Sudan Journal of Medical Sciences
Volume 18, Issue no. 3, DOI 10.18502/sjms.v18i3.14086
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Research Article

Validation of the Arabic Version of Medication Regimen Complexity Index Among Older Patients - Validation of the "MRCI-Arabic"

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Abstract

The medication regimen complexity index is widely used in clinical practice and many studies, to assess the complexity of medication regimens. The goal of this study is to validate the medication regimen complexity index-Arabic (MRCI-Arabic) version among older patients. **Methods:** This methodologic study was conducted in older patients (≥ 65 years old) who were native Arabic speakers at a community pharmacy located in Istanbul, Turkey. After the translation and cultural adaptation process finished, medication regimens of 30 patients were evaluated for test-retest reliability three weeks apart by the rater who was a native Arabic speaker. The inter-rater correlation was calculated in study population (n =100). The link between the number of medications and the score of medication regimen complexity was used to assess convergent validity. The difference in the score of pharmaceutical regimen complexity in stratified age groups was used to examine discriminant validity. **Results:** The inter-rater and test-retest reliability of the MRCI-Arabic total scale and its subsection were extremely high (Spearman's rho ranged from 0.996 to 1; p <0.001). There was a strong and positive correlation between the total MRCI-Arabic score and the number of medications (r = 0.830; p < 0.001), the number of chronic diseases (r = 0.641; p < 0.001). **Conclusion:** The Arabic validation of the MRCI is a validated tool that can be used by native Arabic-speaking healthcare professionals to determine the complexity of their patients' medication regimens.

Keywords: medication regimen complexity index, Arabic version, validation, older patients, clinical practice

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Received 28 October 2022
Accepted 30 January 2023
Published 27 September 2023

Production and Hosting by Knowledge E

Editor-in-Chief:
Prof. Nazik Elmalaika Obaid Seid Ahmed Husain, MD, M.Sc, MHPE, PhD.

1. Introduction

Comorbidity is the simultaneous presence of more than one medical condition in a patient and seems to be directly proportional to age, where it is seen abundantly in individuals over 65 years of age. According to statistics, the percentage of pensioners

afflicted by comorbidity ranges between 55% and 98%; with all the cases struggling with chronic conditions that individually require multiple medication therapies [1].

Polypharmacy refers to the practice of using more than 5 different types of medications at a given period. While extremely common among seniors, polypharmacy has significantly contributed to medication-related problems [2]. Various studies have also displayed a positive relationship between increased therapeutic complexity and lack of patient adherence to treatment. With the demonstrated data, it was evident that it is necessary to investigate the risk factors of polypharmacy to enhance pharmacotherapies adherence among patients [3].

It was observed that the primary factor nurturing poor habits of medication adherence was the complexity of the treatment plan. Non-adherence to medications was more prevalent among patients following a complex medication regimen because it facilitates error making, where patients might find it difficult to follow-up with the directions, doses, and times. Inappropriate consumption of medications is a critical concern provided the adverse health complications they impose [4]. Medication regimen complexity frequently results in decreased effectiveness and an increased chance of treatment failure, as well as nonadherence and greater rates of hospitalization [5-6]. A systematic review of 23 studies that used the medication regimen complexity index revealed that hospitalization, hospital readmission, and medication adherence are some health outcomes that may be influenced by medication regimen complexity [7-8]. In order to tackle the therapeutic complexity and progress toward eliminating it, the pharmacotherapeutic factors nurturing the affair need to be assessed. These factors include the number of medications prescribed, the pharmaceutical forms, schedule management by the patients and/or caregivers, dose regulation, and additional instructions given by the health-care provider [9]. The aforementioned factors can be calculated through the medication regimen complexity index (MRCI) [8], a scale that was validated in Turkish [9], Spanish [10], German [11], Portuguese [12], Korean [13] and Japanese [14].

Polypharmacy affects 46% and 74.9% of older patients in Saudi Arabia and Jordan, respectively [15, 16]. Furthermore, nonadherence to medications is believed to range from 1.4% to 88% in Arab countries. [17]. This high rate of polypharmacy in most Arabic nations necessitates an additional investigation into the factors that influence patients' nonadherence to medications. Arabic pharmacists practicing in patient-oriented settings, such as clinical pharmacy and pharmaceutical care, would benefit greatly from an Arabic version of the MRCI. This tool would help them assess the therapeutic complexity of their patients and identify contributing factors to nonadherence to medication use.

