electronic health record (EHR)'s used nationally[17]. The EQUiPPED team developed templates for geriatric outpatient pharmacy order sets for common ED discharge diagnoses among older adults with dose adjustments for renal impairment, point-of-prescribing education regarding medications to avoid, and links to synthesized geriatric content within EPIC system. The order sets encourage safer medications and was the first order sets focused on medication safety for older adults discharged from the ED. Additionally, Best Practice Alerts (BPAs), a pop-up system which will fire when an order considered inappropriate by the pre-defined program, implemented into the EPIC^{TM} system was used to promote safer medication as well.

2.2.2. Provider feedback:

Staff providers were required a monthly audit and feedback of individual prescribing patterns and received anonymous peer benchmarking comparing individual performance with that of other ED providers at the same site[18,19]. The feedback was a one-on-one meeting with a follow up email detailing the prescribing patterns. The feedback was used to improve provider education and to optimize the EHR-based system.

2.3. Data collection and measures:

Prescribing data from August 1st, 2016 to Sep 30th, 2018 were collected for analysis at a monthly rate and maintained in a Redcap database at Emory. The prescribing data were divided into three periods: Pre-intervention (May 1st, 2016 to October 31st, 2016), Intervention (November 1st, 2016 to March 31st, 2017) and Post-intervention (April 1st, 2017 to September 30th, 2018). As described before, PIMs were defined by the Beers criteria (revised in 2015[5]). Our primary outcome of interest was the rate of PIMs prescribed for people aged 65+ discharged from the ED in the three periods, especially the rate of PIMs before the implementation of EQUiPPED and post intervention. Provider characteristics were collected in the survey at the end of the implementation of EQUiPPED.

2.4. Data analysis:

PIMs rate was calculated by the number of PIMs divided by the number of all prescriptions. Both weekly- and monthly-PIMs rate were calculated. Trends were compared through figures. A Bonferroni adjusted test of proportions was performed to compare the PIMs rate. An exact rate ratio test was performed to confirm the difference between the rate of PIMs before the first implementation of core EQUiPPED interventions and five months after it. In order to get the adjusted effect of EQUiPPED periods, regression models were fitted and model selection on both modeling methods and covariates were conducted.

2.4.1. Model selection on different modeling methods:

Poisson regression can be used to model count data. However, it has very strict assumptions. One that is often violated is the distributional assumption that the mean equals the variance, which, when violated, is known as overdispersion. Another is that sometimes the variance of count outcome of interest is too large because there are many zeroes as well as a few very high values. This is called excess zeroes. Due to overdispersion and excess zeroes of the data, we fitted five different models with PIMs rate as the dependent variable, EQUiPPED period (before or after the program implementation) as the only independent covariate and the number of prescriptions adjusted as offset:

Poisson regression:

Let Y refers to the number of PIMs. Z refers to whether it's at least five months prior to first EQUiPPED intervention (0) or at least five months after the EQUiPPED intervention (1). The following Poisson regression model was fitted:

$\Pr(Y = y_i \mid \mu_i) = \frac{\mu_i^{y_i}\exp(-\mu_i)}{y_i!}$

Where $\text{Log}(\mu_i) = \beta_0 + \beta_1 Z_i$

The β_1 here represents the log of PIMs count after the EQUiPPED intervention divided by PIMs count before the EQUiPPED intervention. A β_1 equals 0 means there is no difference between the PIMS count before and after the EQUiPPED program, indicating EQUiPPED couldn't help to decrease the number of PIMs. A hypothesis test (null hypothesis: $\beta_1 = 0$ vs alternative hypothesis: $\beta_1 \neq 0$) was conducted to check the impact of EQUiPPED.

