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Evaluation of medication use and polypharmacy in postoperative cardiac patients: The clinical pharmacist's imperative in a public institute of Pakistan

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Abstract: As a major concern in the healthcare sector, polypharmacy is correlated with an increased risk of potential drug-drug interactions (pDDIs), treatment costs and adverse drug reactions (ADR). To assess the prevalence of polypharmacy and its associated factors among postoperative cardiac patients admitted to the National Institute of Cardiovascular Diseases (NICVD), a hospital-based cross-sectional study was conducted between November 2021 and April 2022. Medication charts of postoperative patients were reviewed for medication utilization and polypharmacy. Data was collected using a form approved by the Ethical Review Committee (ERC) regarding patient's clinical and demographic characteristics and medications administered. Statistical analysis was performed using the SPSS software version 25.0. Patients were taking an average of 10.3±1.7 medications. The minimum number of drugs taken per patient was 5, while the maximum was 15 drugs. Only 114 (29.7%) received polypharmacy (5-9 drugs) and hyper-polypharmacy (≥10 drugs) was 270 (70.3%). The mean±SD cardiovascular drugs used were 5.45±1.18 and the mean±SD non-cardiovascular drugs were 4.83±1.18. The prevalence of hyper-polypharmacy suggests a critical need for optimized medication management strategies in this population. Incorporating clinical pharmacists within public healthcare institutions can address polypharmacy-related challenges and enhance medication safety, adherence and patient outcomes.

Keywords: Polypharmacy, hyper-polypharmacy, cardiovascular disease (CVD), hospitalized patients, co-morbidities.

INTRODUCTION

A combination of pharmacotherapy has been influential in treating many socially significant diseases, including cardiovascular diseases. However, it is also responsible for the increased frequency of adverse reactions because of the increased number of medicines used. Complex pharmacotherapy is often called polypharmacy (Georgiev, *et al*., 2022). Polypharmacy is the usage of five or more medications concurrently by a single patient for one or more conditions. In comparison, hyper-polypharmacy is the usage of ten or more medications concurrently. Evidence shows that the number of adverse events increases beyond five medications for the broader population (Marcum *et al*., 2012). Due to drug-drug interactions, polypharmacy can result in adverse drug reactions and function impairment (Assefa *et al*., 2020). Despite improvements in medicine and pharmaceutical care, polypharmacy has resulted in a higher burden of medication use. Over the past decade, the number of people using five or more prescription drugs has increased by 70% (Tefera *et al*., 2020). There are various levels of polypharmacy based on the number of medications prescribed, i.e., appropriate polypharmacy and problematic polypharmacy (Kral *et al*., 2020, Sechana and Rashmi, 2020). Although polypharmacy can occur in patients of any age group, it is mainly seen in the elderly due to the high prevalence of coexisting chronic diseases. A cross-sectional study in Saudi Arabia reported that patients with cardiovascular diseases are all linked with polypharmacy (Alwhaibi *et al*., 2018). Several cardiovascular disorders (CVDs) are interrelated, as one may manifest as a complication of another. Consequently, cardiovascular patients can be afflicted with multiple conditions and rely on various medications, adding to their medication burdens. Moreover, patients with cardiovascular diseases may require different medications due to the complexity of their conditions and multiple co-morbid vulnerabilities. Therefore, polypharmacy use affects geriatric and general cardiovascular disorder patients (Tefera *et al*., 2020).

Polypharmacy prescriptions are highest for cardiovascular disorders; up to 82% of the incidence has been stated in older patients with cardiovascular diseases (Al-Arifi *et al*., 2014a). Polypharmacy endangers cardiovascular patients for an extended period. In CVDs, Polypharmacy is associated with several factors. These factors include the onset of complications, various morbidities, the progression of disease stages and increasing age (Volpe,

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et al., 2010). There is a link between polypharmacy and adverse outcomes in cardiovascular patients, such as acute kidney injury, adverse events and drug-drug interactions (Chao *et al*., 2015). As a result, it boosts the likelihood of pDDIs and ADR, which leads to a higher risk for collapses, hospitalization, inadequate functional status, non-adherence to medicines, inappropriate prescribing, morbidity, and mortality. Consequently, polypharmacy causes various drug-related problems and excessive medication burdens among cardiovascular patients (Fried *et al*., 2014). It is important to prevent and manage these problems through pharmaceutical care, which involves reviewing the medications prescribed and optimizing their use, especially by a clinical pharmacist.