Therefore, the study aims to develop and validate the medication regimen complexity index-Arabic (MRCI-Arabic) version among older patients.

2. Methods

2.1. Study population and setting

This methodological study was conducted in older patients (≥ 65 years old) who were native Arabic speakers at a community pharmacy located in Istanbul, Turkey between the 15th of August to the 15th of October 2021.The study population was allocated consecutively, by using convenience sampling technique. The selected community pharmacy was located within the vicinity of the city's financial center where hospitals and touristic monuments are placed. Ethical approval for the study protocol was provided by the Ethical Committee of Altınbaş University (2021\83). The patients gave their permission after being informed.

2.2. Variables

To obtain clinical information demographic variables like sex, age, marital status, education level, smoking, and patient profile "the number of medications and the number of chronic diseases" were considered.

The MRCI scale comprises 3 sections A, B, and C; totaling 65 items that address and assess dosage forms and frequency as well as for instructions. Every section is evaluated and then scored to display the magnitude of complexity through a number that represents the sum of all 3 sections. Section A explores the factor of pharmaceutical forms, Section B investigates dose frequencies, and Section C addresses additional instructions [8].

2.3. Translation and cultural adaption process

Following the receiving approval from the scale's developing author, it was then translated into Arabic with the assistance of two fluent English-speaking native Arabic clinical pharmacists. Once the two translations were obtained, they were forwarded to an independent team to discuss language discrepancies and reconcile the variations. The final version underwent back translation conducted by native English-speaking individuals who were well-versed in the medical field and who had an excellent command of the

Arabic language. The back-translated copies and the English version of the MRCI scale were compared. The latest adaptation was done by editing for grammar and conceptual discrepancies.

2.4. Validation process

For test-retest reliability, the researcher (NO) calculated the MRCI-Arabic score for the medication regimen of 30 older patients (out of the study data set) twice (baseline and within three weeks following the baseline evaluation).

For inter-rater reliability, researchers (NA and NO) individually evaluated every medication regimen of older patients and calculated medication regimen complexity by using the MRCI-Arabic tool. The link between the number of drugs and the score of medication regimen complexity was used to assess convergent validity. The difference in the score of pharmaceutical regimen complexity in stratified age groups was used to examine discriminant validity.

2.5. Statistical analysis

Descriptive statistics are presented as median (interquartile range [IQR]). The Kolmogorov-Smirnov test evaluated the assessment of the normal distribution of the data. Test-retest reliability (the baseline and after three weeks score of the scale) and inter-rater reliability were evaluated by Wilcoxon test and Spearman correlation, respectively. Mann-Whitney U test and Kruskal-Wallis test were used to assess the differences between the independent variables, with a significance threshold of 0.05.

3. Results

The study included a total of 100 patients from different age groups, education levels, and comorbidity frequencies.

Female older patients were found to be present at a high rate (51.1%); and the median age of the study population was 68.58 ± 4.31. The patients' median number of medicines used was 5 (3.25-7) and the median number of chronic diseases was 1.5 (1-2). The lowest mean MRCI-Arabic was calculated in older patients who used less than four medications, while the highest score was observed in older patients who used more than 10 medications. Table 1 shows the descriptive characteristics of patients. The inter-rater and test-retest reliability of the MRCI-Arabic total scale and its subsection were

extremely high (Spearman's rho ranged from 0.996 to 1; $p < 0.001$). No significant differences were observed between the section scores or between the total scores in the test-pretest analysis. The inter-rater and test-retest reliabilities, with adequate internal consistency between items, are shown in Table 2.

Table 3 shows that there are strong and significant relationships between the number of drugs per prescription and the whole MRCI-Arabic score ($r = 0.839$, $p < 0.001$), as well as the number of comorbidities and the total MRCI-Arabic score ($r = 0.641$, $p < 0.001$).

