The Need for Medication Reconciliation Increases with Age

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ABSTRACT: **Background:** Medication reconciliation (MR) at hospital admission, transfer, and discharge has been designated as a required hospital practice to reduce adverse drug events.

Objectives: To perform MR among elderly patients admitted to the hospital and to determine factors that influence differences between the various lists of prescribed drugs as well as their actual consumption.

Methods: We studied patients aged 65 years and older who had been admitted to the hospital and were taking at least one prescription drug.

Results: The medication evaluation and recording was performed within 24 hours of admission (94%). The mean number of medications was 7.8 per patients, 86% consumed 5 or more medications. Mismatching between medication prescribed by a primary care physician (PCP) and by real medication use (RMU) was found in 82% of patients. In PCP the most common mismatched medications were cardiovascular drugs (39%), followed by those affecting the alimentary tract and metabolism (24%) and the nervous (12%) system. In RMU, the most commonly mismatched medications were those affecting the alimentary tract and metabolism (36%). Among all causes of mismatched medications, discrepancies in one drug were found in 67%, in two drugs in 21%, and in three drugs in 13%. The mismatching was more common in females (85%) than in males (46%, $P = 0.042$).

Conclusions: This study provided evidence in a small sample of patients on differences of drug prescription and their use on admission and on discharge from hospital. MR processes have a high potential to identify clinically important discrepancies for all patients.

IMAJ 2017; 19: 625–630

KEY WORDS: medication reconciliation, hospitalization, discharge, geriatric medicine, polypharmacy

The proportion of older people in the population is increasing globally. According to the Israel Central Bureau of Statistics, at the end of 2014, Israel had a population of 8.3 million people. The elderly population (65 years and older) was 900,000 (11%) of the general population.

One in four households in Israel included someone aged 65 or over [1]. The use of health services and drugs, including multiple medications, is increasing year-by-year, especially among the elderly [2-3]. Appropriate prescription of medicines in the elderly and especially in the old elderly is a major clinical and economic concern. Provision of appropriate healthcare and medicines in this group is one of the major challenges facing healthcare systems [4]. Prescribing for older adults is complex. Increased life expectancy is associated with increased numbers of certain chronic illnesses, which often involve recurrent hospital admissions, multiple medications and associated adverse drug events (ADE), and adverse drug reactions (ADR). The presence of co-morbid diseases, multiple medications, and age-related changes in renal and liver function all require careful attention to avoid a variety of prescribing pitfalls, including excessive medication doses, drug–disease interactions, drug–drug interactions, drug–food interactions, and low compliance [5-7].

Medication reconciliation (MR) is the formal process of checking the complete, accurate list of a patient's medications and comparing it with the prescriptions after a transition of care [8]. The main goals of MR are to prevent and reduce errors. This process is accomplished by detecting potential adverse drug events at all steps of medical treatment including continuous prescription use in the community, changes in a patient's medical regimen after specialist consultation and at admission to the hospital as well as on discharge, and transfer to other medical institutions. Without MR, confusion and incomplete information may cause interrupted or inappropriate drug therapy, patient discomfort, and adverse drug reactions.

The purpose of this study was to perform MR among elderly patients admitted to the hospital and to determine factors that affect the differences between the various lists of prescribed drugs.

PATIENTS AND METHODS

The study was conducted by one of the author (R.R.) during the time dedicated for research, as part of a specialization in geriatric medicine.

Consecutive elderly patients admitted to an internal medicine department from April 2013 through August 2013 were assessed for this study. All patients 65 years of age and older admitted to the hospital from home who were taking at least one prescription drug were enrolled. Exclusion criteria included discharge in less than 24 hours, death within 24 hours of admission, inability to communicate, and regularly taking non-prescription medications such as over-the-counter (OTC) drugs or herbal preparations, including nutrient supplements and vitamins.

