Department of Medicine[1], ABDA – Federal Union of German Associations of Pharmacists; Department of Clinical Pharmacy and Biochemistry[2], Institute of Pharmacy, Freie Universität, Berlin; Department of Internal Medicine III - Cardiology, Angiology and Intensive Care Medicine[3], Saarland University Medical Center, Homburg/Saar, Germany

Do patients with diabetes type 2 or chronic heart failure understand a medication plan?

L. Botermann[1,2], A. Wachter[3], K. Monzel[3], K. Krueger[1], S. Ewen[3], F. Mahfoud[3], N. Griese-Mammen[1], M. Schulz[1,2,*], U. Laufs[3]

Received July 11, 2017, accepted August 11, 2017

** Corresponding author: Prof. Dr. Martin Schulz, Department of Medicine, ABDA – Federal Union of German Associations of Pharmacists, Berlin, Germany*
arzneimittel@abda.de

Pharmazie 72: 764–768 (2017) *doi: 10.1691/ph.2017.7773*

A standardized medication plan (MP) was recently enacted into German law (§ 31a SGB V). The purpose of our study was to assess if patients with chronic diseases requiring polymedication understand the standardized MP and can transfer the given information into practice. 100 patients who took at least five medicines regularly were prospectively included in a cross-sectional study: 50 patients with the primary diagnosis chronic heart failure (CHF), and 50 with diabetes mellitus type 2 (DMT2). We performed a structured test-scenario studying the handling of a provided MP then evaluated the execution of the information on the MP by filling pill boxes and requested patients' opinion. An established weighted scoring system, the "Evaluation Tool to test the handling of the Medication Plan" (ET-MP) was applied to quantitate the ability of the patients to handle the MP. In addition, signs of depression, cognitive function and self-care behavior in chronic heart failure were characterized using the PHQ-9, Mini-Cog, and G9-EHFScB-9 questionnaires, respectively. The understanding of the MP was poor and irrespective of the underlying primary diagnosis. Only 32% of all patients were able to handle the MP without difficulties (ET-MP score >90%), the median ET-MP score was 83 [(IQR) 50-98]. Comprehension of the MP was better in patients aged <70 years compared to ≥70 years ($p<0.01$). Patients ≥10 years of education achieved higher ET-MP results than patients with <10 years of education ($p<0.01$). Patients with signs of cognitive impairment exhibited significantly lower ET-MP scores than patients without cognitive impairment ($p<0.001$). There were no significant correlations of the ET-MP score with number of daily medications, living situation, sex, the Charlson Comorbidity Index, the PHQ-9 score, and use of a dosing aid or possession of a medication list.

1. Introduction

Chronic heart failure (CHF) and diabetes mellitus type two (DMT2) are two of the most common chronic diseases causing distress and requiring polymedication. HF is also the leading diagnosis for hospitalizations (Sapkota et al. 2015; Ewen et al. 2015; Scrutinio et al. 2016). For both conditions improvement of evidence-based medication management is important to reduce disease progression (Adler et al. 2000; Fitzgerald et al. 2011; Stratton et al. 2000). Polymedication is associated with adverse drug reactions and medication errors. This, in turn, is associated with increased morbidity and mortality (Sokol et al. 2005; Martin et al. 2005; Brown and Bussell 2011; Laufs et al. 2011; San-Jose et al. 2014). Adverse effects account for a significant proportion of hospital admissions in older patients and appear to be preventable to a significant extent (Budnitz et al. 2007; Gurwitz et al. 2003; Leendertse et al. 2008; van der Hooft et al. 2008; Hartholt et al. 2010).

