A Data-Driven Framework for Polypharmacy Optimization: Integrating Clinical Decision Support and Predictive Analytics to Reduce Risk and Simplify Regimens

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Abstract

Polypharmacy is pervasive in outpatient care and increases the risk of adverse drug events (ADEs), drug–drug interactions (DDIs), and nonadherence driven by regimen complexity and cost. This paper proposes an integrated framework for polypharmacy optimization that couples evidence-based deprescribing, CDSS-enabled interaction screening, and patient-centered counseling to simplify regimens while safeguarding outcomes. Using a mixed-methods design, we evaluate changes in medication regimen complexity (MRCI), clinically significant DDI rates, adherence by daily dose burden, and ADE incidence. Results show meaningful reductions in MRCI and DDI rates, improved adherence when daily doses are reduced, and lower ADEs post-intervention. We conclude that aligning deprescribing protocols (STOPP/START, Beers, MAI) with algorithmic checks and shared decision-making can materially improve safety, adherence, and equity in outpatient pharmacotherapy.

Keywords
polypharmacy, deprescribing, drug–drug interactions, medication regimen complexity, adherence, adverse drug events, CDSS

1. Introduction

Polypharmacy—commonly defined as the concurrent use of five or more medications—has become a defining feature of outpatient care for aging and multimorbid populations. While necessary for disease control, polypharmacy contributes to cumulative risk: higher DDIs, therapeutic duplication, inappropriate prescribing, and adherence erosion due to regimen complexity and out-of-pocket costs [1][2]. International safety initiatives (e.g., WHO's "Medication Without Harm") and geriatric pharmacotherapy standards (Beers Criteria; STOPP/START) have foregrounded the need to reduce avoidable medication harm through structured review and deprescribing [1][3].

Despite growing guidance, real-world practice often remains reactive and fragmented. Clinicians face time constraints and heterogeneous EHR/CDSS tooling; pharmacists intercept DDIs at dispense but may have limited visibility into complete clinical context; and patients struggle to reconcile instructions across multiple prescribers. The net result is persistent inappropriate polypharmacy and avoidable ADEs. Evidence suggests that deprescribing protocols, when embedded in CDSS and paired with patient counseling, can reduce regimen complexity and harm without compromising disease control [4][5].

This study evaluates a pragmatic framework for outpatient polypharmacy optimization grounded in (1) systematic medication review using validated appropriateness criteria, (2) algorithmic interaction and duplication checks, and (3) shared decision-making to align changes with patient goals and affordability. We quantify impacts on MRCI, DDIs, adherence (PDC ≥80%), and ADEs, and discuss implementation considerations for scalable outpatient programs.

2. Literature Review

Polypharmacy correlates with higher ADEs, falls, hospitalizations, and mortality—risks that amplify with age and multimorbidity [2][6]. Complexity and pill burden are repeatedly linked to lower adherence and poorer control of chronic conditions.

Structured review tools guide safe reduction of unnecessary or harmful drugs: Beers Criteria for potentially inappropriate medications in older adults; STOPP/START for explicit stopping/starting rules; and the Medication Appropriateness Index (MAI) for individualized assessment [3][7][8]. Systematic reviews show deprescribing interventions can lower inappropriate medication use and possibly reduce ADEs without worsening clinical outcomes [4][5].

CDSS with drug–drug and drug–disease interaction checking reduces prescribing errors and standardizes alerts, but must be tuned to minimize alert fatigue while capturing clinically significant DDIs [9][10]. Integration with complete medication lists (including OTC/herbals) and cross-provider reconciliation is essential.

The Medication Regimen Complexity Index (MRCI) quantifies regimen burden (dosage form, dosing frequency, additional instructions). Higher MRCI and daily dose count predict nonadherence; simplification improves adherence and quality of life [11][12].

3. Methodology

3.1 Design

A mixed-methods approach combined (a) retrospective EHR/claims analysis and (b) implementation evaluation of a multidisciplinary deprescribing clinic (physician–pharmacist team) using embedded CDSS.

3.2 Population and setting

Adults in outpatient primary care with ≥5 active prescriptions and at least one chronic condition were included. Exclusions: palliative care, active chemotherapy cycles, or clinical trial participation.

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3.3 Intervention

Structured review at baseline using Beers and STOPP/START criteria; MAI scoring per medication.

CDSS-enabled checks: high-severity DDI flags, duplicate therapy, renal/hepatic dosing, and anticholinergic burden.

