ABSTRACT

Intravenous (IV) hydralazine, enalapril and labetalol are oftentimes used without indication for the treatment of asymptomatic hypertension in the hospital setting and have been shown to have substantial adverse effects that are associated with increased morbidity and mortality, as well as longer length of stay. Their use is also associated with greater monetary costs. In this project, we studied the frequency of use and consequences of these medications before and after a series of education cycles which clarified when and when not to use intravenous antihypertensives (IVAHs). Our initial aim was to decrease the unindicated use of IVAH by at least 25% in the setting of asymptomatic hypertension in our community hospital within a 1-year period after introducing education on the topic. Multidisciplinary involvement throughout three Plan-Do-Study-Act (PDSA) cycles yielded favorable results. We focused on education towards a hospital-wide knowledge gap stemming from a lack of guidelines regarding the treatment of asymptomatic hypertension, as well as the guideline indications for IVAH. After three cycles of education targeting different groups, the unindicated use of IVAH fell by a total of 66%, decreasing patient exposure to IVAH unless otherwise indicated was driven by repetitive education and group discussion to close the gap created by a lack of guidelines.

INTRODUCTION

There is no agreement on the treatment of asymptomatic hypertension nor is there a systematic approach to evaluating hypertension in the hospital setting. The prevalence of hypertension in the outpatient setting is approximately 29% in comparison with an estimated 72% in the inpatient setting. The stress and complications of acute illness in the hospital likely contribute to abnormally elevated blood pressures (BPs) without an established outpatient diagnosis of hypertension (table 1). Aggressive treatment of elevated BP with intravenous antihypertensive (IVAH) in the hospital setting is indicated for specific conditions which have proven mortality benefit from rapid BP reduction. These conditions include, but are not exclusive to: hypertensive emergency, acute phase ischaemic stroke, acute aortic dissection, intracerebral haemorrhage and eclampsia. Various studies have shown that reducing BPs aggressively in the presence of end-organ damage may salvage the affected organ system, however, there is no such evidence for treating elevated BPs without end-organ damage or symptoms, in fact doing so can cause significant harm. There is increasing concern about the use of IVAH as well as the increased use of these agents in treating asymptomatic hypertension without any established guidelines about when and when not to use them. Clinical evidence thus far recommends conservative management of asymptomatic hypertension in the hospital setting with observation, oral antihypertensive medication and outpatient follow-up with a primary care provider.

Definition of hypertension by the American College of Cardiology and the American Heart Association:

- Normal: <120/80 mm Hg.
- Elevated: systolic between 120 and 129 and diastolic <80.
- Stage 1: systolic between 130 and 139 or diastolic between 80 and 89.
- Stage 2: systolic at least 140 or diastolic at least 90 mm Hg.
- Hypertensive urgency: systolic at least 180 or diastolic at least 120, without end-organ damage.
- Hypertensive emergency: systolic at least 180 or diastolic at least 120 with end-organ damage.
Table 1  Evaluation of hypertension in the hospital setting

<table>
<thead>
<tr>
<th>Missed home medication doses</th>
<th>Antihypertensive medications</th>
</tr>
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<tbody>
<tr>
<td>Associated with hospital condition</td>
<td>Pain</td>
</tr>
<tr>
<td></td>
<td>Anxiety</td>
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<tr>
<td></td>
<td>Physiologic stress</td>
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<td>Urinary retention</td>
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<td>Respiratory distress</td>
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<td>Other</td>
<td>Work stress</td>
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<td>Family stress</td>
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<td></td>
<td>Anger</td>
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<tr>
<td>Drugs</td>
<td>Alcohol withdrawal</td>
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<tr>
<td></td>
<td>Other drug withdrawal</td>
</tr>
</tbody>
</table>