Poisson regression with offset:

Poisson regression is typically used to model count data. However, the number of prescriptions one provider prescribes varies so that it may be more relevant to model PIMs rates rather than PIMs counts. Let C refers to the total number of prescriptions one provider prescribe. A Poisson regression model with an offset was fit:

$\Pr(Y = y_i \mid \mu_i) = \frac{\mu_i^{y_i}\exp(-\mu_i)}{y_i!}$

Where $\text{Log}(\mu_i) = \text{Log}(C) + \beta_0 + \beta_1 Z_i$

The β_1 here represents the log of PIMs rate after the EQUiPPED intervention divided by PIMs rate before the EQUiPPED intervention. A β_1 equals 0 means there is no difference between the PIMS rate before and after the EQUiPPED program, indicating EQUiPPED couldn't help to improve the prescription quality. A hypothesis test (null hypothesis: $\beta_1 = 0$ vs alternative hypothesis: $\beta_1 \neq 0$) was conducted to check the impact of EQUiPPED. A score test for over-dispersion with the mean-variance equality null hypothesis was conducted to test for over-dispersion[20].

Negative binomial regression:

Negative binomial regression is considered another method to deal with overdispersion[20]. The following Negative binomial regression model was fitted:

$$\Pr(Y = y_i \mid \mu_i, \alpha) = \frac{\Gamma(y_i + \alpha^{-1})}{\Gamma(y_i + 1)\Gamma(\alpha^{-1})}\left(\frac{\alpha^{-1}}{\alpha^{-1} + \mu_i}\right)^{\alpha^{-1}}\left(\frac{\mu_i}{\alpha^{-1} + \mu_i}\right)^{y_i}$$

Where $\mathrm{Log}(\mu_i) = \mathrm{Log}(C) + \beta_0 + \beta_1 Z_i$

The β_1 here represents the log of PIMs rate after the EQUiPPED intervention divided by PIMs rate before the EQUiPPED intervention. A hypothesis test (null hypothesis: $\beta_1 = 0$ vs alternative hypothesis: $\beta_1 \neq 0$) was conducted to check the impact of EQUiPPED.

Zero-inflated Poisson regression (ZIP):

Zero-inflated Poisson (ZIP) regression model was proposed to account for overdispersion. A logit (or log odds) distribution is used to model the conditional probability of having zero PIMs, and a Poisson distribution is used to model the conditional distribution of positive-valued PIMs. The following ZIP model was fitted:

$$\Pr(Y = y_i | \mu_i, \pi_i) = \begin{cases} \pi_i + (1-\pi_i)\, exp(-\mu_i)\,, & if \text{ yi} = 0 \\ (1-\pi_i)\, \frac{{\mu_i}^{y_i} exp(-\mu_i)}{y_i!}, & if \text{ yi} \neq 0 \end{cases}$$

Where Log(μ_i) = Log(C) + β_0+$\beta_1 Z_i$ and

$$\text{Log}(\frac{\pi_i}{1-\pi_i}) = \gamma_0 + \gamma_1 Z_i$$

The β_1 here represents the log of PIMs rate after the EQUiPPED intervention divided by PIMs rate before the EQUiPPED intervention. A hypothesis test (null hypothesis: $\beta_1 = 0$ vs alternative hypothesis: $\beta_1 \neq 0$) was conducted to check the impact of EQUiPPED. The Vuong test[19] would be used to compare a Poisson model and a zero-inflated Poisson model fitting.

Zero-inflated Negative binomial regression (ZINB):

Similarly, the following zero-inflated Negative binomial regression was fitted:

$$\Pr(Y = y_i | \mu_i, \pi_i, \alpha) = \begin{cases} \pi_i + (1-\pi_i)\, \frac{\Gamma(\alpha^{-1})}{\Gamma(1)\Gamma(\alpha^{-1})} (\frac{\alpha^{-1}}{\alpha^{-1} + \mu_i})^{\alpha^{-1}} & , if \text{ yi} = 0 \\ (1-\pi_i)\, \frac{\Gamma(y_i + \alpha^{-1})}{\Gamma(y_i + 1)\Gamma(\alpha^{-1})} (\frac{\alpha^{-1}}{\alpha^{-1} + \mu_i})^{\alpha^{-1}} (\frac{\mu_i}{\alpha^{-1} + \mu_i})^{y_i}, & if \text{ yi} \neq 0 \end{cases}$$

Where Log(μ_i) = Log(C) + β_0+$\beta_1 Z_i$ and

$$\text{Log}(\frac{\pi_i}{1-\pi_i}) = \gamma_0 + \gamma_1 Z_i$$

The β_1 here represents the log of PIMs rate after the EQUiPPED intervention divided by PIMs rate before the EQUiPPED intervention. A hypothesis test (null hypothesis: $\beta_1 = 0$ vs alternative hypothesis: $\beta_1 \neq 0$) was conducted to check the impact of EQUiPPED. The Vuong test[19] would be used to compare a Negative binomial model and a zero-inflated Negative binomial model fitting.