Initially, 126 patients who were taking one or more medications at the time of hospital admission were eligible for the study. After further evaluation, 76 patients who were regularly taking a non-prescription medication, such as OTC drugs or herbal preparations were excluded.

The patients were divided into three groups according to age: young elderly (65–74 years, 12%), old elderly (75–84 years, 54%) and old-old elderly (85 years and older, 34%).

A comprehensive interview with the patient and/or caregiver was conducted. Questions included demographic information, ethnicity, reason for hospitalization, and medical as well as medication history. The medication history was compiled from the hospitalization referral letter at the patient's primary care physician (PCP), actual daily medication list, bottle labels, and self-prepared medication list.

Fifty patients met the inclusion criteria and were enrolled in the study. All patients provided written informed consent. The institutional ethics committee approved the study.

Patients were divided into three groups according to prescription medication history and actual drug consumption:

- Medications prescribed in an ambulatory setting according to the cover letter of the PCP
- Real medication use (RMU) by patients on admission, as reported by the patient or family member according to the drugs brought to the hospital
- Medications recommended on discharge (ROD) from the hospital

All medications were categorized according to the codes of the Anatomical Therapeutic Chemical (ATC) Classification System [9]. This pharmaceutical coding system groups drugs according to the organ or system on which they act, and according to their pharmaceutical characteristics.

According to the Joint Commission on National Patient Safety (USA) [10], the MR process consists of five steps:

- Develop a list of current medications
- Develop a list of medications to be prescribed
- Compare the medications on the two lists
- Make clinical decisions based on the comparison
- Communicate the new list to the appropriate caregivers and to the patient

The Institute for Healthcare Improvement has further simplified the process of medication reconciliation into three steps [11]:

- Verification (collect the medication history)
- Clarify (ensure that the medications and doses are appropriate)
- Reconciliation (document changes in the orders). Both views of the process should be considered when medication reconciliation is provided

STATISTICAL ANALYSIS

Descriptive statistics were used for all parameters and were reported as mean and standard deviation or range for continuous variables, and count and/or percent for dichotomous variables. Differential statistics were conducted using Mann–Whitney and Kruskal–Wallis tests for continuous variables, and chi-square test for dichotomous variables. Possible associations between the medication and continuous variables were examined by Pearson's correlation coefficient. Results were considered statistically significant if the P-value was < 0.05. The Yates correction for the chi-square test was conducted whenever any of the cells in a 2×2 table was less than five and the unadjusted chi-square was 3.84. All statistical analyses were conducted by using SPSS software version 16 (SPSS Inc., Chicago, IL, USA).

RESULTS

Among the 50 patients studied, medication evaluation and recording was performed within 24 hours of admission for (94%). The mean age was 81.7 years (range 65–97). The largest group of patients (54%) were old-elderly (79.7 ± 1.5 years), followed by old-old elderly (34%, 88.35 ± 2.98 years) and young-elderly (12%, 70.0 ± 2.8 years). Male patients were older (82.9 ± 6.7 years) than females (80.2 ± 5.8 years, $P > 0.05$). Of the participants, 48% were married, 44% were widowed and 8% were single. Most patients (94%) had at least one child [Table 1].

The mean number of co-morbid diseases per patient was 4.2 (4.5 among females and 3.9 among males, $P < 0.04$). The most common co-morbid diseases were cardiovascular (90%), followed by metabolic diseases (62%) mainly diabetes mellitus, and gastrointestinal (46%) [Table 1].

Patients were prescribed a mean of 7.8 drugs each [Table 2]. At admission, the mean number of medications actually consumed was 7.7 and 7.4 at discharge. Most of the group, 43 (86%), consumed 5 or more medications. In addition, 39 (78%) consumed 6 or more, 36 (72%) 7 or more, 32 (64%) 8 or more, 24 (48%) 9 or more and 17 (34%) 10 or more medications.