PROBLEM

Problem areas were isolated using a fishbone diagram after evaluating baseline data and habits within the healthcare environment (figure 1). Areas of concern included physician orders, reasoning, nursing, pharmacy checkpoints, patient evaluation and admission processes. Due to the lack of official guidelines directing the treatment of asymptomatic hypertension in the hospital, providers turned to pharmacological agents to remedy high BP values. The drug of choice was often an IVAH and on further questioning, medical staff as a whole was unaware of the risk or rates of adverse effects when using these agents. Patients rarely had a thorough evaluation to assess for underlying causes of hypertensive state (table 1). Not all nurses were aware of all the causes of hypertension and did not know when hypertension posed a danger to the patient. As a result, physicians received calls for elevated BPs and gave verbal orders for one time IVAH doses or asked nurses to defer to as needed IVAH orders already placed as an electronic order despite systolic doses being well below 180 mm Hg (figure 1). The electronic health record (EHR) system itself did not alert the ordering individual that oral medications were available nor did it alarm that the patient did not qualify for IVAH administration. Instead, asymptomatic elevations in BP were being treated with IVAH based on numerical value and without any supporting evidence for their use. On further investigation, the most common reasons that IVAH was used were due to a lack of knowledge of appropriate use and lack of guidelines in treating asymptomatic hypertension. Other issues that compounded the problem were a lack of timely medication reconciliation and not considering alternative therapies, which all stemmed from the main problem: a lack of structure in tackling the treatment of asymptomatic hypertension on the general medical floor. Various studies have already explored this topic including the American Heart Association and Journal of Clinical Hypertension with both agreeing that an aggressive approach to treating asymptomatic hypertension (with IVAH) may be harmful and has no proven value.69

Figure 1  Fishbone diagram depicting problem areas within the bigger picture of why IVAH are commonly used despite lack of medically proven indication. BP, blood pressure; IVAH, intravenous antihypertensive; IVAHs, intravenous antihypertensives; PRN, pro re nata; IV, intravenous.
INITIAL AIM: To decrease the unindicated use of IVAHs in the treatment of asymptomatic hypertension by at least 25% in our community hospital over a 3-month period following a 9-month intervention with education in the year of 2015.

Patient population and data collection
This study takes place at Crittenton Hospital Medical Centre, a community hospital in Rochester Hills, Michigan, USA. There is diversity between both private and teaching attendings as well as residents within the institution. This is a retrospective study taking place over three full PDSA cycles thus far. Study participants were first identified via EHR between 1 October and 31 December 2014 from a list of all hospitalised patients who have a documented order for either IV enalapril, IV hydralazine and/or IV labetalol. Qualified patients included adults over the age of 18 years who were admitted to the general medical floor and had a diet order in place. Exclusion criteria included patients admitted with hypertensive emergency, stroke or other conditions in which IVAH use was indicated and those who had nil-per-os (NPO) orders, as well as all other patients who were admitted to any floor other than the general medical floor.

Baseline measurement
Baseline data were collected retrospectively from the aforementioned 3-month period prior to any intervention to evaluate how often IVAHs were being used without indication. With the help of IT services and pharmacy, 480 charts were found in the EHR that fit our inclusion criteria with the remainder exhibiting appropriate guideline-mediated use of IVAH, thus being excluded from the study. This started us off with a 32% rate of indicated IVAH use and a 68% rate of the unindicated use of IVAHs. The goal of this study was to reduce the percentage of unindicated use of IVAH as we then excluded patients who were given IVAH appropriately as guideline-mediated treatment. We also reviewed patient chart data to identify associated adverse effects occurring within the first 24 hours for those patients who received IVAH without clear guideline-based indication (table 2).

Following administration of IVAHs, the most common adverse effects were hypotension and acute kidney injury, which were noted in 24.6% of the IV hydralazine group, 21.2% of the IV labetalol group and 34.6% of the IV enalapril group. On average, at least 25% of patients suffered adverse effects which could have been prevented and over 80% of these patients had alternative oral medications available which were not given either due to delay in medication reconciliation, lack of orders or the initiation of IVAH without any indicated reason. Hundred percent of these patients had no contraindication to receiving alternative therapies or home medications.

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Adverse effects of IVAH use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypotension</td>
<td>SBP &lt;100 mm Hg</td>
</tr>
<tr>
<td>Symptomatic hypotension</td>
<td>Altered mental status, Dizziness, Light headedness, Non-mechanical fall</td>
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<tr>
<td>Nephrogenic</td>
<td>Acute kidney injury, Oliguria</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Elevated troponins, Non-ST-elevation MI, MI, Tachycardia, Palpitations</td>
</tr>
<tr>
<td>Cerebrovascular accident</td>
<td>Stroke, Transient ischaemic attack</td>
</tr>
</tbody>
</table>

IVAH, intravenous antihypertensive; MI, myocardial infarction.