In terms of total MRCI-Arabic scores, no significant variations were observed between groups according to sex, marital status, or educational level ($p > 0.05$) (Table 4).

4. Discussion

The number of native Arabic speakers residing in Turkey has risen significantly in recent years. In addition, the number of pharmacy students studying in Turkey and continuing their careers in Turkey is growing. Even though the majority of pharmacists know Turkish and English, many studies show that language is a barrier to optimizing medication therapy outcomes, and providing healthcare in the patient's native language is necessary [18, 19]. The medication regimen complexity index was developed to evaluate the complexity of the medication regimen with the aim to simplify these regimes to improve patient adherence and outcomes [8]. The translation and adaptation of MRCI to Arabic will benefit not only the Arabic native speakers in Turkey but all over the world. The MRCI-Arab is the first Arabic version of the MRCI that has been validated based on cross-cultural adaption.

The discriminant validation was validated by lack of correlations between MRCI-Arab scores and factors not connected to pharmaceuticals such as age, sex, marital status, education level, and smoking status.

Furthermore, convergent validation was revealed by the positive correlation between MRCI-Arab scores and the number of medications. These findings matched those of the original MRCI and the other validations indicating that the MRCI-Arab is a viable tool for assessing medication complexity for native Arabic speakers [8–14].

The average MRCI-Arab score in our study was significantly lower than in the other validations, which could be attributed to the nature of our study population, which primarily included patients with type 2 diabetes and/or hypertension who primarily used tablet form, so they only received 1 point from the dosage form section (Section A) [8–13]. Patients who received insulin, for example, had a high score in Section A (3-4), which determines dosage form, yet only a tiny proportion of patients received insulin

Table 1: Characteristics of patients participated in the study (n = 100).

Sex	%
Male	49
Female	51
Age	
Mean ± SD	68.58 ± 4.31
Median (IQR)	67 (66-69.7)
(Min – max)	(65 – 85)
Marital status	
Married (%)	69
Single	41
Education level (%)	
Illiterate	11
Primary school	4
Middle school	32
High school	39
University	14
Smoking	
No	56
1-10 cigarettes daily	16
11-15 daily	8
16-20 daily	17
More than 20 cigarettes a day	3
Number of medications	**Median (IQR)**
1 – 4 (n = 41)	5.00 (4.00 – 6.50)
5 – 9 (n = 50)	11.00 (9.00 – 13.63)
≥10 (n = 9)	18.00 (13.75 — 20.50)
Total medications median	5 (3.25 – 7)
OTC medications	
Median (IQR)	2 (2 – 3)
(Min – max)	(1 – 6)
The number of chronic diseases	
Median (IQR)	1.5 (1-2)
The chronic diseases Hypertension Type 2 diabetes mellitus Other cardiovascular disease Hyperlipidemia Other diseases	38 37 14 9 19
MRCI-Arabic total score	
Median (IQR)	9 (6-12.38)
MRCI- Arabic section A	
Median (IQR)	1(1-3)
MRCI-Arabic Section B	
Median (IQR)	6(4-9)
MRCI-Arabic Section C	
Median (IQR)	1(0-1)

MRCI-Arabic: Medication Regimen Complexity Index Arabic version; IQR: interquartile range

(only 8 patients). It is also not astounding that the highest score was seen primarily

Table 2: The inter-rater and test-retest reliability of the Arabic version of the medication regimen complexity index (MRCI-Arabic).

	Inter-rater reliability	Test-retest reliability (Post 3 weeks)
MRCI-Arabic Section A	0.997	1.000
MRCI-Arabic Section B	0.998	1.000
MRCI-Arabic Section C	0.895	1.000
MRCI-Arabic total	0.996	1.000

The intraclass correlation coefficients (Spearman's rho) are shown in this table. (*p* 0.001), all coefficients are statistically significant. MRCI-Arabic is the Arabic version of the Medication Regimen Complexity Index. The Wilcoxon signed rank test was used to compare the differences between the test and the retest, the *p value* was > 0.05 between all the sections and the total.

Table 3: Correlation between patient characteristics and MRCI-Arabic scores.