Hurdle regression:

Similar to zero-inflated model, a hurdle model could be treated as a binomial process generating zero and a zero-truncated Poisson process generating non-zero outcomes. The following hurdle model was fitted:

$$\Pr(Y = y_i \mid \mu_i, \pi_i) = \begin{cases} \pi_i, & if \text{ yi} = 0 \\ (1-\pi_i)\frac{\mu_i{}^{y_i}}{(e^{\mu_i}-1)y_i!}, & if \text{ yi} \neq 0 \end{cases}$$

Where $\text{Log}(\mu_i) = \text{Log}(C) + \beta_0 + \beta_1 Z_i$ and

$$\text{Log}\left(\frac{\pi_i}{1-\pi_i}\right) = \gamma_0 + \gamma_1 Z_i$$

The β_1 here represents the log of PIMs rate after the EQUiPPED intervention divided by PIMs rate before the EQUiPPED intervention. A hypothesis test (null hypothesis: $\beta_1 = 0$ vs alternative hypothesis: $\beta_1 \neq 0$) was conducted to check the impact of EQUiPPED.

After fitting these models, we then selected a modeling method based on the following information criteria: Two vuong tests were used to compare between Poisson model and ZIP model and Negative binomial model and ZINB model. The dispersion parameter α was used to compare between Poisson model and Negative binomial model and ZIP model and ZINB model. AIC and BIC were used to assist the decision on modeling method. The kernel density estimate of predicted values given by these five models was then plotted and compared to the kernel density estimate of observed values to check whether these models imply marginal distributions that look like the marginal distribution of the observed outcome. If a model picked up by AIC and BIC looked reasonable given this criterion, we used backward covariates selection with AIC and BIC as the criteria for the given covariates were then performed using the selected model. The adjusted effect for EQUiPPED period on the final model(s) was then tested and compared to the unadjusted effect.

All analyses were conducted with R (Version 3.4.4). All hypothesis tests were performed at a 0.05 α level.

3. Results:

3.1. Demographic characteristics:

36 medical service providers were enrolled into this program. The mean practice experience of all providers was 10.69 ± 8.63 (range from 0 to 40) years. These providers had an average of 7.66 ± 7.07 years of ED experience, ranging from 0 to 21 years at the beginning of the study. The percentage of female providers was 54.3%. Most of the providers were physicians (69.4%). More baseline demographic characteristics of the providers are presented in Table 1.

42,284 prescription records were collected. Among them 3,960 were prescribed before the intervention and 30,411 were prescribed five months after the implementation of EQUiPPED. There were 35,339 records categorized as no PIMs (I), 2,474 as PIMs with no conditions (II), 4,347 as PIMS with conditions and conditions met (III) and 73 as PIMs with conditions and conditions were not met or could not be determined (IV). Figure 1 showed the distribution of the number of PIMs and all prescriptions.

3.2. The implementation of EQUiPPED:

During the first five months of EQUiPPED, 25 providers (65.8%) had used the “ED Geriatric Discharge Order Set” and 24 (63.2%) had received a face-to-face feedback. 24 out of 38 providers claimed they had changed their approach to prescribing as a result of the EQUiPPED program. A significant positive correlation had been detected between the use of “ED Geriatric Discharge Order Set” and the claim they had changed their approach to prescribing as a result of the EQUiPPED program with a 0.501 correlation coefficient (P-value <0.001). Another positive significant correlation was detected between the face-to-face feedback and the change of prescribing approach with a 0.299 correlation coefficient (P-value = 0.014).

3.3. Unadjusted effectiveness of EQUiPPED:

The previous study reported the unadjusted effectiveness. So, we checked the unadjusted results first. The mean PIMs rate by month before the implementation of EQUiPPED was 17.5 ± 1.09% while five months after the implementation, the average PIMs rate by month was 15.6 ± 1.79%. The overall PIMs rate before and after the EQUiPPED implementation were 17.5% and 7.9%, respectively. A slight decrease trend for PIMs rate could be seen from Figure. 2 and Figure. 3, which showed the PIMs rate change in months and weeks respectively. When unadjusted, both the Bonferroni corrected test of proportion and the exact rate ratio test indicate significant difference between the PIMs rate before and after the EQUiPPED implementation.

