Minimizing STOPP and Beers Criteria Risks in PIM Treatments Using PM-TOM and ChatGPT: A Case Study

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Abstract. PM-TOM (Personalized Medicine-Therapy Optimization Method) is a clinical decision-support tool designed to optimize polypharmacy treatments by minimizing their adverse drug reactions (ADRs) caused by individual drugs or drug interactions (DDIs, DCIs, DFIs, DGIs), along with the risks identified by the STOPP and Beers criteria. On the other hand, AI tools like ChatGPT 4.0, trained on medical literature texts, can provide broader clinical reasoning and insights tailored to individual patient contexts. By referring to a documented deprescribing case, this study demonstrates the synergistic power of PM-TOM and ChatGPT in optimizing potentially inappropriate medication (PIM) treatments. A malnourished older woman was admitted to a deprescribing facility with recurrent falls, hypertension, ischemic heart disease, depression, osteoarthritis, osteoporosis, and GERD. She was initially prescribed acetaminophen, alendronate, omeprazole, lisinopril, metoprolol, aspirin, citalopram, and vitamin D, which were assessed as inadequate. While the discharge regimen improved some conditions by replacing alendronate with zoledronic acid and reducing some drug dosages, PM-TOM revealed that key risks, stemming primarily from omeprazole, aspirin, and citalopram, remained unaddressed. The discharge treatment was optimized with PM-TOM after considering alternative drug classes suggested by ChatGPT and elaborated in the available medical literature. In the optimized treatment, omeprazole (PPI) was replaced with famotidine (H2-blocker), citalopram (SSRI) with agomelatine (atypical antidepressant), zoledronic acid (bisphosphonate) with denosumab (RANK ligand inhibitor), aspirin (NSAID) with ticagrelor (antiplatelet), and lisinopril with benazepril (ACE inhibitor). These changes significantly reduced possible ADRs and the geriatric care criteria risks. Finally, ChatGPT validated the proposed adjustments, confirming their alignment with the guidelines and highlighting the potential for longer-term benefits. This case study illustrates how a combined use of PM-TOM and AI tools can effectively support the clinical decision-making process by optimizing polypharmacy treatments and minimizing their PIMs, major contributors to morbidity in older adults and high healthcare costs.

Keywords. PM-TOM, ChatGPT, ADR, STOPP/START Criteria, Beers Criteria

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1. Introduction

Adverse drug reactions (ADRs) from potentially inappropriate medications (PIM) are estimated by the US FDA [1] to be the fourth leading cause of death in the United States. A study [2] also reported that in 2016, the US's annual cost of drug-related morbidity and mortality was projected at $528.4 billion, accounting for approximately 16% of US healthcare expenses. The above FDA report concludes that ADRs represent a significant but largely preventable public health concern.

However, clinical decision support systems issue numerous alerts regarding potential ADRs in PIM treatments without suggesting viable alternatives, leading to a phenomenon known as alert fatigue [3], where clinicians override 90% of alerts. ADRs are also often treated as new conditions, triggering a "prescribing cascade" – adding new medications and thus increasing the PIM treatment risks. Older adults are particularly vulnerable to ADRs due to the prevalence of multiple chronic conditions. Established guidelines, such as the Beers criteria [4] and the STOPP/START criteria [5], recommend avoiding or cautiously using certain drugs and drug combinations in this population.

Optimizing PIM treatments has become a critical healthcare priority that requires innovative solutions. This study proposes that analytical tools, such as PM-TOM (Personalized Medicine - Therapy Optimization Method), supported by AI tools such as ChatGPT 4.0, could assist healthcare providers (clinicians, clinical pharmacists, specialists, and primary care providers) in identifying suitable polypharmacy treatments and preventing PIM prescriptions. With its structured drug database, PM-TOM can efficiently identify treatments with reduced ADRs and minimized STOPP and Beers criteria risks. Meanwhile, ChatGPT can review these regimens and suggest their improvements based on knowledge compiled from available medical literature.