Ninety-two percent of medications consumed at the time of hospital admission belonged to four groups of the ATC drug classification system. Among which, 40% were medications affecting the cardiovascular system, followed by the alimentary tract and metabolism (20%). Blood and blood forming organs

Table 1. General characteristics of studied patients

Characteristic	Mean ± SD
Age	81.67 ± 6.17
Female, n (%)	26 (52)
Co-morbid diseases	4.22 ± 1.22
Gender	
Female	4.50 ± 1.24
Male	3.88 ± 1.16
Age groups (years)	
65–74	3.67 ± 1.51
75–84	4.41 ± 1.19
≥ 85	4.06 ± 1.14
Affected system, n (%)	
Cardiovascular	45 (90)
Metabolic	31 (62)
Gastrointestinal	23 (46)
Renal	22 (44)
Neurological	19 (38)
Hematologic	18 (36)
Orthopedic	18 (46)
Pulmonary	11 (22)
Cognitive	5 (10)
Other	19 (38)

Table 2. Mean medication use according to gender and age related groups

	PCP (Mean ± SD)	RMU (Mean ± SD)	ROD (Mean ± SD)
All patients	7.78 ± 2.25	7.68 ± 2.48	7.38 ± 2.56
Female	8.04 ± 2.27	7.96 ± 2.20	7.54 ± 2.77
Male	7.50 ± 2.25	7.38 ± 2.76	7.21 ± 2.36
Age groups (years)			
65–74	6.83 ± 2.40	6.67 ± 2.50	7.33 ± 3.20
75–84	8.33 ± 1.98	8.44 ± 1.87	7.85 ± 2.30
≥ 85	7.24 ± 2.49	6.82 ± 3.00	6.65 ± 2.71

PCP = prescribed by primary care physician, RMU = real medication use, ROD =medications recommended on discharge from hospital

and the nervous system accounted for 14% each; 8% of medications belonged to other groups.

The number of co-morbid disease was significantly correlated with the mean number of medications in both in PCP (r = 0.416, P = 0.003) and in RMU (r = 0.329, P = 0.02) groups of patients. The group of cardiovascular diseases was the most common to correlate with the mean number of medications in both of the studied groups (r = 0.356, P = 0.01 in PCP, and r = 0.364, P = 0.009 in RMU groups, respectively).

Gender differences were as follows:

- In female patients, factors correlated with PCP and RMU medications were the mean number of co-morbid diseases (r = 0.666, P < 0.001 and r = 0.665, P < 0.001, respectively), metabolic diseases (r = 0.498, P = 0.01 and r = 0.684, P < 0.001), and hematologic diseases (r = 0.483, P = 0.012 and r = 0.527, P = 0.006).
- In male patients, an inverse correlation between the presence of hematologic diseases was found with PCP and RMU medications (r = -0.442, P = 0.03 and r = -0.425, P = 0.039, respectively). There was a positive correlation between cardiovascular diseases and PCP medications (r = 0.458, P = 0.025). An inverse correlation was found between RMU medications and advanced age (r = -0.441, P = 0.031) and family status (r = -0.417, P = 0.043).

A positive correlation between the mean number of co-morbid diseases with the number of drugs in the PCP and with RMU was found in old-elderly (r = 0.517, P = 0.06 and r = 0.433, P = 0.024, respectively), and in the old-old elderly (r = 0.8, P < 0.01 and r = 0.597, P = 0.011) patients.

There was a mismatch between PCP and RMU in 82% of the patients, which represents 11% of all medications prescribed by PCP and 9% of all RMU. In PCP, the most common mismatched medications were cardiovascular drug (38%), followed by medications affecting the alimentary tract and metabolism (24%) and the nervous (12%) system. In RMU, the most commonly mismatched medications were those affecting the alimentary tract and metabolism (36%), followed by cardiovascular (28%) and nervous (18%) systems.