3.4. Modelling method selection:

The mean number of PIMs per month was 34.58. The sample variance was 1463.20, suggesting over-dispersion. Indeed, an over-dispersion test for the Poisson regression model rejected the null hypothesis of equal mean and variance ($P < 0.01$). The alpha dispersion parameter for Negative binomial model is estimated to be 17.782, indicating that the Negative binomial model might be better than Poisson model.

The Vuong test for zero-inflated Poisson regression model versus Poisson regression indicated the zero-inflated Poisson model fit worse than the regular Poisson model (P-value = 0.002). The Vuong test for zero-inflated Negative binomial regression model versus Negative binomial regression model suggested the Negative binomial model was better than the zero-inflated model (P-value = 0.005). Table 2 shows the AIC and BIC statistics for the six fitted models. The Poisson regression without offset fitted the worst with much worse information criteria compared to others followed by the regular Poisson regression. The Negative binomial seems the best with the lowest AIC and BIC.
Based on the alpha dispersion parameter, over-dispersion test, Vuong test and statistics of the goodness of fit, Negative binomial model was an optimum model fitting the count of PIMs and would be selected to conduct the following covariate selection.

Figure 4 shows the kernel density estimates of predicted values of five fitted models and the kernel density estimation of observed values. The Poisson regression without offset predicts the PIMs counts while others predicts the PIMs rates. As a result, it is not showed on the graph. All of the models predicted very similarly and was often overlapping, especially the Poisson model and zero-inflated Poisson one and the Negative binomial model and the zero-inflated Negative binomial one. Among these four models, the Negative binomial model and the zero-inflated Negative binomial model seemed to generate the most similar estimation of kernel density of prediction values to the kernel density of observed counts. They outperformed the hurdle model, Poisson model and zero-inflated Poisson model. Based on these results, we selected the Negative binomial model.

3.5. Model selection of Negative binomial model and adjusted effectiveness:

Backward selection was used to select adjusted variables in order to get an adjusted effect for EQUiPPED period, which was forced into the model. AIC and BIC were used as criteria for model selection separately. Potential covariates to be selected are as follows: gender, age group (<30, 30-39, 40-49, 50-64), ethnicity, race, professional background (General Medicine, Emergency Medicine, Toxicology Fellowship, Geriatrics Fellowship, Other Established Specialists, Other training), years of experience in medical practice, years of experience in emergency department, hours per week in emergency department, usual shift length. When using AIC as the criteria, general medicine professional background, gender, ethnicity, years of experience in emergency department and time per week in emergency department were selected (Model 1). Gender, general medicine professional background and time per week in emergency department were included in the model selected by BIC (Model 2). Table 3 showed the regression coefficients and other basic features of Model 1 and Model 2.

Unfortunately, in both the selected models, the t test for the null hypothesis that EQUiPPED coefficient of intervention equaled zero did not reject the null hypothesis, providing no evidence of an association between EQUiPPED period and number of PIMs ($p>.05$) after adjusting the potential covariates and offsets.

4. Discussion:

Figure 2 and Figure 3 showed the change trend of PIMS rate in months and weeks respectively. The PIMs rate increased a little when the EQUiPPED firstly being conducted. A possible explanation is that providers had to get used to the new program so that they were distracted, which resulted in the slight increase on PIMs rate. During the implementation of EQUiPPED, generally speaking, the raw PIMs rate appeared to decreas, indicating the possibility that the EQUiPPED program successfully reduced PIMs rate. This trend continuous to month 19, when the PIMs rate reached its valley value. However, the PIMs rate dramatically increased at month 20, the March of 2018. Our analysis showed that the PIMs rate fluctuates greatly month to month. The ED is a dynamic environment, one in which providers do not work on a consistent basis. Additionally, the influx of students and residents result in a constantly changing workforce within the ED. Changing trend in PIMs in weeks showed so much noise and so many rises and downs that it was hard to detect any evidence from this figure. Considering the periodic noise, it’s hard to identify valid evidence of EQUiPPED by just observing the plots.