Section 2 summarizes basic PM-TOM features, including references to several studies demonstrating its ability to minimize drug interactions in complex polypharmacy treatments. Section 3 explains the optimization of a documented deprescribing case using these two tools, while Section 4 summarizes the benefits of the proposed method.

2. PM-TOM

PM-TOM finds polypharmacy treatments with minimal drug interactions (DDIs, DCIs, DGIs, and DFIs), as well as the STOPP and Beers criteria risks. It assists healthcare providers by letting them select candidate drugs applicable to patients' conditions and then finding their optimal combination. Articles [6], [7], [8] and [9] provide further details about PM-TOM, its algorithm, database and applications.

The PM-TOM inputs are the patient's conditions and candidate drugs or drug classes that the healthcare providers consider after examining the patient's record. Optionally, they select an initial treatment (IT) as a starting point for further optimization. The optimization process is based on the Cumulative Adverse Drug Interaction Indicator (CADI), a weighted sum of counts of various types of possible ADRs. PM-TOM calculates CADI for each candidate treatment to find one that minimizes this score.

PM-TOM output is an optimized therapy with the lowest CADI score and a detailed report outlining the number, types, and effects of potential ADRs, along with the

STOPP and Beers risks.

PM-TOM heuristic algorithm [6] assesses only a limited number of alternative therapies, enabling its high efficiency in finding improved PIM treatments.

3. Case Study

An older malnourished woman with recurrent falls was admitted to a specialized medical facility for the assessment and adjustment of her PIM treatment, as documented in an article by Fujita K. et al. [10]. Her conditions and medications at admission and discharge are detailed in Table 1. The optimized treatment is listed as well (to be discussed). The PM-TOM analysis of all treatments, summarized in Table 2, shows counts of possible ADRs, directly caused by individual drugs or drug interactions, and the counts of the Beers and STOPP criteria risks.

Comprehensive reports of this case are available in the Mendeley Library [11].

Table 1. Conditions and the admission, discharge and optimized treatments. (APAP: acetaminophen).

Conditions/ Treatment	Osteoarthritis	Osteoporosis	GERD	Hyper-tension	Ischemic heart disease	Depression
Admission	APAP	alendronate, vitamin D	omeprazole	lisinopril	metoprolol, aspirin	citalopram
Discharge	APAP	zoledronic acid, Vitamin D	omeprazole	lisinopril	metoprolol, aspirin	citalopram
Optimized	APAP	denosumab, vitamin D	famotidine	benazepril	metoprolol, ticagrelor	agomelatine

The medical team assessed the admission treatment and found it inadequate as it could cause falls and malnourishment. In the discharge treatment, alendronate was replaced with zoledronic acid, and some medications' dosages were reduced.

While these changes improved the patient's condition, the analysis shown in Table 2 exposed that the counts of the PIM risks remained similar, raising concerns about the stability of the discharge treatment in the long run.

Table 2. Counts of adverse drug reactions and interactions, and the Beers and STOPP criteria risks. The first column shows ADRs possibly directly caused by single drugs, like falls, depression, or cardiac issues.

Version	ADR (direct)	DDI Critical	DDI Other	DCI	DFI	Beers Criteria	STOPP Criteria
Admission	9	5	15	3	23	6	**6**
Discharge	7	5	14	4	23	6	**6**
Optimized	4	1	8	1	11	2	**1**

After consulting ChatGPT and guidelines, the following alternatives were considered: (1) replacing omeprazole (PPI) with an H2-blocker, (2) citalopram (SSRI) with an atypical antidepressant, (3) lisinopril with an alternative ACE inhibitor, (4) aspirin with another antiplatelet, and (5) zoledronic acid with denosumab (RANK ligand inhibitor). The optimized treatment (Table 1 and Table 2) showed a reduction of ADRs (direct) from 7 to 4, critical DDIs from 5 to 1, other DDIs from 14 to 8, DCIs from 4 to

1, and DFIs from 23 to 11. Also, the STOPP and Beers criteria risks decreased significantly from 6 to 1 and 6 to 2 (cautions).

ChatGPT 4.0 review and findings are listed in Table 3, confirming that the optimized treatment is aligned with the STOPP/START and Beers criteria and would likely offer a more sustainable, safer option for the patient.