Table 2: Adverse effects of IVAH use

Strategic education
During education, we reviewed the definition of asymptomatic hypertension: elevated BP of any level which does not exhibit end-organ damage or symptoms, and we explained when patients were excluded from this criterion. Our goal was to implement a culture change to move away from the overuse of IVAH. In order to tackle the multiple issues that stemmed from the lack of awareness of when and why to use IVAH and when to avoid them, we created a power-point presentation about existing hypertension research and guidelines which included a list of...
IVAHs are a part of the standard of care was made available inpatient setting. Alternatively, a list of conditions in which lines for the treatment of asymptomatic hypertension in the IVAH and data was presented to date. There are no guide-our findings and audits to decrease the unindicated use of cycle as will be described next. All staff were informed about nurses, pharmacists and residents, separated by the PDSA individual education for the physicians, mid-


The PowerPoint was presented as a series of lectures and individual education for the physicians, mid-level providers, nurses, pharmacists and residents, separated by the PDSA cycle as will be described next. All staff were informed about our findings and audits to decrease the unindicated use of IVAH and data was presented to date. There are no guide-

PDSA cycles
PDSA cycle 1: physician education
The aim of PDSA cycle 1 was to reduce use of IVAH by 25% in cases of asymptomatic hypertension compared with the baseline rate during a 3 month observation period. Over a 9-month period from 1 January 2015 to 30 September 2015, cycles of education were implemented at physician board meetings, internal medicine staff meetings, and at various other physician meetings which included both physicians and mid-level providers and occasionally residents. Sessions lasted approximately 15–20 min with time for questions. After 9 months of these sessions, we again selected qualified patients from a 3-month period between 1 October 2015 to 31 December 2015 with all inclusion and exclusion criteria as our original data collection and found that educating physicians and mid-level providers made a positive impact.

PDSA cycle 2: nursing and pharmacist education
The goal of PDSA cycle 2 was to reduce the use of IVAH by 40% compared with the baseline rate during a 3-month observation period. Again over 9 months, we continued to provide educational sessions to physicians, but this time, we also expanded to the general medical floor nursing staff and principle pharmacists. From 31 January 2016 to 30 September 2016, education sessions took place monthly on the general medical floors for nurses and several meetings were scheduled with the principle pharmacists to go over goals and how they can help limit the use of IVAH to only when indicated. Nurses were additionally instructed to check for completion of medication reconciliation and how to assess a patient for other reasons for elevated BP before contacting providers. The PowerPoint was presented once a month. After 9 months of these sessions, we again selected qualified patients from a 3-month period between 1 October 2016 to 31 December 2016 with all inclusion and exclusion criteria as our original data collection and found that by expanding education we also improved patient safety (figure 2).

PDSA cycle 3: resident education
The goal of PDSA cycle 3 was to reduce the use of IVAH by 50% compared with the baseline rate during a 3-month observation period following intervention. Over a 9-month period from 1 January 2017 to 30 September 2017, cycles of education were implemented at resident noon lecture for internal medicine once every month and also a family medicine morning report once every month. Education also continued for physicians, mid-level providers, nurses and pharmacists. Again, results were even greater by adding another focused education group.

RESULTS
With three PDSA cycles over a course of 4 years, this quality improvement project was able to decrease the unindicated use of IVAH by a total 51%, with a 100% decrease among residents. Meaning, when residents did order IVAH, it was only for conditions in which IVAs were correctly indicated. This project not only proved that repetitive education was useful, but that results were sustainable. Each PDSA cycle continued to build on itself
with a continual decrease in unindicated IVAH use with enough time for our change to become a habit. As a secondary endpoint, we also found that the cost of IVAH was so great that the switch away from administering these agents saved the hospital thousands of dollars each year (figures 3 and 4).