Several non-pharmacological approaches to reduce risks and to improve outcomes have been tested (Balu et al. 2009; Bangalore et al. 2007; Hussein et al. 2010). A medication list is regarded as an important contribution to patient safety (Kuske et al. 2012; Wenger and Young 2007; Wolf et al. 2016). Therefore, the German Federal Ministry of Health developed a standardized medication plan (MP) within the scope of the German "Action Plan for Medication Safety" (Bundesministerium für Gesundheit 2013). A MP is a document for patients providing a complete list of their medication including self-medication with information on the medication and its application (Schulz 2014). The standardized MP is offered to statutory health insured patients in Germany taking three or more prescribed drugs (Bundesministerium für Gesundheit 2015).

Interestingly, despite the recommended and widespread use of medication lists, systematic evaluation of its use is still insufficient. Specifically, the understanding and the practical application of the national MP for the patient should be broadly evaluated. For this purpose Botermann et al. developed the "Evaluation Tool to test the handling of the Medication Plan" (ET-MP) (Botermann et al. 2016a).

The aim of this study was to evaluate the understandability and the handling of the MP in two prevalent groups of patients with polymedication – patients with the primary diagnosis CHF and patients with DMT2.

2. Investigations and results

2.1. Study design and setting

We conducted a cross-sectional study, which was approved by the local ethics committee (Nr. 146/15). Patients were recruited in a hospital or general practitioner (GP) practice. In the hospital setting eligible patients were approached consecutively during their stay or at discharge; in the outpatient setting eligible patients were pre-screened by the GP and invited to the practice if willing to participate. Patient screening was done using medical records or by asking the ward physicians for suitable patients.

Patients were eligible if they were 18 years or older with a primary diagnosis of CHF or DMT2 in stable medical condition. Additional inclusion criteria were: application of at least five drugs daily, ability to read and understand German fluently without significant impairment of vision or hearing and willingness to participate in

the study. Patients with professional pharmaceutical or medical background were excluded from the study.

2.2. Data collection

After written informed consent was obtained, a trained medical student (KM) conducted a standardized face-to-face interview (Botermann et al. 2016a and 2016b). The study took place in a quiet room to protect patients' privacy. First, we collected vital signs, height and weight, recording of co-morbidities, educational level, living situation and the prescribed medication from the patients' medical record. Next, patients answered questionnaires concerning cognition (*Mini-Cog* (Borson et al. 2003, 2006)), depression (*Patient Health questionnaire* (PHQ-9) (Kroenke et al. 2001), cut-off ≥10 (Manea, Gilbody and McMillan 2012)), and only for CHF patients self-care (*European Heart Failure Self-care Behavior Scale* (G9-EHFScB-9) (Jaarsma et al. 2009; Koberich et al. 2013)). All patients were also asked to give their personal opinion on the MP by commenting on four predefined statements (Table 1) regarding the design, the expected benefit and use in practice.

Table 1: Statements regarding patients' attitude towards the medication plan

„The MP is clearly arranged"
„The MP would help me with my medication"
„I would use a MP"
„I would take my MP to every doctor's or pharmacy appointment/visit"

To test patients' understandability of the standardized MP, the interview included a test case: patients had to handle a dummy MP and sort the six listed drugs in a dosing aid for 2 days according to the given dosing regimen. The filled dosing aids were photo documented and rated using the ET-MP (Botermann et al. 2016a). The ET-MP is a weighted tool assessing the daily dose, the day, and the time of the day for each medication. The ET-MP score is the percentage of the achieved number of points based on the total amount of points possible. An ET-MP score of >90% was classified as understanding the MP. This cut-off was set based on the readability guideline for package leaflets (European Commission 2009).

2.3. Statistical analyses

Statistical analysis was performed using IBM® SPSS® Statistics software (IBM® SPSS®Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.). Data is presented as median and inter quartile range (IQR) or numbers and percentages. Patient characteristics were analyzed using Chi-square test for categorical variables and Wilcoxon-Mann-Whitney test for continuous variables. Differences in the ET-MP scores between the groups were determined using the Wilcoxon-Mann-Whitney test. To screen for correlations between variables and the ET-MP score the Spearman's rank correlation coefficient was calculated. A $p\ value < 0.05$ was considered statistically significant.