In addition, there are increasing arguments about cardiovascular polypharmacy; some contend it should not be understood as dangerous, symbolizes poor care and could be facilitated concerning CVDs. Others, however, argue cardiovascular polypharmacy has been misjudged, and polypharmacy should not be evaluated based on the number of drugs but the number of pharmacologically numerous medicines in the cardiovascular system (Abolhassani, 2018).

Since polypharmacy is a growing problem associated with potentially inappropriate prescribing and adverse health outcomes, especially in geriatric cardiovascular disorder patients, it is vital to identify the extent of polypharmacy in these patients (Tseng *et al*., 2016). Polypharmacy is associated with increased medication-related burden in cardiovascular patients due to interference with daily activities, adverse effects, pDDIs and adverse psychological effects (Mohammed *et al*., 2018).

Thus, this study was designed to evaluate the prevalence of polypharmacy and its covariates in postoperative cardiovascular patients at the NICVD in Karachi, Pakistan.

MATERIALS AND METHODS

Study design and setting

A hospital-based cross-sectional study was conducted in Karachi between November 2021 and April 2022 at the NICVD in Karachi, Pakistan. As the first tertiary cardiac centre in South Asia, it is the premier facility for cardiology in Pakistan, providing patient care, education, training for medical professionals and research and development in cardiac care. The NICVD offers cardiovascular services for patients from all provinces of Pakistan, Afghan refugees and patients from neighbouring countries.

Study population and sample selection

The study population included only postoperative patients in the surgical ward during the abovementioned time frame.

Inclusion criteria

In our study, we included patients aged at least 18 years (both genders) and who received at least two drugs (all routes of administration). All medications during the entire hospitalization were included.

Exclusion criteria

Patients that were excluded from the study were Patients younger than 18 years of age and patients on herbal medication.

Sample size

We calculated the sample size using Daniel's formula for sample size calculation, i.e., $n = Z^2P (1-P)/d^2$ (Daniel and Cross, 2018). Based on previous studies, P = expected prevalence in the population (P=0.50, d=precision (d= 0.05) (Ismail *et al*., 2013). Using Daniel's formula mentioned above, our study had a sample size of 384 patients.

Data collection and analysis

The data were compiled using an Ethical Review Committee (ERC) approved data collection form. The data collection form is confined to the patient's socio-demographics, clinical history, and prescribed medications. Patients prescribed medications were listed by their generic names. Data were obtained on an MS Excel™ spreadsheet and double-checked for accuracy and completeness by the co-supervisor. The SPSS (Version 25.0) was applied to evaluate the data. Data were analyzed using frequencies, percentages, means, and standard deviations. Pearson correlation was performed among total, CV and non-CV drugs.

Ethical approval

The study obtained approval from the ERC of the NICVD (ERC-117/2021). Informed consent was not applicable because the study was based on prescription records.

RESULTS

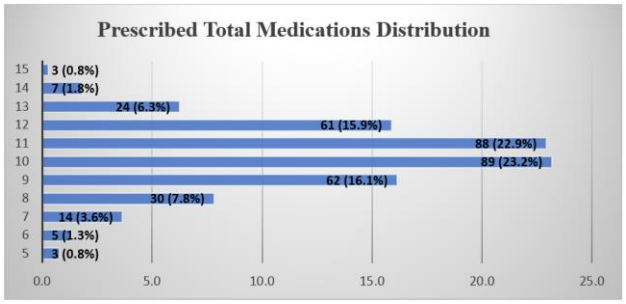
Statistics on sociodemographics and associated profiles

The current study reviewed 384 medication charts of admitted patients to this hospital. The minimum age was 18 years, while the maximum was 75 years. The mean age was 48.93±13.9 years. From the admitted charts reviewed, most patients were 46-60 years old, i.e., 178 (46.4%). The male gender comprised 269 (70.1%), while the female gender comprised 115 (29.9%) of the study population. From the total study participant's distribution of co-morbidity, Hypertension was the most common, 168 (43.8%), followed by Diabetes Mellitus 42 (10.9%), and patients with no known co-morbidities were 112 (29.2%), as depicted in table 1.