**Data interpretation**

During PDSA cycle 1 there was a total decrease of unindicated IVAH (IV hydralazine, IV labetalol and IV enalapril) use by 38% (278 doses) and a decrease in total cost by 57% (US$3498.68) during the 3-month interval following educational intervention over the prior 9 months to attending physicians and mid-level providers alone when compared with baseline (figure 5). This surpassed our original goal of decreasing use by at least 25%. The second PDSA cycle focused on the addition of nursing staff and pharmacists to the education sessions and after 9 months of reviewing and reiterating information the next 3-month study interval yielded a 55% (408 doses) decrease of IVAH use and a 56% (US$2063.10) reduction in cost from our baseline and an additional 29% decrease in IV labetalol use and cost in comparison to PDSA1. The third PDSA continued with special attention to resident education, yielding 100% compliance after education. Meanwhile, the 9-month interval continued to focus on providing education to all three groups: physicians, nursing and pharmacists plus residents and results were again collected during the last 3 months of the year. PDSA cycle 3 resulted in a 66% reduction in IVAH use and overall, there were favourable outcomes for patients’ safety with adverse effects reduced by 52% total after the three PDSA cycles and decreasing the number of exposed patients by an estimated 248 cases during a 3-month observation period (figure 2). The hospital also saw positive results in absolute cost by cutting down unnecessary IVAH use saving an estimated US$59,954.92 since the project started in 2014. Unindicated IV hydralazine use in our community hospital decreased from 464 to 162 doses dispensed (65% reduction) and the total charge fell from US$7191.23 to US$2513.25 (65% reduction). Since 2014, the unindicated use of labetalol decreased from 165 to 45 doses dispensed (73% reduction) and the total cost fell from US$1816.62 to US$493.20 (73% reduction). In the Enalapril group, the unindicated use decreased from 103 to 42 doses dispensed (60% reduction) and the total charge fell from US$465.46 to US$188.00 (60% reduction) (figures 3–5).

The total data gathered showed a decrease of unindicated IVAH use and directly decreased the number of patients negatively affected by their use. Education proved to be a very important factor to improving the care of patients with asymptomatic hypertension in the hospital setting.

**Secondary endpoint**

As discussed earlier, the primary outcome of this quality improvement project was the betterment of patient safety...
and reduction in the use of IVAH (figures 2 and 4). As the unindicated use of IVAH was drastically decreased, we saw an increase in absolute cost savings. These medications were much more expensive than oral medications, or not using any antihypertensive medications at all. Indirect costs were more difficult to measure and will not be discussed here although in our research we did note that patients with IVAH use may have incurred longer length of stay in the hospital due to adverse effects attributed to IVAH, additional medications and fluids required to correct insults, and transfer to higher acuity floors. Acute kidney injury, for example, may increase the length of stay by up to 3.5 days.²

The cost of medication is different based on the size of the hospital and other factors, however, despite this, IVAHs are much more expensive than their oral counterparts.¹²-¹⁴ The average cost of hydralazine was US$0.64 for an oral tablet of any dose (10, 25 and 50 mg) or US$15.49 per 20 mg/mL vial. The average cost of enalapril was US$0.75 for an oral tablet of any dose (2.5, 5, 10 and 20 mg) or US$4.53 per 1.25 mg/mL vial. The average cost of labetalol was US$0.70 for an oral tablet of any dose (100 mg, 200 mg, and 300 mg) or US$10.96 per 100 mg/20 mg vial. We found that the majority of the time the remainder of a vial is wasted if not used completely.

**DISCUSSION**

Since this project started in 2014, education continues to have a clinical impact on the lives of our patients with asymptomatic hypertension by reducing the unnecessary use of IVAH, decreasing the number of iatrogenic side effects, and improving patient safety. Our study proved that IV hydralazine, IV labetalol and IV enalapril were being ordered despite lack of symptoms or end-organ damage to fulfil criteria for hypertensive emergency or other clear indication for IVAHs. Instead, asymptomatic elevations in BP were being treated with IVAH based on a numerical value. Education proved to be a

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**Figure 4** Decrease in absolute doses of unindicated IVAH use compared with secondary endpoint of cost reduction from baseline (2014) through PDSA 3 (2017). IVAH, intravenous antihypertensive; PDSA, Plan-Do-Study-Act.