Table 3. ChatGPT 4.0 review of the discharge and optimized treatments: concerns and recommendations.

Review of the discharge (D) and optimized (O) treatments:
Osteoarthritis: D: and O: Acetaminophen is generally recommended for osteoarthritis in older adults, avoiding the risks associated with NSAIDs. **Osteoporosis: D:** Zoledronic Acid (bisphosphonate) requires monitoring in older adults to prevent renal impairment. **O:** Denosumab offers effective fracture prevention without the renal risks linked to bisphosphonates. Cholecalciferol is essential in both treatments. **GERD: D:** Long-term omeprazole (PPI) use could exacerbate malnutrition and increase fracture risk, given the patient's osteoporosis. **O:** Famotidine (H2 Blocker) is a safe alternative, avoiding long-term nutritional or fracture risks associated with PPIs. **Hypertension:** Lisinopril and benazepril (ACE Inhibitors) are generally suitable for elderly adults. **D:** Lisinopril can cause hypotension, especially in combination with metoprolol, which may heighten fall risk. **O:** Benazepril offers slight advantages in precise dosing for this profile. **Ischemic heart disease: D: and O:** While metoprolol is not contraindicated, beta-blockers carry cautionary notes for elderly patients with a history of falls or orthostatic hypotension. **D:** Aspirin elevates bleeding risk, which is particularly concerning in a patient with recurrent falls. **O:** Ticagrelor presents a lower risk of gastrointestinal bleeding, a key advantage for this patient. **Depression: D:** Citalopram (SSRI) increases fall risk, with concerns around QT prolongation and electrolyte imbalance. **O**: Agomelatine (melatonergic antidepressant) avoids QT prolongation and hyponatremia, making it safer for this patient, with minimal risk of sedation or cognitive effects.
Recommendation:
The optimized treatment aligns more effectively with the STOPP/START and Beers criteria. Here is why: 1. **Reduced Fall and Bleeding Risks**: Removing aspirin and citalopram minimizes bleeding and fall risks, which is critical for this elderly patient. 2. **Bone Health Management**: Denosumab offers effective osteoporosis management without exacerbating renal issues, making it safer for an older adult with malnutrition. 3. **Improved Nutritional and Bone Health Impact**: Famotidine replaces omeprazole for GERD management, reducing nutrient deficiency and fracture risks. 4. **Safer Antidepressant Option**: Agomelatine avoids QT prolongation and falls risks while effectively treating depression. This optimized regimen better addresses the patient's needs while minimizing adverse effects, aligning well with geriatric care guidelines.

4. Conclusions

This case study highlights the benefits of PM-TOM's data-driven, risk-quantification, and evidence-based approach to optimizing polypharmacy treatments. AI tools like ChatGPT complement PM-TOM by evaluating alternatives, offering insights, reviewing optimized treatments, and explaining the reasoning in plain language.

It is important to note that while AI tools add significant value to this process, they cannot replace analytical tools like PM-TOM, which rely on structured and curated drug databases and can accurately identify all drug interactions and risk profiles.

The integrated approach offers the following key advantages:

1. It simplifies finding effective drug regimens, allowing healthcare providers to leverage their expertise efficiently.
2. Detailed PM-TOM reports facilitate the involvement of pharmacists in monitoring and adjusting polypharmacy treatments.
3. Targeted recommendations help reduce non-actionable alerts, mitigate alert fatigue, and prevent prescription errors, including prescription cascades.
4. PM-TOM rapidly evaluates and optimizes complex treatment plans, enabling efficient consideration of multiple alternatives.
5. AI tools like ChatGPT can suggest alternative approaches, review the optimized treatments and provide additional insights.
6. When applied at the primary care level, this approach could prevent PIM prescribing and reduce the need for costly deprescribing procedures.

In conclusion, combining analytical optimization tools like PM-TOM with AI tools like ChatGPT provides powerful support for clinical decision-making, helping to prevent PIM polypharmacy and enabling safer, more effective treatments while reducing health risks and costs.

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