Among all causes of mismatched medications, discrepancies in one drug were found in 67%, 21% in two drugs, and 13% in three drugs. The mismatching was more common in females (85%) than in males (46%; chi square = 4.16, P = 0.042), as well as in the old-old elderly (80%), compared to the old-elderly (67%) and young-elderly (12%, P = 0.038). Factors correlated with mismatching of medications were advanced age (r = 0.389, P = 0.005) and female gender (r = 0.332, P = 0.019).

Table 3 summarized the significant results of mismatch.

DISCUSSION

Population aging is challenging healthcare systems globally. Increased life expectancy is proportionally associated with increased disease burden on each patient, as well as impaired functional capacity and cognitive decline. The use of drugs in the older population is increasing annually [2-3].

Aging has a strong impact on the pharmacokinetics and pharmacodynamics, co-morbidity, and patterns of medication prescription that contribute to an increased risk of adverse events [12]. Elderly patients often have age-related or disease-related physiological and pathological changes that affect pharmacokinetics and pharmacodynamics, such as impaired renal and hepatic function, altered body composition and altered homeostatic mechanisms. The presence of co-morbid diseases, multiple medications, and renal impairment require careful attention to avoid a variety of prescribing pitfalls, including excessive doses, drug-disease interactions, drug-drug interactions, and use of any of a long

Table 3. Summary finding in the study

	PCP	RMU
Number of mismatched drugs, n (%)		
Drug affecting cardiovascular system	19 (38)	14 (28)
Drug affecting alimentary system	12 (24)	18 (36)
Drug affecting metabolism	12 (24)	18 (36)
Drug affecting nervous system	6 (12)	9 (18)
Correlation *r* (*P*)		
Co-morbid diseases		
Female	0.666 (0.001)	0.665 (0.001)
Metabolic diseases		
Female	0.498 (0.01)	0.684 (0.001)
Hematologic diseases		
Female	0.483 (0.012)	0.527 (0.006)
Male	-0.442 (0.039)	-0.425 (0.039)
Cardiovascular diseases		
Male	0.458 (0.025)	

PCP = prescribed by primary care physician, RMU = real medication use

list of medications that should typically be avoided in older adults [5-7].

This study aimed to perform careful MR among a group of elderly patients to determine factors that affect the mismatches between prescribed drugs and their actual consumption. In 94%, the MR was performed in first 24 hours of hospitalization. We compared the lists of medications prescribed by family physician and actual medications consumed. Ninety-two percent of all medications in the RMU group were found in four groups of the ATC drug classification system [9] drugs: those affecting the cardiovascular system, alimentary tract and metabolism, blood and blood forming organs, and the nervous system.

In this study, difference was demonstrated between gender and in the number of medications. In both groups females showed significant correlation of mean number of medications and co-morbidity ($r = 0.666$, $P < 0.001$, and $r = 0.665$, $P < 0.001$, respectively in PCP and RMU groups). While in RMU male patients showed an inverse correlation between age and mean number of medications ($r = -0.441$, $P = 0.031$). This discrepancy may reflect differences in certain aspects of compliance between genders. Overall, in stratification according to age related groups in old (75–84 years) and old-old (≥ 85 year) elderly patients, significant correlation of the mean number of medication and co-morbidity was found ($r = 0.517$, $P = 0.06$ and $r = 0.433$, $P = 0.024$, respectively in old-elderly from the PCP and RMU groups; $r = 0.8$, $P < 0.01$ and $r = 0.597$, $P = 0.011$, respectively in old-old elderly from the PCP and RMU groups [Table 3]).

The patients were taking a mean 7.68 medications. This number is lower than that presented in the hospital admission (7.78) and then was verified in the ambulatory clinic computer database. The mean number of medications per patient in PCP and RMU groups was higher in females (8.04 and 7.96, respectively) than in males (7.50 and 7.38, respectively).