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**Figure 5** (Top) Decrease in unindicated IVAH doses organised by respective drug, from the baseline in 2014 prior to any intervention the total doses of IV hydralazine dispensed was 464.25, after one round of education (PDSA1), the unindicated use dropped to 320.5 doses. After the second round of education (PDSA 2), the unindicated use dropped to 227.25 doses, and after three rounds of education, the unindicated use of IV hydralazine dropped to 162.25 doses. From the baseline in 2014 prior to any intervention, the total doses of IV labetalol dispensed was 165.75. After one round of education (PDSA 1), the unindicated use dropped to 62.5 doses. After the second round of education (PDSA 2), the unindicated use dropped to 47.5 doses, and after three rounds of education, the unindicated use of IV labetalol dropped to 45 doses. From the baseline in 2014 prior to any intervention, the total doses of IV enalapril dispensed was 102.75. After one round of education (PDSA 1), the unindicated use dropped to 71.75 doses. After the second round of education (PDSA 2), the unindicated use dropped to 50 doses, and after three rounds of education, the unindicated use of IV enalapril dropped to 41.5 doses. (Bottom) Absolute cost reduction by respective drug. From the baseline in 2014 prior to any intervention the total cost of IV hydralazine dispensed for unindicated reasons was US$7191.23. After one round of education (PDSA 1), the cost of unindicated IV hydralazine use dropped to US$4964.55. After the second round of education (PDSA 2), the cost of unindicated IV hydralazine use dropped to US$3520.10 doses, and after three rounds of education, the cost of unindicated IV hydralazine use dropped to US$2513.25. From the baseline in 2014 prior to any intervention, the total cost of IV labetalol dispensed for unindicated reasons was US$1816.62. After one round of education (PDSA 1), the cost of unindicated IV labetalol use dropped to US$685.00. After the second round of education (PDSA 2), the cost of unindicated IV labetalol use dropped to US$520.60, and after three rounds of education cost of unindicated IV labetalol use dropped to US$493.20. From the baseline in 2014 prior to any intervention, the total cost of IV enalapril dispensed for unindicated reasons was US$465.46. After one round of education (PDSA 1), the cost of unindicated IV enalapril use dropped to US$325.03. After the second round of education (PDSA 2), the cost of unindicated IV enalapril use dropped to US$226.50, and after three rounds of education, the cost of unindicated IV labetalol use dropped to US$188.00. IVAH, intravenous antihypertensive; PDSA, Plan-Do-Study-Act.
very important factor in improving the care of patients with asymptomatic hypertension. Factors such as other interacting medications, diet habits, individual physiologic response and combination of comorbid conditions cannot be correlated due to a myriad of confounding variables when administering IVAHs. This is true not only for this quality improvement study and analysis, but also in real time with patients. There is no way to predict their effect on an individual or the adverse event that may take place. However, we do know that using IVAHs puts patients at a greater risk for an adverse effect. A very minor proportion of patients received more than one dose of IVAH during their hospital stay versus most patients who received only one dose, which may have led to an increased risk of an adverse effect in those patients, although this pattern was not observed. Additionally, we only studied the use of the three most common IVAHs used in our hospital, namely IV hydralazine, IV labetalol and IV enalapril. Despite this, our education did recommend using all IVAHs only for guideline-directed therapies when indicated (excluded from this study) and never to use them for asymptomatic hypertension. Other confounding variables included the efficacy of reaching all healthcare providers, the quality of education and retention of materials presented, and understanding of the material by different healthcare providers. We attempted to remedy this by holding several sessions and presented the same PowerPoint with the same group and reached out to physicians individually if their attendance was not recorded. During sessions, we surveyed participants and found that with each session a greater majority acknowledged that they were aware of the project and/or they were implementing the appropriate assessment and treatment of inpatient hypertension as a change in their practice. Another limitation to this study was the location at one rural hospital in comparison with a larger facility with a larger patient base for data collection which would have improved the power of the study, although the advantage was a smaller medical staff to which education was presented. There are no confounding variables that could attest to the significant drops in unindicated usage of the three studied IVAHs in our hospital other than the provided education and acknowledged implementation by medical staff.