Count outcomes are often used in clinical research but are often inappropriately treated as continuous outcomes[23]. In this study, we fit five different models that are commonly used to fit count outcomes: Poisson regression model, zero-inflated Poisson regression model, Negative binomial model, zero-inflated Negative binomial model and hurdle model. The Negative binomial model appear to provide the best fit of the PIMs data.

Given the fact that there was evidence of over-dispersion, it is not surprising that the Negative binomial provided better fit than Poisson model, since it's better in dealing with over-dispersion. It's interesting that Vuong tests for both Poisson model vs. zero-inflated Poisson model and Negative binomial model vs. zero-inflated Negative binomial model supported the non-zero-inflated model. We could see from Figure 4 that all the models predicted more zeroes than the observed one. Zero-inflated models, while often necessary to account for excess zeros, may in fact lead to too many zeros. This situation, which is called zero-deflation, is less commonly discussed in the literature than zero-inflation. Dietz[24] et al. and Angers[25] et al. discussed this issue and proposed a zero-modified model for modelling both zero-inflated and zero-deflated data, which has the ZIP and zero-deflated Poisson (ZDP) distribution as particular cases. This model, as well as the ZDP model, might be more appropriate to fit the PIMs data.

Different selection criteria chose different models. Using AIC as the criteria, general medicine professional background, gender, ethnicity, years of experience in emergency department and time per week in emergency department were selected while using BIC or P-value as the criteria, gender, general medicine professional background and time per week in emergency department were included in the model. As for the gender, females tended to prescribe fewer PIMs than males. Providers with general medicine professional background prescribed more PIMs than other professional backgrounds (mainly from emergency medicine). Non-Hispanic population tended to have fewer PIMs than Hispanics. The more hours per week a provider worked in emergency department, s/he would prescribe more PIMs.

Additionally, the estimated kernel density of prediction values generated by regression models fitted well with the observed one at lower number of prescriptions but differs a lot at higher number of prescriptions. This might because the lack of information on higher number of prescriptions. With additional post intervention EQUiPPED data, we could get more large-scale prescriptions and the estimate would be more precise.

It was easily noticed that the unadjusted results and adjusted outcomes from the adjusted Negative binomial regression contradicted each other on the effect of EQUiPPED period on PIMs rate. The unadjusted result we got is consistent with the former study[10], where Poisson regression with only number of prescriptions adjusted as offset was used. This pilot study implemented EQUiPPED in 4 VA sites and found that unadjusted coefficients of EQUiPPED period (before the implementation of EQUiPPED and six months after it) were significant in all of the four sites (P-value <0.001 for site 1, 2 and 3, = 0.04 for site 4). After adjusting for the general medicine professional background, gender, ethnicity, years of experience in emergency department and time per week in emergency department, the adjusted coefficients for EQUiPPED period showed negative, but non-significant point estimate (P-value = 0.39 in the adjusted Negative binomial models). Because of the observational nature of the data, a covariate adjusted regression should give us a more reliable estimate of association because it accounts for the potential confounders. Therefore, the results of the previous study[10], which did not adjust for covariates, should be interpreted cautiously.

In our analysis, we pooled all time periods into Pre-Intervention, Intervention and Post-Intervention periods. This approach may not allow us to fully capture changing trends over time. An alternative analysis might include weeks/months into the regression, for example using time-series regression. In this approach, we can study more subtle trends over time.

Our analysis is limited by the fact that the sample size we had was relatively small. Moreover, a serious limitation of our work is that the independence assumption required by Poisson/Negative binomial regressions may be violated. In our analysis, the unit of analysis (represented by a row of data) is the provider in a particular EQUiPPED period. Because some providers were observed both pre- and post-intervention, the observations are unlikely to be independent, with the same provider given different EQUiPPED period likely to prescribe in a similar pattern. In the future, we will consider appropriate techniques for accounting for this correlation, such as generalized estimating equations or random effects models.

While we found a trend towards the EQUiPPED intervention leading to a decreased PIMs rate, we did not find strong evidence of reduced PIMs rate. Given the conflicting results of our analysis and the previous one, further work should be done in order to get more evidence on the efficacy of EQUiPPED.