The correlation coefficient (Spearman's rho)								
	MRCI-Arabic total		**Section A**		**Section B**		**Section C**	
	r	**P**	**r**	**P**	**R**	**p**	**R**	**p**
The number of medications	0.839**	<0.001	0.389**	<0.001	0.890**	<0.001	0.360**	<0.001
Age	0.022	>0.05	1.000	>0.05	-0.024	>0.05	-0.045	>0.05
The number of chronic diseases	0.641**	<0.001	0.353**	<0.001	0.671	<0.001	0.203**	<0.001

MCRI-Arabic: Medication Regimen Complexity Index Arabic version.
**. Correlation is significant at the <0.001 level (2-tailed).

in Section B in our study, as well as in most studies that use MRCI. Section B scores were determined by dosing frequency, and even if the medication was taken on a need basis it will take at least 0.5 points, thus the complexity of our medication study was primarily driven by dosing frequency. Complex-dose formulations led the most to higher MRCI scores of COPD-specific medications, according to Negewo et al., whereas dosing frequency predominantly drove the complexity associated with non-COPD medications [20]. Given that none of our patients have COPD and do not use inhalation medication, Negewo et al's findings confirm our findings.

The validation findings demonstrated strong inter-rater and test retest reliabilities, with adequate internal consistency between items. The results of the Portuguese, Korean, and Turkish versions were relatively similar to those of our study, whereas the first German validation version had low inter-rater reliability, which improved with the development of the second version [9, 11-13].

Because the instrument is designed to be filled out by a healthcare professional rather than a patient, its methodology allows for the inclusion of several prescriptions and additional information, broadening the scope of the assessment. Furthermore, there

Table 4: Patient characteristics and medication regimen complexity.

	Total score of MRCI-Arabic Median (IQR)	p
Sex		
Male	10.0 (5.5 - 13)	NS
Female	7.0 (6-12)	
Marital status		
Single	9 (6 – 12)	NS
Married	10 (5 - 12.7)	
Smoking		
No Smoking	9.5 (6.2 – 12.8)	NS
1-10	10 (5 – 12)	
16-20	8.50 (5 – 12)	
More than 20	13 (5 – 0)	
Education level		
Illiterate	9 (5.5 – 15)	NS
Primary school	11.75 (7.5 – 14.5)	
Middle school	7.50 (5 – 12.3)	
High School	10 (5 – 13)	
University	10 (6.7 – 11.2)	

NS: non-significant

was no need for significant changes when translating from the original to Arabic. This can also be seen in other validations, such as Turkish and German, where only minor changes are required [9, 11].

The lowest mean MRCI was observed when the total number of medications received was less than four, while the highest average was observed when medication numbers exceeded 10. This finding is supported by the presence of a strong and positive correlation between the total MRCI score and the number of medications, which was found to be valid across all index subsections. These findings are consistent with previous researchers [9-12, 18, 20]. Polypharmacy, which is defined as taking five or more prescriptions at the same time, is highly common among older patients [21]. Polypharmacy was found in 59% of the people in our study versus 45% in the Turkish validation, which could be because our study included OTC medications versus Okuyan et al's study, which only included prescribed medications [9]. In general, our findings were compared with those of Kaufman et al., who reported that 57% of US women aged ≥ 65 years took ≥ 5 prescription medications, and 12% took ≥ 10 medications. This is also consistent with the findings of a large European study (N = 2707; mean age, 82.2 years) which found that 51% of patients took ≥ 6 medications per day [22, 23]. In our study, the mean value of the OTC used by the participated patients is 2.41 ± 1.17

with at least one OTC medication for each patient in agreement with another study, which has been done on 1059 rural community-dwelling older patients (mean age, 74.5 years) showed that nearly 90% of the patients took ≥ 1 and nearly 50% took 2 to 4 OTC medications [24].

It is also not strange that an increase in the number of comorbidities correlates strongly and positively with the total MRCI as well as its three subsections. Wimmer and colleagues conducted a large cross-sectional population-based study involving 3348 subjects in order to assess factors other than the MRCI that were associated with higher MRCI scores [6]. The number of drugs administered to such individuals increased as the number of comorbidities increased. Large numbers of prescriptions, intricate schedules, or extra instructions might all contribute to the patient's problems or lack of interest in following treatment recommendations, resulting in poor clinical results in our research and all other studies that measure medication complexity [4].