The use of IVAH comes with various side effects and daunting costs. Repetitive education proved to have a huge impact on hospital culture and the move away from IVAH in the treatment of asymptomatic hypertension. We were able to improve patient safety by decreasing the number of patients exposed to the risks of IVAH use and as a secondary endpoint, the decrease in IVAH use for reasons other than guideline-indicated conditions was found to be financially favourable when evaluating the absolute cost. This does not include indirect costs that were incurred by an adverse effect (ie, acute kidney injury). Patients are now actively evaluated for other causes of hypertension and if an antihypertensive medication is required, then oral options are preferred.

Looking back on the progress with this quality improvement, it would be more efficient if we had more participants on the project to lead education sessions, data collection and implementation. The more educational sessions and more physicians, we could reach even on an individual basis which would be faster with more people on the project. A larger hospital with a larger patient base would also support numerical data even more, however, then there will be more healthcare personnel to reach with education sessions. This would require more people to be involved in the project as well. The more participants are engaged in teaching and monitoring progress would be ideal to make this quality improvement initiative more efficient. Very helpful resources in monitoring progress were both IT services, medical records and pharmacists; these individuals are key to accurately collect and interpret data.

CONCLUSIONS

This quality improvement project started with the initiative of improving patient safety in our community hospital in the context of the overuse of IVAHs. We noted that there were various adverse effects associated with their use and that many times these drugs are being given without any specific reason but instead because they are an ‘easy’ option. By auditing the use of the most commonly used IVAHs in the hospital (IV hydralazine, IV labetalol and IV enalapril), we noted a large number of instances in which these drugs were being used without indication. On further investigation of various articles and past published research, we found that there continues to be no set guideline on the treatment of asymptomatic hypertension in the hospital. Therefore, we created a subset of ‘rules’ in our education sessions which provided a systematic approach to evaluating asymptomatic hypertension, and then treatment if necessary. By doing this, we calculated an estimated decrease in unnecessary adverse side effects and improvement in patient safety all based on initial data which were collected prior to the initiation of any intervention.

This project can be easily reproduced at any sized institution by first evaluating the culture of use of IVAH medications and comparing use for guideline indicated reasons versus without any specific indication. Next, it is important to find an easily accessible group such as nurses on a particular floor, a particular group of physicians or residents. From here, it is a matter of collecting data as education is implemented. Education should implement both visual and numerical information given in a form that stimulates both auditory and visual learning, in our case, a PowerPoint presentation. Humans are a creature of habit and once education is given several times, not only do they continue to abide by this knowledge, but they also teach others. Continued education sessions that implement progress in reducing IVAH use are encouraging to the groups involved as the project moves forward. We have seen a sustained improvement in the avoidance
of IVAH when not indicated and expect to see minimal usage except for guideline-recommended conditions due to the number of healthcare professionals we were able to reach with our repeated sessions.

The unindicated use of IVAH medications among others stems from the lack of guidelines in the treatment of asymptomatic hypertension. By implementing education in our community hospital, we have affected the culture of treating asymptomatic hypertension and were able to sustain results by repetitive education and observing a continual decrease in unindicated usage of these medications. Physicians, nurses, pharmacists and residents are now aware of the clear cut indications for IVAH use and avoid using them in asymptomatic hypertension. Our hospital is now able to actively re-evaluate for pain, anxiety, respiratory distress, inaccurate BP readings and more in an effort to minimise medicating and maximise thorough examinations. When medications are indicated, a systematic approach by first reviewing the medication reconciliation, ordered medications and given medications allow an informed decision to be made by the healthcare provider. If an antihypertensive medication is required, oral options are preferred. With this change in our system which was primed over the last 3 years, we are seeing substantial improvement in the quality of patient care and safety. The next steps include modifying the EHR itself to make a more efficient medication reconciliation process as well as an alert system to clarify when IVAHs are indicated and when other options should be reviewed.

Acknowledgements The authors would like to thank Heidi Kenaga, PhD, Research Coordinator at Wayne State University School of Medicine Graduate Medical Education and R. Brent Stansfield, PhD, Director of Education at Wayne State University School of Medicine Graduate Medical Education for their continued support during the extent of this project.

Contributors JS, AS: wrote manuscript, edited manuscript, planned study, collected and interpreted data, conducted intervention. RB: planned study, collected and interpreted data, conducted intervention. DP: collected data, conducted intervention. NC: collected data, conducted intervention. JT: collected data, VT: planned study, collected data. SK: faculty advisor, edited manuscript.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article.

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