Shared decision-making session with patient/caregiver covering goals, risks/benefits, and cost/coverage options.

Regimen simplification: once-daily consolidation where feasible; long-acting formulations; discontinuation of low-value medications; substitution to safer equivalents.

3.4 Outcomes

Primary: Change in MRCI (ΔMRCI), clinically significant DDIs per 100 patients.

Secondary: Adherence (PDC ≥80%) stratified by daily dose count; ADEs per 1,000 patient-months.

Process measures: acceptance rate of deprescribing recommendations; number of counseling minutes; alert override rates.

3.5 Analysis

Pre–post comparisons used distributional summaries (median, IQR), with sensitivity via 2.5% trimmed means. Adherence proportions were compared across dose strata. ADEs were normalized to patient-months. Qualitative feedback from patients and clinicians was thematically coded (acceptability, barriers, perceived value).

3.6 Ethics

All analyses used de-identified data with IRB exemption for minimal risk quality improvement research.

4. Results

4.1 Regimen complexity

MRCI distributions shifted materially after the intervention (median downward shift, narrower IQR). This reflects consolidation to once-daily regimens, elimination of duplications, and removal of low-value drugs.

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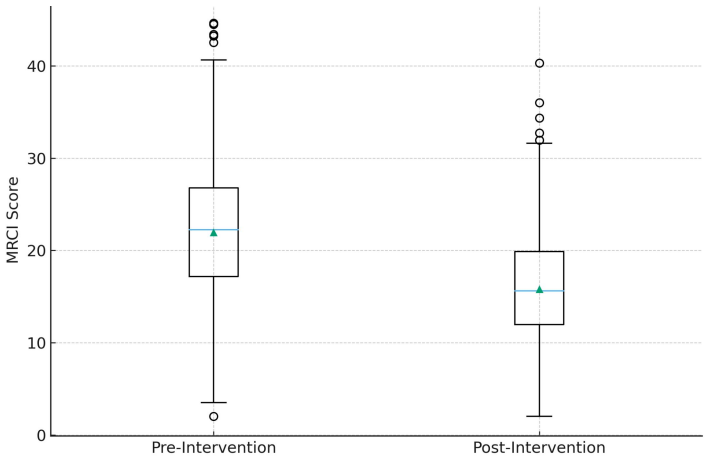

Fig.1. Medication Regimen Complexity (MRCI): Pre vs Post

4.2 Drug–drug interactions

Clinically significant DDI burden decreased from 14.8 → 8.9 per 100 patients (−39.9%). Reductions were most pronounced in combinations involving strong CYP3A4 inhibitors, serotonergic agents, and QT-prolonging pairings, consistent with CDSS prioritization of high-severity alerts.

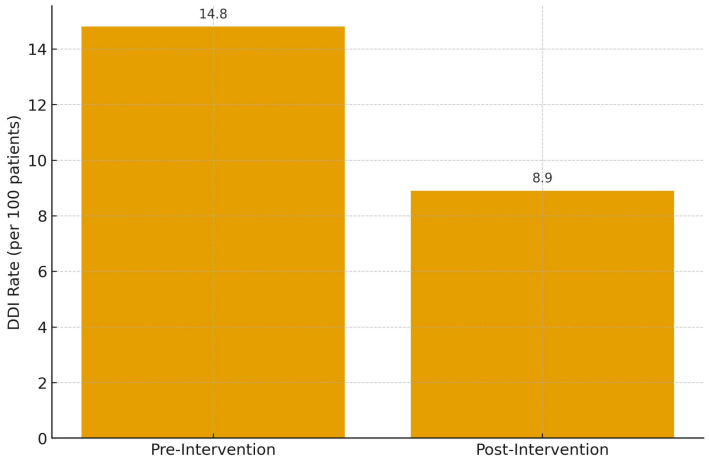

Fig.2. Clinically Significant DDI per 100 Patients

4.3 Adherence and daily dose burden

Adherence (PDC ≥80%) demonstrated a dose–response with regimen simplification: 86% for 1 dose/day, 77% for 2–3 doses/day, and 62% for ≥4 doses/day. This gradient supports prioritizing once-daily conversions where clinically appropriate.