As there is no knowledge on a required sample size, we chose a convenient sample of 100 patients, 50 in each group. This also reflects the 2.5 fold of the suggested amount of patients for the readability testing of package leaflets by the European Commission (European Commission 2009).

2.4. Study population

We included 100 individuals, 50 with CHF and 50 with DMT2 (Table 2). The median age was 69 (61-77) 40% were female. Patients in the DMT2 group had a higher median weight (88 kg (81-94)) compared to CHF patients (80 kg (70-90); p=0.02)). Participation in a disease management program (DMP) was more often documented in the DMT2 group (p=0.02). Possession of a medication list was significantly higher in the CHF group (p=0.02). Otherwise, the patients' characteristics were comparable.

The Mini-Cog and PHQ-9 questionnaires assessing cognition and depression did not show significantly different results between the two disease groups. According to the patients, 81% would use a MP if provided by their GP or pharmacist and 53% would take it to every visit. 61% considered the document to be clearly arranged. For 68% of all patients the MP would be helpful for their regular medication intake.

Table 2: Characteristics of the study groups

Characteristic	CHF (n=50)	DMT2 (n=50)	Total (N=100)	p value
Age (years)	73 (62-79)	67 (61-71)	69 (61-77)	0.1
Sex, female	20 (40)	20 (40)	40 (40)	1
BP systolic (mmHg)	130 (118-140)	130 (130-140)	130 (120-140)	0.42
BP diastolic (mmHg)	73 (70-80)	80 (70-80)	75 (70-80)	0.43
Heart rate (min-1)	69 (65-72)	72 (68-80)	72 (68-78)	0.02
Height (m)	1.70 (1.63-1.67)	1.68 (1.65-1.75)	1.69 (1.64-1.75)	0.75
Weight (kg)	80 (70-94)	88 (81-94)	85 (74-94)	0.02
BMI	28 (25-31)	29 (27-34)	29 (26-33)	0.01
Creatinine (mg/dl)	1.1 (0.9-1.4)	1.1 (0.9-1.3)	1.1 (0.9-1.3)	0.71
eGFR (ml/min)	62.2 (44.2-75.9)	64 (52.3-73.9)	62.6 (48.5-74.7)	0.62
eGFR < 60ml/min	39 (78)	21 (42)	60 (60)	0.13
Living situation, alone	16 (32)	16 (32)	32 (32)	0.83
Highest educational degree				
None	5 (10)	5 (10)	10 (10)	1
8/9 years	30 (60)	30 (60)	60 (60)	1
10 years	9 (18)	11 (22)	20 (20)	0.62
12/13 years	4 (8)	2 (4)	6 (6)	0.40
College/University	2 (4)	2 (4)	4 (4)	1
Number of daily medication (tablets)	9 (8-11)	8 (6-10)	9 (7-11)	0.03
Possession of a medication lista,b	41 (86)	30 (60)	71 (71)	0.02
Charlson Comorbidity Index	2 (1-2)	2 (1-3)	2 (1-3)	0.93
Comorbidities				
Diabetes mellitus type 2	17 (34)	50 (100)	67 (67)	<0.001
Heart failure	50 (100)	14 (28)	64 (64)	<0.001