The use of five or more long-term medications at the same time is defined quantitatively as polypharmacy [13-15]. Polypharmacy is defined qualitatively as "The administration of more medications than are clinically indicated" [6]. In the current study, 86% of patients were consuming at least five medications, and 34% were taking ten medications daily. Polypharmacy, thus, involves serious risks to patient safety. It is associated with reduced ability to perform tasks of daily living, with increased risk for impaired cognitive capacity and increasing incidence of geriatric syndromes such as delirium, falls, and urinary incontinence. In addition, patients with polypharmacy have an increased rate of ADR and ADE [16,17]. Polypharmacy is common in persons admitted to the hospital [18] and multi-morbidity is a strong predictor of unplanned hospitalization [19]. Studies have also shown that the number of medications a patient takes is of value in predicting hospitalization [20] and, indeed may add to the predictive validity of other co-morbidity measures [18].

This study found a high mismatch in medication and prescription use between the studied groups. Appropriate prescribing of medicines in the elderly and especially in the old-old elderly is a major clinical and economic issue. The group of the oldest old people (85 years and older) is increasing and will increase even more in western countries in the coming years. Therefore, health management and appropriate use of medicines in this group is one of the major challenges facing healthcare systems in these countries [4].

A patient's medication regimen may be changed during hospitalization, including temporary cessation or addition of new drugs. Therefore, hospitalized patients are at high risk for medication errors and changes that may cause side effects and dangers. This study found a non-significant decrease in the number of medications on discharge.

The Joint Commission International National Patient Safety Goals Effective [21] recognized that organizations face challenges in implementing medication reconciliation. The effectiveness of this procedure requires a thorough understanding of the patient's current prescriptions and the drugs used at home. This process is part of the list of National Patient Safety Goals for the Accreditation of Hospitals, which is incorporated as target number three: "Enhancing drug use safety" [21].

The process of MR has three important elements: verification (obtaining the most up-to-date medication list), clarification (determining current dosage, utilization, and adherence), and reconciliation (deciding on required changes and ensuring that this information is available to other treating physicians) [11]. Although effective MR represents a critical component of safe transitioning from or between healthcare settings, medical trainees have traditionally received little or no formal training and/or tools for eliciting a proper medication history, review, and reconciliation [22].

We found that 82% of the studied patients had a mismatch between PCP and RMU of at least one medication, which

represents 11% of all PCP and 9% of all RMU medications. Among all of the mismatched medications in the PCP group, 83% represent three codes of the ATC system [9]: cardiovascular drug (39%), followed by medications affecting the alimentary tract, metabolism (24%), and nervous (12%) system. In the RMU group, most mismatched medications were drugs affecting the alimentary tract and metabolism (36%), followed by cardiovascular (28%) and nervous (17%) systems. The mismatching of medication was higher in females (85%) than in males (46%, $\chi^2 = 4.16$, $P = 0.042$), and among the old-old elderly (80%) than in the old-elderly (67%) and young-elderly (12%, $P = 0.038$). Factors correlated to mismatching of medications were advanced age ($r = 0.389$, $P = 0.005$) and female gender ($r = 0.332$, $P = 0.019$).

Hospital admissions are associated with unintentional discontinuations or changes in medication regimens for chronic conditions [23]. The medication list provided by the hospital may not be complete at the time of discharge, resulting in patients inadvertently stopping medications for chronic conditions or starting new medications that may adversely affect existing conditions or other medications [24].

The hospital physician needs to have a detailed list of the patient's current medications to avoid adverse drug reaction and errors and to prevent unintentional, unnecessary, and potentially dangerous changes in drugs and to avoid interactions as well as to assess the appropriateness of treatment. Obtaining a list of current drugs is easy and safe with some patients, while in other cases, it can be difficult (e.g., emergency admission of patients in unstable conditions, elderly patients with impaired cognitive function, and patients with inadequately documented polypharmacy who do not know their drug history). Thus, the existing current medication list often has to be assembled by using a combination of admission letters, written instructions (if existing), and patient history. However, in clinical practice, these sources of information are often incomplete and sometimes contradictory, making a medication survey difficult.