Study participant's clinical characteristics

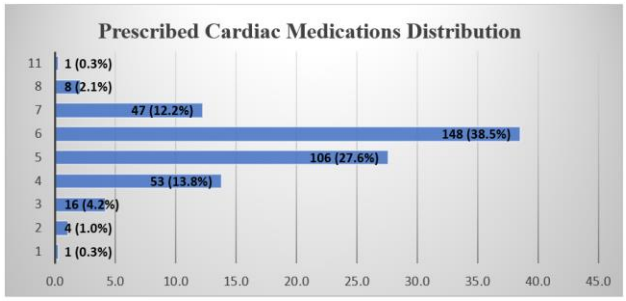
The most commonly diagnosed cardiovascular disorder was three-vessel disease (3VD) from the study participants admitted to the surgical ward. It contributed

to 208 (54.2%) of all diseases, followed by Severe Mitral Regurgitation (MR) 43 (11.2%), Severe Aortic Stenosis (AS) 30 (7.8%), Severe Mitral Stenosis (MS) 25 (6.5%), Severe Aortic Regurgitation (AR) 20 (5.2%) and wound infections 25 (6.5%) as shown in table 1. As mentioned in table 1, the highest percentage of surgeries was CABG 208 (54.2%), followed by Mitral Valve Replacement (MVR) 58 (15.1%), Aortic Valve Replacement (AVR) 39 (10.2%), Double Valve Replacement (DVR) 21 (5.5%), Wound Debridement 25 (6.5%) and Atrial Septal Defect (ASD) Closure 19 (5.0%).



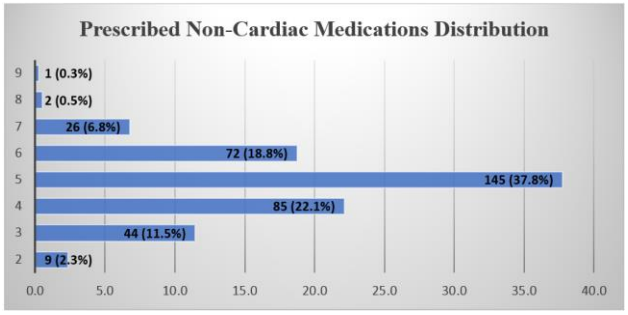
Note: The vertical column shows the total number of drugs prescribed per patient.

Fig. 1: Total prescribed drugs frequency (%)



Note: The vertical column shows the total number of CV drugs prescribed per patient.

Fig. 2: Prescribed CV Drugs Frequency (%)



Note: The vertical column shows the total number of non-CV drugs prescribed per patient.

Fig. 3: Prescribed non-CV drugs frequency (%)

Statistics on prescribed medications

The most frequently prescribed CV drug class was anti-platelet 351 (91.4%), diuretics 348 (90.6%), beta-blocker 319 (83.1%), HMG CoA reductase inhibitor 220 (57.3%), and anti-coagulant 157 (40.9%) table. 2. Regarding non-CV drug classes, antimicrobials were the highest prescribed drug class, 381 (99.2%), followed by proton pump inhibitor 347 (90.4%), analgesic 311 (81.0%), gastrointestinal agent/anti-emetic 236 (61.5%) and anticholinergic/bronchodilator 187 (48.7%) table 3.

Table 1: Demographic and clinical characteristics of study participants (N=384)

Variables	Frequency (%)
Gender	
Male	269 (70.1)
Female	115 (29.9)
Age (years)	
Mean±SD	48.93 ± 13.9
Min - Max	18 - 75
18-30 years	49 (12.8)
31-45 years	81 (21.1)
46-60 years	178 (46.4)
Above 60 years	76 (19.8)
Most Common Co-Morbidities	
Hypertension	168 (43.8)
Diabetes Mellitus	42 (10.9)
Smoking/Tobacco	18 (4.7)
Ischemic Heart Disease	16 (4.2)
NKCM (No Known Co-Morbidity)	112 (29.2)
Most Common Diagnosis	
3VD	208 (54.2)
Severe MR	43 (11.2)
Severe AS	30 (7.8)
Severe MS	25 (6.5)
Severe AR	20 (5.2)
ASD	19 (5.0)
Wound Infection	25 (6.5)
LA Myxoma	7 (1.8)
Most Common Procedures/Surgeries	
CABG	208 (54.2)
MVR	58 (15.1)
AVR	39 (10.2)
DVR	21 (5.5)
ASD Closure	19 (5.0)
Wound Debridement	25 (6.5)
Excision of Myxoma	7 (1.8)