Characteristic	CHF (n=50)	DMT2 (n=50)	Total (N=100)	p value
Hypertension	42 (84)	39 (78)	81 (81)	0.44
Coronary heart disease	33 (66)	16 (32)	49 (49)	0.001
Asthma/COPD	6 (12)	9 (18)	15 (15)	0.40
Depression	3 (6)	4 (8)	7 (7)	0.7
Chronic kidney disease	12 (24)	6 (12)	18 (18)	0.12
Most common medication classes				
Statins	41 (82)	45 (90)	86 (86)	0.25
Beta-blockers	43 (86)	40 (80)	83 (83)	0.42
Oral anti-diabetics	14 (28)	38 (76)	52 (52)	<0.001
Diuretics	39 (78)	22 (44)	61 (61)	<0.001
ACE inhibitors	29 (58)	22 (44)	51 (51)	0.16
Insulins	0 (0)	14 (28)	14 (14)	<0.001
Questionnaires				
Cognitive impairement	23 (46)	15 (30)	38 (38)	0.1
PHQ 9 (total score)	5 (2-10)	5 (2-9)	5 (2-9)	0.9
DE EHFScB-9 (total score)	19.5 (14.3-24)	not applicable		
Participation DMPa				
Yes	1 (2)	9 (18)	10 (10)	0.01
No	12 (24)	14 (28)	26 (26)	0.65
Unknown	37 (74)	27 (54)	64 (64)	0.04

Data presented as median (IQR) or n (%).

Abbreviations: CHF, chronic heart failure; DMT2, diabetes mellitus type 2; BP, blood pressure; DMP, disease management program; eGFR, estimated glomerular filtration rate; DE EHFScBS-9, 9-Item European Heart Failure Self-care Behaviour Scale, German Version; PHQ-9, The Patient Health Questionnaire; COPD, chronic obstructive pulmonary disease.

Note: [a]According to the patient; [b]partly self made or manually corrected and outdated

2.5. Evaluation tool to test the handling of the medication plan (ET-MP)

32% of all patients (n=100) were considered to understand the MP (ET-MP score >90%). The median ET-MP score of the total cohort (n=100) was 83% (50-98). CHF patients showed a median ET-MP score of 83% (61-99) versus 81% (42-93) in patients with DMT2 (p=0.13) (Fig. 1).

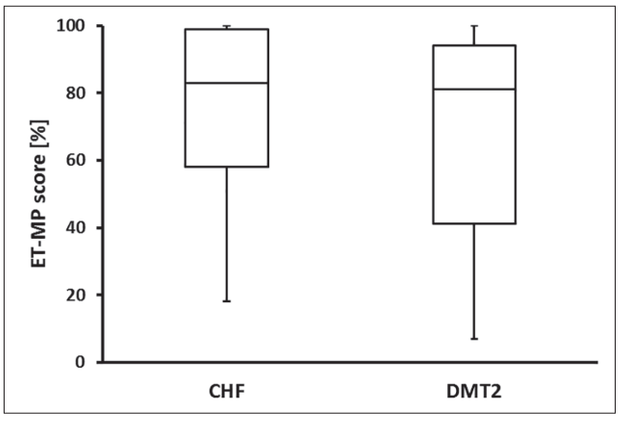

Fig. 1: Boxplots of the ET-MP scores (%) CHF (n=50) vs. DMT2 (n=50). p=n.s. Abbreviations: ET-MP, "Evaluation Tool to test the Medication Plan"

Further analyses showed that the understanding of the MP was better in patients aged <70 years (90% (68-99)) compared to patients aged ≥70 years (76% (39-89.5), *p*=0.003). Patients with more or equal than 10 years of education achieved higher results (91% (82-99)) in the ET-MP score than patients with <10 years (80% (46-90), *p*=0.002). Cognitively impaired patients exhibited a significantly (p<0.001) lower ET-MP score (58% (39-89)) than patients without cognitive impairment (90% (77-99)). The ET-MP scores according to the co-variables are depicted in Table 3.