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6. Figures and Tables:

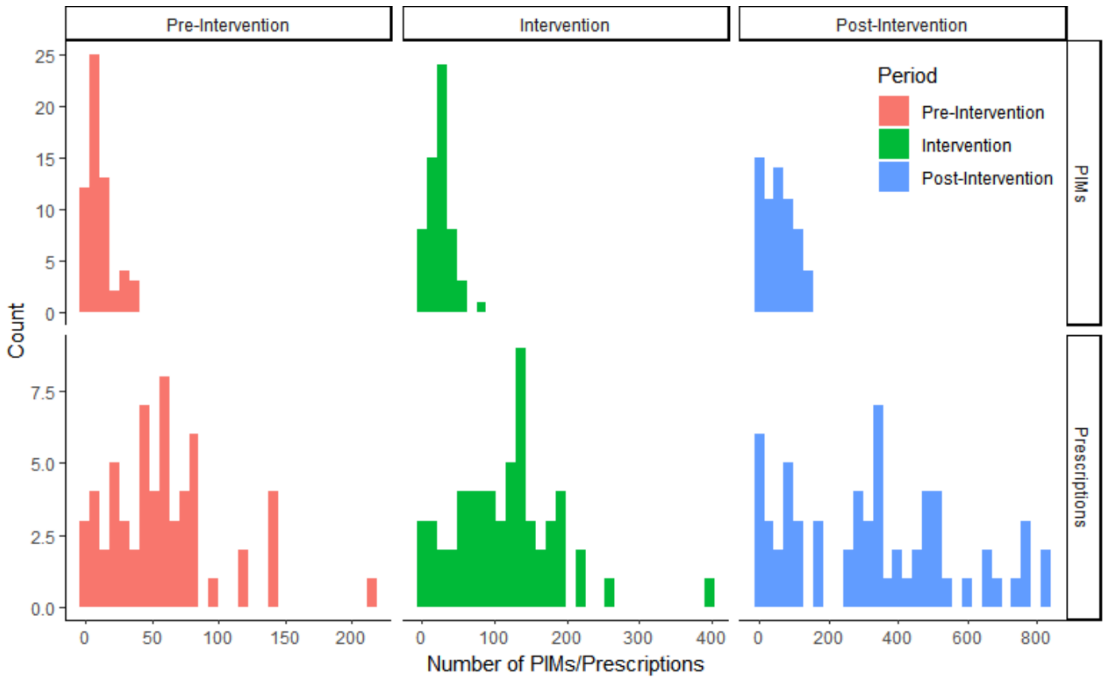

Figure 1. The distribution of PIMs and Prescriptions

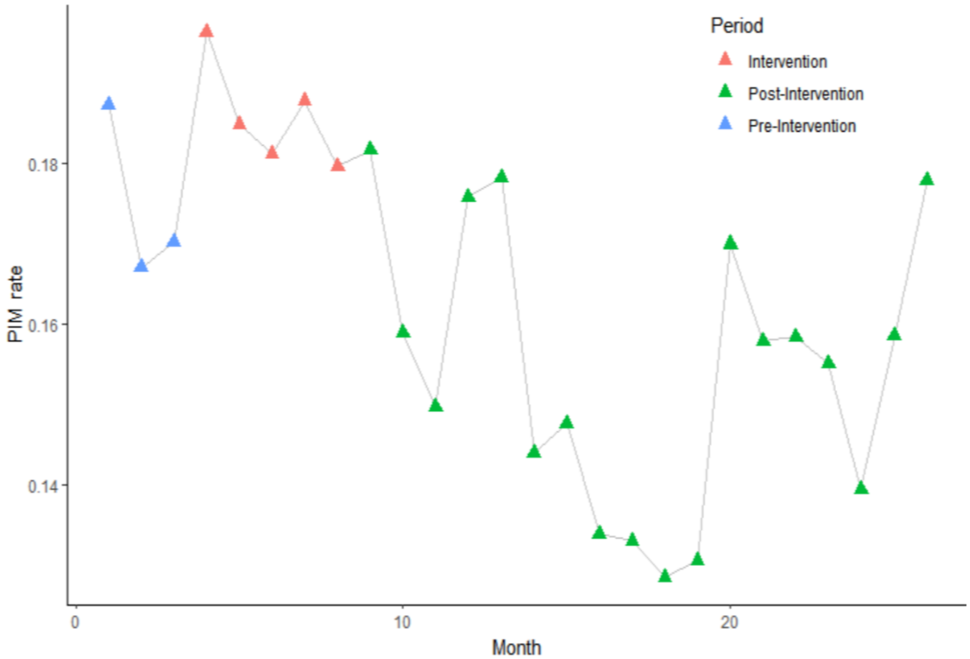

Figure 2. PIMs rate in months

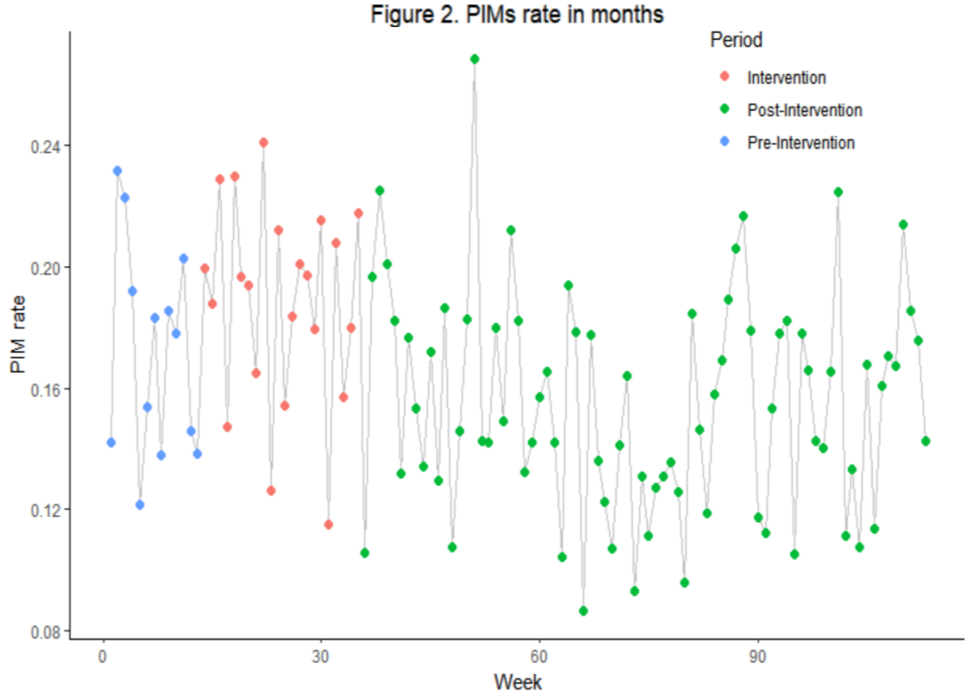

Figure 3. PIMs rate in weeks

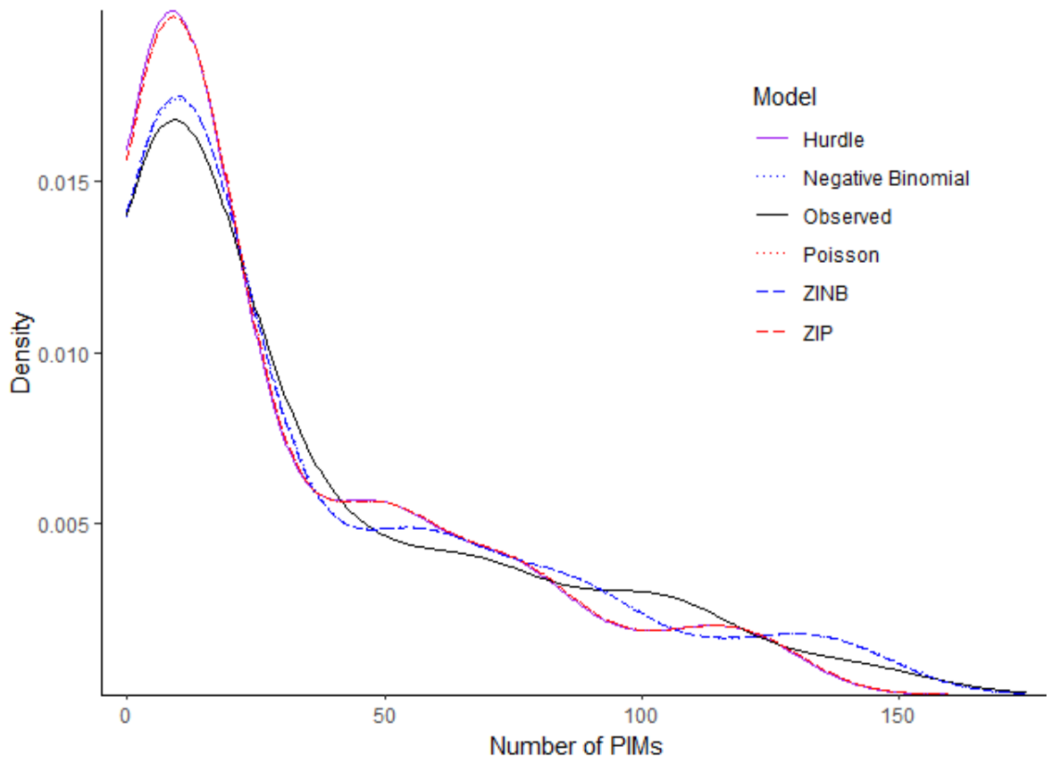

Figure 4. Kernel density estimation of predicted probability of five models and the kernel density of observed probability

**The predictive curve of Poisson model and Zero-inflated Poisson model and Negative binomial model and Zero-inflated Negative binomial model are extremely similar and overlapping*

Table. 1: Baseline Demographic characteristics of medical service providers

Baseline characteristics	N = 38
Age, n(%) *	