Prevalence of polypharmacy

The minimum number of drugs taken per patient was 5, while the maximum was 15 drugs of different classes. The average number of medications (mean) prescribed per prescription was 10.3±1.7, indicating hyper-polypharmacy practice in the surgical ward. Among the study participants, hyper-polypharmacy was 270 (70.3%), mean CV drugs were 5.45±1.18 and non-CV drugs were 4.83±1.18, as shown in table 4. Of the total study participants, 89 (23.2%) patients were taking ten (10) drugs, which was the highest percentage, followed by 88 (22.9%) patients were taking eleven (11 drugs) and 62

(16.1%) patients were taking twelve (9) drugs fig. 1. The highest number of CV drugs was 6 per patient, 148 (38.5) fig. 2 and the highest number of non-CV medicines used was 5 per patient, 145 (37.8), as in fig. 3.

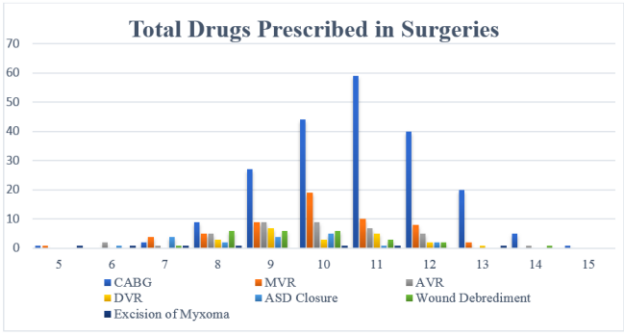
Table 2: Most common cardiovascular (CV) drugs

Variables	Frequency (%)
Anti-Platelate	**351 (91.4)**
Aspirin	224 (58.3)
Clopidogrel	206 (53.6)
Aspirin (Soluble)	122 (31.8)
Diuretic	**348 (90.6)**
Amiloride and Furosemide	265 (69)
Furosemide	138 (35.9)
Spironolactone	14 (3.6)
Beta Blocker	**319 (83.1)**
Metoprolol	210 (54.7)
Bisoprolol	105 (27.3)
Carvedilol	2 (0.5)
HMG CoA Reductase Inhibitor	**220 (57.3)**
Rosuvastatin	157 (40.9)
Atorvastatin	63 (16.4)
Anti-Coagulant	**157 (40.9)**
Warfarin	120 (31.3)
Enoxaparin	101 (26.3)
Rivaroxaban	7 (1.8)
Heparin	1 (0.3)
ACE Inhibitor	**34 (8.9)**
Enalapril	33 (8.6)
Captopril	1 (0.3)
Anti-Arrhythmic	**34 (8.9)**
Amiodarone	18 (4.7)
Digoxin	18 (4.7)
Calcium Channel Blocker	**30 (7.8)**
Amlodipine	28 (7.3)
Diltiazem	1 (0.3)
Verapamil	1 (0.3)
Angiotensin Receptor Blocker	**14 (3.6)**
Losartan Potassium	8 (2.1)
Valsartan	6 (1.6)
Phosphodiesterase Inhibitors	**10 (2.6)**
Sildenafil	10 (2.6)
Vasodilator	**6 (1.6)**
Hydralazine	5 (1.3)

The 384 medication charts assessed found the highest polypharmacy in CABG patients. CABG patients have been prescribed 11 drugs 59 (15.4%), 10 drugs 43 (11.2%) and 12 drugs 40 (10.4%) fig. 4.

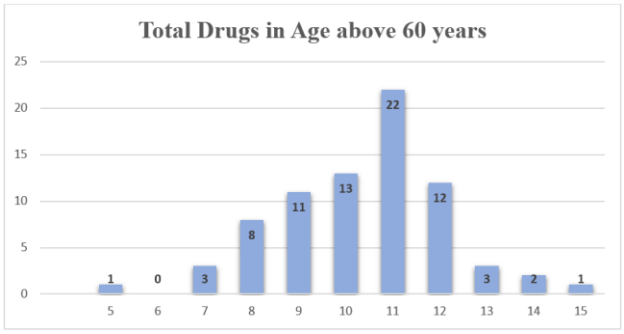
The prevalence of polypharmacy was high in geriatric patients; however, the association between polypharmacy and age was statistically insignificant. However, the highest prescribed drugs, i.e., 15, were prescribed to the patient over 60 years. Similarly, the most frequent total drugs used was 11 in the age above 60 years, i.e., 22 (29%) of total above 60 years patients fig. 5.