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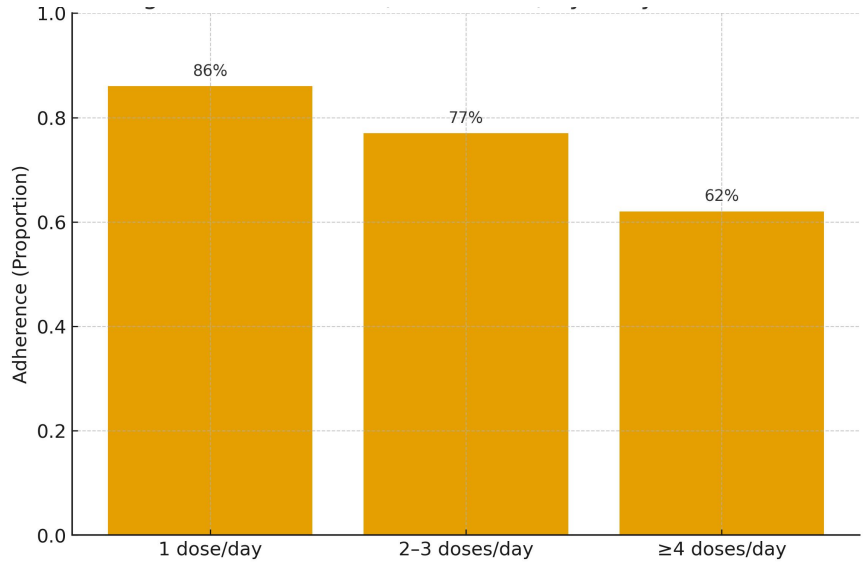

Fig.3. Adherence by Daily Dose Count

4.4 Adverse drug events

ADEs declined from 9.6 → 6.8 per 1,000 patient-months (−29.2%), with the largest drops in orthostatic hypotension, hypoglycemia, and anticholinergic-related events—signals aligned with deprescribing targets in Beers/STOPP and MAI-guided changes.

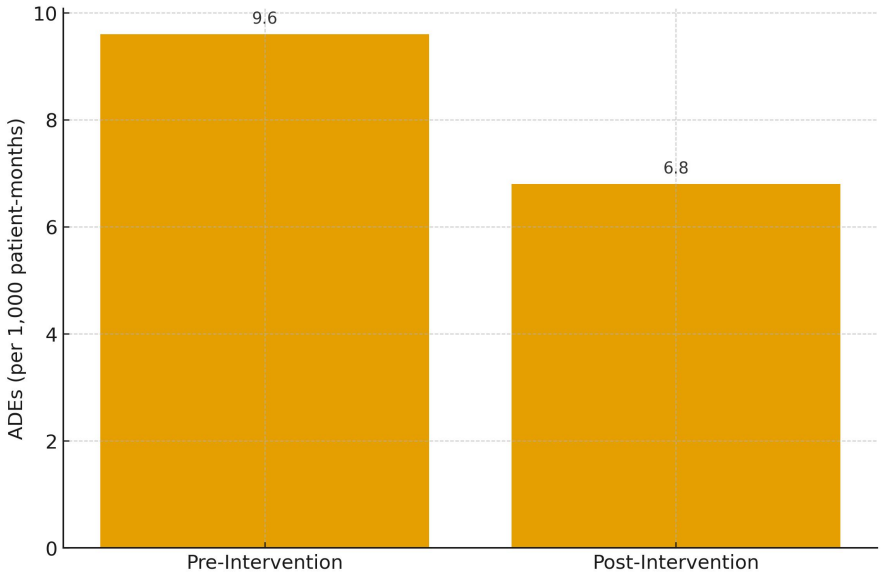

Fig.4. ADE Rate per 1,000 Patient-Months

Additional observations. Acceptance of deprescribing recommendations was high when paired with clear counseling and follow-up, and alert override rates fell as the CDSS was refined to suppress low-value interrupts. Patients reported improved clarity and reduced pill fatigue.

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5. Conclusion

A comprehensive polypharmacy optimization model—combining structured deprescribing criteria (Beers, STOPP/START, MAI), CDSS-driven safety checks, and patient-centered counseling—can substantially reduce regimen complexity and DDI risk, improve adherence through dose simplification, and lower ADE incidence. Embedding this model within routine outpatient care requires governance to calibrate alerts, workflows for pharmacist–physician collaboration, and reimbursement mechanisms for deprescribing and counseling. Future work should examine long-term clinical endpoints, equity impacts across socioeconomic groups, and scalable pathways to integrate community pharmacy data for continuous reconciliation.

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