<30	1 (2.9%)
30-39	16 (45.7%)
40-49	10 (28.6%)
50-64	8 (22.9%)
Gender, n (%) *	
Male	16 (45.7%)
Female	19 (54.3%)
Practice experience, y *	10.69 ± 8.63
Range	0-40
ED experience, y**	7.66 ± 7.07
Range	0-21
Race, n (%) **	
White	26 (68.4%)
Black	5 (13.2%)
Asain	1 (2.6%)
Other	2 (5.3%)
Ethnicity, n (%) *	
Hispanic	2 (5.7%)
Non-Hispanic	33 (94.3%)
Role, n (%)***	
Physician	25 (69.4%)
Nurse Practitioner	8 (22.2%)
Physician assistant	3 (8.3%)
Time at ED per week, hr***	27.29 ± 10.59
Range	5-40
Typical shift, n (%)***	
8 hours	25 (69.4%)
12 hours	11 (30.6%)

*N = 35
**N = 34
***N = 36

Table. 2: AIC and BIC for six different models

Model	AIC	BIC
Poisson w/o offset	7403.20	7408.84
Poisson	1082.84	1088.48
ZIP	1086.84	1098.12
Negative binomial	859.97	868.43
ZINB	863.97	878.07
Hurdle	1087.84	1099.12

*ZIP, Zero-inflated Poisson;
ZINB, Zero-inflated Negative binomial

Table 3: Regression coefficients and other features of selected Negative binomial model

Model	Variables	β	Standard Error	Z	P-value	AIC	BIC
Model1	General medicine professional background	0.0068	0.0048	1.41	0.16	299.59	314.22
	Gender	-0.24	0.052	-4.697	<0.001		
	Ethnicity	-0.21	0.096	-2.17	0.03		
	Years of experience in ED	1.38	0.16	8.78	<0.001		
	Time per week in ED	0.011	0.0039	2.89	0.0039		
	Intercept	-1.76	0.15	-11.51	<0.001		
	EQUiPPED period	-0.054	0.064	-0.85	0.4		
Model2	General medicine professional background	1.36	0.16	8.35	<0.001	300.55	311.52
	Gender	-0.22	0.054	-4.14	<0.001		
	Time per week in ED	0.007	0.0029	2.38	0.018		
	Intercept	-1.8	0.1	-18	<0.001		
	EQUiPPED period	-0.051	0.067	-0.77	0.44		