We evaluated all the medications that the patient received, including over-the-counter medications, because researchers in past studies generated MRCI ratings for all medications utilized. The Turkish validation only looked at prescription medications, which they consider a limitation of their research [27-30].

Although our study did not directly assess the role of pharmacists in simplifying medication regimens and improving adherence, Arabic validation for this scale will assist native Arabic pharmacists in conducting studies that evaluate the effect of MRCI on patient mortality, quality of life, medication adherence, hospitalization, and readmission, similar to many studies that used different validated versions of MRCI [31-35]. One of our study's limitations is that it was conducted in a single central site, a pharmacy with a pharmacist who is a native Arabic speaker. However, we were able to collect the 100 patients required for our study's sample, which was calculated based on data from previous validations. In terms of validation, 20 German, 96 Portuguese, and 100 Turkish patients participated, respectively. [9, 11, 12]. Other limitations in the study were the over-the-counter medications, patient comorbidities, and other study variables that were collected subjectively from the patients because many of them were newly arrived in Turkey or were tourists who were not covered by the government insurance system. As a result, this information, which was obtained verbally from the patient and was not confirmed by the insurance system, is prone to bias. Even so, this bias has no bearing on our validation because the MRCI is a tool that is completed by the pharmacist rather than the patient. In conclusion, the Arabic validation of the MRCI was a validated tool that can be used by native Arabic-speaking healthcare professionals to assess the complexity

of their patients' regimens and then uses this data in their studies and clinical practices to improve their patients' therapeutic outcomes.

Acknowledgments

None.

Ethical Considerations

Ethical approval for the study protocol was provided by the Ethical Committee of Altınbaş University (2021\83). Written informed consent was obtained from all the patients.

Competing Interests

There are no relevant financial or non-monetary interests to report for the authors.

Availability of Data and Material

The datasets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Funding

None.

Author Contributions

1. Concepts, Literature search [Nilay Aksoy, Nur Ozturk, Betul Okuyan and Mesut Sancar]
2. Clinical studies, Experimental studies [Nilay Aksoy and Nur Ozturk].
3. Data acquisition, Data analysis, Statistical analysis [Nilay Aksoy and Nur Ozturk].
4. Manuscript preparation, Manuscript editing, Manuscript review. [Nilay Aksoy, Nur Ozturk, Betul Okuyan and Mesut Sancar].

5. Final Approval of the version to be published. [Nilay Aksoy, Nur Ozturk, Betul Okuyan and Mesut Sancar].

References

[1] Linjakumpu, T., Hartikainen, S., Klaukka, T., Veijola, J., Kivelä, S. L., & Isoaho, R. (2002). Use of medications and polypharmacy are increasing among the elderly. Journal of clinical epidemiology, 55(8), 809-817.

[2] Masnoon, N., Shakib, S., Kalisch-Ellett, L., & Caughey, G. E. (2017). What is polypharmacy? A systematic review of definitions. *BMC geriatrics, 17*(1), 1-10.

[3] Advinha, A. M., de Oliveira-Martins, S., Mateus, V., Pajote, S. G., & Lopes, M. J. (2014). Medication regimen complexity in institutionalized elderly people in an aging society. *International Journal of Clinical Pharmacy*, *36*(4), 750-756.

[4] De Geest, S., & Sabaté, E. (2003). Adherence to long-term therapies: evidence for action. *European Journal of Cardiovascular Nursing, 2*(4), 323-323.

[5] Jimmy, B., & Jose, J. (2011). Patient medication adherence: measures in daily practice. *Oman Medical Journal, 26*(3), 155.

[6] Wimmer, B. C., Cross, A. J., Jokanovic, N., Wiese, M. D., George, J., Johnell, K., Diug, D., & Bell, J. S. (2017). Clinical outcomes associated with medication regimen complexity in older people: A systematic review. *Journal of the American Geriatrics Society*, *65*(4), 747-753.

[7] Alves-Conceicao, V., Rocha, K. S. S., Silva, F. V. N., Silva, R. O. S., Silva, D. T. D., & Lyra-Jr, D. P. D. (2018). Medication regimen complexity measured by MRCI: A systematic review to identify health outcomes. *Annals of Pharmacotherapy*, *52*(11), 1117-1134.