During acute care, evaluation of the patient's drugs is critical for safety and exact diagnosis of medical conditions. Nevertheless the critical phases may present difficulty in assessing the validity of the PCP and the medication record. The capacity of the patient to inform, especially during acute conditions, and due to memory impairments, may be difficult. The MR during the period of hospitalization, although time consuming, is the best method to provide the important information of drug use that may affect the patient's health, wellbeing, and safety.

The strength of this study is in the comparative exact data achieved about drug use in elderly patients who are hospitalized for acute conditions who also present with chronic conditions. The limitations of the study are derived from its small size, short period, and absence of post discharge follow-up. Several factors were not included in the study, such as the reason for hospitalization. Patients with dementia were excluded from the study. We have to extrapolate to their medication use according to the information provided by their caregivers. In the study medical information was obtained for the non-demented patients from both caregivers and patients. We focused mainly on the continuation of care in drug use in the elderly. Thus the importance of drugs as a reason for hospitalization was not considered in this study.

The results of this study strengthen the findings that mismatching of medication use is common among the elderly. Female gender and advanced age are risk factors for this discrepancy. Thus MR is of increasing importance in these groups.

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Capsule

Tracing development of the dendritic cell lineage

Dendritic cells (DCs) are important components of the immune system that form from the bone marrow into two major cell lineages: plasmacytoid DCs and conventional DCs. See and co-authors applied single-cell RNA sequencing and cytometry by time-of-flight to characterize the developmental pathways of these cells. They identified blood DC precursors that shared surface markers with plasmacytoid DCs but that were functionally distinct. This unsuspected level of complexity in pre-DC populations reveals additional cell types and refines understanding of known cell types.

Science 2017; 356: eaag3009

Eitan Israeli

Capsule

A promising therapeutic target in HIV pathogenesis

Antiretroviral therapy (ART) effectively limits human immunodeficiency virus (HIV) replication. Nevertheless, HIV+ individuals need to be medicated for life because ART withdrawal results in rebound of persistent virus. One emerging approach to target HIV is an antibody against integrin α4β7. Integrin α4β7 is a receptor that facilitates homing of CD4+ T cells to the gut, a key site for HIV persistence. Guzzo and colleagues found that integrin α4β7 is incorporated into the HIV envelope, suggesting that antibody treatment may directly interfere with the ability of HIV to home to intestinal tissues. Their results change our perception of the role of integrin α4β7, a promising therapeutic target in HIV pathogenesis.

Sci Immunol 2017; 2: eaam7341

Eitan Israeli

Capsule

Seven-year outcomes of the silicone arthroplasty in rheumatoid arthritis prospective cohort study

Rheumatoid arthritis (RA) causes destruction of the metacarpophalangeal (MCP) joints, leading to hand deformities, pain, and loss of function. Chung and co-authors prospectively assessed long-term functional and health-related quality-of-life outcomes in RA patients with severe deformity at the MCP joints. RA patients between ages 18 to 80 years with severe deformity at the MCP joints were referred to one of the three study sites. Subjects who elected to undergo silicone metacarpophalangeal joint arthroplasty (SMPA) while continuing with medical management were followed in the SMPA cohort. Subjects who elected to continue with medical management alone without surgery were followed in the non-SMPA cohort. Objective measurements included grip and pinch strength as well as arc of motion, ulnar drift, and extensor lag of the MCP joints. Patient-reported outcomes included the Michigan Hand Questionnaire (MHQ) and the Arthritis Impact Measurement Scales questionnaire. Radiographs of SMPA implants were assessed and graded as intact, deformed, or fractured. MHQ scores showed large improvements post-SMPA, and baseline-adjusted expected outcomes in the SMPA group were significantly better at year 7 in function, aesthetics, satisfaction, and overall score compared to non-SMPA. SMPA subjects did not improve in grip or pinch strength, but achieved significant improvement and maintained the improvement long term in ulnar drift and extensor lag.

Arthritis Care & Res 2017; 69: 973

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