Table 3: ET-MP scores according to co-variables (N=100)

Variable		ET-MP score (%)	p value
Sex			
female	(n=40)	82 (45-94)	0.29
male	(n=60)	84 (58-99)	
Age (years)			
<70	(n=53)	90 (68-99)	0.003
≥70	(n=47)	76 (39-90)	
Education (years)			
<10	(n=70)	80% (46-90)	0.002
≥10	(n=30)	91% (82-99)	
Living situation			
alone	(n=32)	84 (38-95)	0.52
not alone	(n= 68)	83 (55-99)	
Number of prescribed drugs			
<7	(n=54)	82 (54-94)	0.49
≥7	(n= 46)	85 (46-99)	
Charlson Comorbidity Index			
<2	(n=38)	90 (50-99)	0.33
≥2	(n=62)	83 (50-92)	
Cognitive impairement			
yes	(n=38)	58% (39-89)	<0.001
no	(n=62)	90% (77-99)	
Medication list			
yes	(n=71)	85 (55-99)	0.22
no	(n=29)	76 (49-90)	
Weekly dosing aid			
yes	(n=70)	84 (61-99)	0.15
no	(n=30)	69 (33-96)	
PHQ-9			
<5	(n=45)	83 (68-99)	0.11
≥5	(n=55)	83 (43-92)	
<10	(n=75)	83 (54-98)	0.37
≥10	(n=25)	75 (43-94)	

Median (IQR)

Abbreviations: ET-MP, „Evaluation Tool to test the handling of the Medication Plan"; PHQ-9, The Patient Health Questionnaire.

The Spearman correlation showed moderate correlations between higher ET-MP scores and lower age (r=-0.40; p<0.001), higher level of education (r=0.32; p<0.01), and cognitive impairment (r=-0.38; p<0.001). There were no significant correlations of the ET-MP score with the number of daily medications, living situation, sex, the Charlson Comorbidity Index, the PHQ-9 score, assessment in the hospital or outpatient setting and the use of a dosing aid or a medication list.

3. Discussion

The main finding of our study is that many patients with CHF or DMT2 and polymedication experience problems using the standardized MP. Overall, only 32% of the patients achieved an ET-MP score over 90%. The median ET-MP score was 83% (50-98). Importantly, there was no difference between patients with CHF and DMT2. Patients with higher age (≥70 years), lower education (<10 years) and cognitive impairment showed a lower comprehension of the MP (lower ET-MP scores). Overall, the patients judged the standardized MP as clearly arranged (61%), potentially helpful (68%) and 81% would use it if provided. This indicates the self-assessed necessity for patients and hence hopefully its broad use in practice.

Many experts have recommended a medication list as part of a comprehensive strategy to improve medication safety (Kuske et al. 2012; Wenger and Young 2007; Committee on Identifying and Preventing Medication Errors 2006; Rose et al. 2017). Only if a patient's complete medication including self-medication is known, medication errors e.g. duplications or interactions can be avoided (Steinman 2016; Hutchinson et al. 1986). In addition the current European guideline for the diagnosis and treatment of CHF stressed the importance of additional written instructions for patients as well (Ponikowski et al. 2016). The recent implementation of a standardized MP in Germany by law represents an important approach to improve medication safety and adherence. However, broad evidence on the handling of the MP is still rare (Botermann et al. 2016a, 2016b). To the best of our knowledge, a MP has never been prospectively assessed in patients with DMT2 and, hence, there is no information on the ability to handle this document in this patient population. These data may provide important information for the continuous improvement of the MP and policies. Besides, the authors do not know any studies that verify the increase of patients´ safety due to the standardized MP. Further research in this area is needed.

Our results show that patients have difficulties to use the MP practically. Only one out of three patients was able to fully understand the MP. This clearly shows that additional strategies are needed, especially for risk groups, to successfully implement the MP in practice. Patients need to be counselled not only on their medication but also on the MP itself. A continuous monitoring of patients' knowledge on their medication would seem appropriate. Older age (>70 years), lower level of education and signs of cognitive impairment might help to identify patients with the need of further assistance with their pharmacotherapy by health care professionals in practice. Our findings also support previous observations on risk factors for poor medication adherence (Gehi et al. 2005; Krueger et al. 2005; Rieckmann et al. 2006; Wang et al. 2002).