[8] George, J., Phun, Y. T., Bailey, M. J., Kong, D. C., & Stewart, K. (2004). Development and validation of the medication regimen complexity index. *Annals of Pharmacotherapy*, *38*(9), 1369-1376.

[9] Okuyan, B., Babi, B., Sancar, M., Ay, P., Yücel, E., Yücel, A., & Izzettin, F. V. (2016). Validation of the Turkish version of medication regimen complexity index among elderly patients. *Journal of Evaluation in Clinical Practice*, *22*(5), 732-736.

[10] Saez de la Fuente, J., Such Diaz, A., Cañamares-Orbis, I., Ramila, E., Izquierdo-Garcia, E., Esteban, C., & Escobar-Rodríguez, I. (2016). Cross-cultural adaptation and validation of the medication regimen complexity index adapted to Spanish. *Annals of Pharmacotherapy*, *50*(11), 918-925.

[11] Stange, D., Kriston, L., Langebrake, C., Cameron, L. K., Wollacott, J. D., Baehr, M., & Dartsch, D. C. (2012). Development and psychometric evaluation of the German

version of the Medication Regimen Complexity Index (MRCI□D). *Journal of Evaluation in Clinical Practice*, *18*(3), 515-522.

[12] Deliza, R., Rosenthal, A., & Costa, M. C. D. (2003). Tradução e validação para a língua portuguesa de questionário utilizado em estudos de consumidor. *Food Science and Technology*, *23*, 43-48.

[13] Hahn, J., Lok Min, K., hee Jung, E., sun Oh, K., Cho, R., Jung Chang, M. (2019). Development and validation of the Korean version of the medication regimen complexity index. *PLoS One,14*, e0216805.

[14] Masumoto, S., Sato, M., Momo, K., Matsushita, A., Suzuki, K., Shimamura, H., Shimamura, H., & Hamano, J. (2021). Development of medication regimen complexity index: Japanese version and application in elderly patients. *International Journal of Clinical Pharmacy*, *43*(4), 858-863.

[15] Masumoto, S., Sato, M., Momo, K., Matsushita, A., Suzuki, K., Shimamura, H., ... & Hamano, J. (2021). Development of medication regimen complexity index: Japanese version and application in elderly patients. *International Journal of Clinical Pharmacy*, *43*(4), 858-863.

[16] Al-Qerem, W., Jarrar, Y. B., Al-Sheikh, I., & ElMaadani, A. (2018). The prevalence of drug-drug interactions and polypharmacy among elderly patients in Jordan. *mortality*, *15*, 16.

[17] Al Qasem, A., Smith, F., & Clifford, S. (2011). Adherence to medication among chronic patients in Middle Eastern countries: Review of studies. *EMHJ-Eastern Mediterranean Health Journal, 17*(4), 356-363.

[18] Westberg, S. M., & Sorensen, T. D. (2005). Pharmacy-related health disparities experienced by Non–English-Speaking patients: Impact of pharmaceutical care. *Journal of the American Pharmacists Association*, *45*(1), 48-54.

[19] Al Shamsi, H., Almutairi, A. G., Al Mashrafi, S., & Al Kalbani, T. (2020). Implications of language barriers for healthcare: A systematic review. *Oman Medical Journal*, *35*(2), e122.

[20] Negewo, N. A., Gibson, P. G., Wark, P. A., Simpson, J. L., & McDonald, V. M. (2017). Treatment burden, clinical outcomes, and comorbidities in COPD: An examination of the utility of medication regimen complexity index in COPD. *International Journal of Chronic Obstructive Pulmonary Disease*, *12*, 2929.

[21] Viktil, K. K., Blix, H. S., Moger, T. A., & Reikvam, A. (2007). Polypharmacy as commonly defined is an indicator of limited value in the assessment of drug□related problems. *British Journal of Clinical Pharmacology*, *63*(2), 187-195.