The Pearson correlation test was analyzed among total, CV and non-CV drugs, as shown in table 5. The association among them was statistically significant (p = 0.000).



Note: The horizontal row shows the total number of prescribed drugs prescribed per patient.

Fig. 4: Total drugs prescribed in all surgeries



Note: The horizontal row shows the total number of prescribed drugs prescribed per patient.

Fig. 5: Total drugs in age above 60 years

DISCUSSION

This prospective study was conducted at a 650-bed, well-known state-of-the-art teaching hospital in Karachi, Pakistan, providing specialized and generalized cardiac care from outpatient services and emergency to cardiac surgical procedures and postoperative care to national and international patients at no cost.

Polypharmacy is common in cardiac vascular diseases among older adults. Polypharmacy is best defined as taking five or more medications together or concurrently. In different populations, the prevalence of polypharmacy varies and increases with age. In a vast clinical trial involving 1742,336 elder subjects, the prevalence was 44% (Khezrian, McNeil *et al*., 2020, Masnoon, Shakib *et al*., 2017). In another scientific Scottish polypharmacy guidance study, 11% of undecided admissions in a hospital were associated with impairment from polypharmacy and nearly 50% of these were avoidable (Mair, Wilson *et al*., 2019).

Chiefly, the polypharmacy prevalence change broadly parallels the age group, by definition, geographical and healthcare setting. In the United States of America, the prevalence of polypharmacy was 26% among adults, and 61% of older people over 65 years had more than one or multiple conditions. Similarly, our study associated polypharmacy with multiple or single co-morbid conditions (Kim *et al*., 2014). In our recent study and another study, the polypharmacy prevalence among older adults with CVD was more than 90%, significantly associated with single or multiple co-morbidities (34.9%), elderly age and heart diseases (Sheikh-Taha and Asmar, 2021).

Table 3: Most common non-cardiovascular (CV) drugs

Variables	Frequency (%)
Anti-Microbials	**381 (99.2)**
Vancomycin	204 (53.1)
Ceftazidime	274 (71.4)
Co-Amoxiclav	80 (20.8)
Ciprofloxacin	55 (14.3)
Meropenem	19 (4.9)
Co-trimoxazole	3 (0.8)
Piperacillin-Tazobactam	3 (0.8)
Moxifloxacin	3 (0.8)
Proton Pump Inhibitor	**347 (90.4)**
Omeprazole	196 (51.0)
Dexlansoprazole	151 (39.3)
Analgesic	**311 (81.0)**
Acetaminophen	250 (65.1)
Orphenadrine + Acetaminophen	61 (15.9)
Gastrointestinal /Anti-Emetic	**236 (61.5)**
Domperidone	235 (61.2)
Ondansetron	1 (0.3)
Anticholinergic/Bronchodilator	**187 (48.7)**
Ipratropium Bromide	151 (39.3)
Beclomethasone Dipropionate	26 (6.8)
Salbutamol	10 (2.6)
Opioid Analgesic	**24 (6.3)**
Tramadol	24 (6.3)
Electrolyte	**13 (3.4)**
Potassium Chloride	13 (3.4)
Anti-Diabetic	**7 (1.8)**
Metformin	6 (1.6)
Glimepiride	3 (0.8)
Sitagliptin	3 (0.8)
Corticosteroid	**6 (1.6)**
Hydrocortisone	4 (1)
Methylprednisolone	1 (0.3)
Antipsychotic	**5 (1.3)**
Quetiapine	3 (0.8)
Levosulpiride	1 (0.3)

Polypharmacy prescriptions are highest for cardiovascular disorders; up to 82% of the incidence has been stated in older patients with cardiovascular diseases (Al-Arifi *et al*., 2014b). Polypharmacy endangers cardiovascular patients for an extended period. In CVDs, Polypharmacy is associated with several factors. These factors include the onset of complications, various morbidities, the progression of disease stages and increasing age (Khezrian *et al*., 2020).