[22] Kaufman, D. W., Kelly, J. P., Rosenberg, L., Anderson, T. E., & Mitchell, A. A. (2002). Recent patterns of medication use in the ambulatory adult population of the United States: the Slone survey. *Jama*, *287*(3), 337-344.

[23] Fialová, D., Topinková, E., Gambassi, G., Finne-Soveri, H., Jónsson, P. V., Carpenter, I., Schroll, M., Onder, G., Sørbye, L. W., Wagner, Reissigová, J., Bernabei, R., AdHOC Project Research Group. (2005). Potentially inappropriate medication use among elderly home care patients in Europe. *Jama*, *293*(11), 1348-1358.

[24] Stoehr, G. P., Ganguli, M., Seaberg, E. C., Echemen, D. A., & Belle, S. (1997). Over□the□counter medication use in an older rural community: The Mo VIES Project. *Journal of the American Geriatrics Society*, *45*(2), 158-165.

[25] Wimmer, B. C., Johnell, K., Fastbom, J., Wiese, M. D., & Bell, J. S. (2015). Factors associated with medication regimen complexity in older people: A cross-sectional population-based study. *European Journal of Clinical Pharmacology*, *71*(9), 1099-1108.

[26] Brysch, E. G., Cauthon, K. A., Kalich, B. A., & Sarbacker, G. B. (2018). Medication regimen complexity index in the elderly in an outpatient setting: A literature review. *The Consultant Pharmacist®*, *33*(9), 484-496.

[27] Linnebur, S. A., Griend, J. P. V., Metz, K. R., Hosokawa, P. W., Hirsch, J. D., & Libby, A. M. (2014). Patient-level medication regimen complexity in older adults with depression. *Clinical Therapeutics*, *36*(11), 1538-1546.

[28] McDonald, M. V., Peng, T. R., Sridharan, S., Foust, J. B., Kogan, P., Pezzin, L. E., & Feldman, P. H. (2013). Automating the medication regimen complexity index. *Journal of the American Medical Informatics Association*, *20*(3), 499-505.

[29] Hirsch, J. D., Metz, K. R., Hosokawa, P. W., & Libby, A. M. (2014). Validation of a patient□level medication regimen complexity index as a possible tool to identify patients for medication therapy management intervention. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy*, *34*(8), 826-835.

[30] Lalic, S., Jamsen, K. M., Wimmer, B. C., Tan, E. C., Hilmer, S. N., Robson, L., ... & Bell, J. S. (2016). Polypharmacy and medication regimen complexity as factors associated with staff informant rated quality of life in residents of aged care facilities: a cross-sectional study. *European Journal of Clinical Pharmacology*, *72*(9), 1117-1124.

[31] Wimmer, B. C., Dent, E., Visvanathan, R., Wiese, M. D., Johnell, K., Chapman, I., & Bell, J. S. (2014). Polypharmacy and medication regimen complexity as factors associated with hospital discharge destination among older people: A prospective cohort study. *Drugs & Aging*, *31*(8), 623-630.

[32] Wimmer, B. C., Dent, E., Bell, J. S., Wiese, M. D., Chapman, I., Johnell, K., & Visvanathan, R. (2014). Medication regimen complexity and unplanned hospital readmissions in older people. *Annals of Pharmacotherapy*, *48*(9), 1120-1128.

[33] Wimmer, B. C., Bell, J. S., Fastbom, J., Wiese, M. D., & Johnell, K. (2016). Medication regimen complexity and number of medications as factors associated with unplanned hospitalizations in older people: a population-based cohort study. *Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences*, *71*(6), 831-837.

[34] Lalic, S., Sluggett, J. K., Ilomäki, J., Wimmer, B. C., Tan, E. C., Robson, L., Emery, T., & Bell, J. S. (2016). Polypharmacy and medication regimen complexity as risk factors for hospitalization among residents of long-term care facilities: A prospective cohort study. *Journal of the American Medical Directors Association*, *17*(11), 1067-e1-1067.e6.

[35] Wimmer, B. C., Bell, J. S., Fastbom, J., Wiese, M. D., & Johnell, K. (2016). Medication regimen complexity and polypharmacy as factors associated with all-cause mortality in older people: A population-based cohort study. *Annals of Pharmacotherapy*, *50*(2), 89-95.