Table 4: Prescribed drugs per patient

Variables		Frequency (%)
Total Drugs		
Total drugs (384 patients)		3956
Total Drugs per patient (Mean±SD)		10.3 ± 1.7
Min - Max		5 - 15
0-4 Drugs	Non-Polypharmacy	0 (0)
5-9 Drugs	Polypharmacy	114 (29.7)
10-15 Drugs	Hyper-polypharmacy	270 (70.3)
Cardiovascular (CV) Drugs		
Drugs per patient (Mean±SD)		5.45 ± 1.18
Min - Max		1 - 11
Total (CV Drugs)		2091 (53)
Non-Cardiovascular (CV) Drugs		
Drugs per patient (Mean±SD)		4.83 ± 1.18
Min - Max		2 - 9
Total (Non-CV Drugs)		1854 (47)

The predominance of heart and vascular is rising regardless of battles to prevent the significant reason of CVD, for instance, diabetes and obesity. Recent CVD clinical guidelines endorse the multiple drugs used to enhance clinical outcomes. On the other hand, it also increases the drug-drug interaction risk and unwanted adverse effects (Abolbashari *et al*., 2017).

A common problem among postoperative cardiac patients is polypharmacy, especially hyper-polypharmacy. Many medications are often required to treat these patients' complex medical histories. However, multi-medication can lead to adverse effects, drug interactions, and decreased medication adherence. In addition to causing poor outcomes, these interactions can lead to hospital readmissions. Polypharmacy assessment is imperative to ensure safe and effective medication use in postoperative cardiac patients.

In Pakistan, a developing country with high cardiovascular disease rates, polypharmacy assessments are critical in postoperative cardiac patients. In Pakistan, many public institutions do not have dedicated clinical pharmacists to conduct such evaluations due to a lack of resources and trained personnel. In such cases, the medication management and outcomes of patients who have undergone cardiac surgery may be suboptimal.

To address this issue, the incorporation of clinical pharmacists in public institutes in Pakistan is essential. The role of clinical pharmacists is to work collaboratively

Table 5: Correlations among drug categories

Correlations		Cardiac Drugs	Non-Cardiac Drugs	Total Drugs
CV Drugs	Pearson Correlation	1	-0.018	.696**
	Sig. (2-tailed)		0.728	0.000
	N	384	384	384
Non-CV Drugs	Pearson Correlation	-0.018	1	.697**
	Sig. (2-tailed)	0.728		0.000
	N	384	384	384
Total Drugs	Pearson Correlation	.696**	.697**	1
	Sig. (2-tailed)	0.000	0.000	
	N	384	384	384
**. Correlation is significant at the 0.01 level (2-tailed).				

with physicians and other healthcare providers to optimize medication regimens and improve patient outcomes. Clinical pharmacists can ensure safe and effective postoperative cardiac care by reviewing comprehensive medication records, identifying drug interactions and recommending medication adjustments.

Several studies have shown clinical pharmacists can aid postoperative cardiac patients with polypharmacy assessment. According to a systematic review and meta-analysis of 16 randomized controlled trials, pharmacists are involved in postoperative care to reduce medication-related problems, hospital readmissions and healthcare costs (Ahmed *et al*., 2021).

To the best of our knowledge, this is the first study conducted at our hospital that observes polypharmacy among older adults, which needs attention to prevent complications in single or multiple co-morbidities to increase compliance and reduce the complications associated with polypharmacy. Prior published studies conducted in other regions like Lahore and Peshawar also reported that older adults are the particular population for inappropriate medicines. Still, their findings were restricted to drug utilization patterns. However, our scientific study features polypharmacy patterns among elderly CVD patients.

CONCLUSION

In summary, hyper-polypharmacy was common among postoperative cardiac patients. The findings support the recommendation to develop various strategies to mitigate the adverse effects of hyper-polypharmacy in postoperative cardiac patients. The reconciliation and optimization of non-CV drugs could reduce the medication burden for cardiac patients and indirectly impact their adherence to guideline-directed medical therapy. Clinical pharmacists can improve medication safety, adherence, and outcomes in this vulnerable patient population by conducting comprehensive medication reviews and making appropriate recommendations.

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