Perhaps, in practice the demonstrated issues understanding the MP are in fact even higher in patients with DMT2. The applications in this patient group are often more difficult, and the dummy MP only contained solid oral dosage forms. In addition, the standardized MP only allows for four dosing intervals (morning, noon, night, at bedtime), and more complex dosing regimens, especially in insulin-dependent DMT2 patients, do not fit in the corresponding data field. An additional 'insulin plan' should be issued with a reference on the MP. These aspects are additional sources of errors. It has to be emphasized that the MP cannot at all replace professional counselling but only serves as a reminder. In our study, we used a single standard dummy MP and did not explicitly test diabetes specific medication due to comparability aspects.

According to patients´ feedback, most of them would use a MP. A majority of the patients was already equipped with some form of a medication list or unstructured dosing schedule. Our study underlines the value of an MP. The MP has to be complete and readable. However, literature shows that the information was commonly not up to date, incomplete, difficult to read or contained handwritten changes (Freigofas et al. 2015; Waltering et al. 2015). Therefore, only an electronically generated printed MP appears useful. This MP should be available to patients and all caregivers, and should be continuously updated by physicians and pharmacists. Additionally, our research clearly shows that extra and structured help is required for the identified subgroups.

This study encounters several limitations. We only included a small convenient sample of 100 patients, 50 in each group. However, since there is no knowledge of the required sample size we chose the 2.5-fold of the European commission's recommended number for the readability tests of package leaflets (European Commission 2009). Our results may not entirely reflect the handling of the MP in real live, because we used a test case and not the patients' own medication. Moreover, the test contained only six easy to understand medicines and no complicated dosage forms. But, the standardized approach allows robust quantification and a comparison of patients without the confounder of prior counseling. Patients that were not able to correctly transfer the given dosing instructions do not necessarily have to be unable to handle their own medication. Patients that were recruited and participated in the study were interested and potentially amenable to new approaches. Therefore, it can be hypothesized that the average patient might even encounter more difficulties.

The study shows that a significant proportion of patients with CHF or DMT2 has difficulties understanding the standardized MP. It has to be emphasized that the MP cannot at all replace professional counseling. Higher age, lower education and cognitive impairment identify patients with problems understanding the MP that require additional assistance. It is important to identify patients at risk to provide the necessary support.

Acknowledgements: The authors would like to thank Peter Monzel, MD, and the Klinikum Garmisch-Partenkirchen GmbH for their support.

Conflicts of interest: The authors declare that they have no competing interests.

References

Adler AI, Stratton IM, Neil HA, Yudkin JS, Matthews DR, Cull CA, Wright AD, Turner RC, Holman RR (2000) Association of systolic blood pressure with macrovascular and microvascular complications of type 2 diabetes (UKPDS 36): prospective observational study. BMJ 321: 412–419.

Balu S, Simko RJ, Quimbo RM, Cziraky MJ (2009) Impact of fixed-dose and multi-pill combination dyslipidemia therapies on medication adherence and the economic burden of sub-optimal adherence. Curr Med Res Opin 25: 2765–2775.

Bangalore S, Kamalakkannan G, Parkar S, Messerli FH (2007) Fixed-dose combinations improve medication compliance. A meta-analysis. Am J Med 120: 713–719.

Borson S, Scanlan JM, Chen P, Ganguli M (2003) The Mini-Cog as a screen for dementia. Validation in a population-based sample. J Am Geriatr Soc 51: 1451–1454.

Borson S, Scanlan JM, Watanabe J, Tu S-P, Lessig M (2006) Improving identification of cognitive impairment in primary care. Int J Geriatr Psychiatry 21:349–355.

Botermann L, Krueger K, Eickhoff C, Kloft C, Schulz M (2016a) Patients' handling of a standardized medication plan: a pilot study and method development. Patient Prefer Adherence 10: 621–630.

Botermann L, Monzel K, Krueger K, Eickhoff C, Wachter A, Kloft C, Laufs U, Schulz M (2016b) Evaluating patients' comprehensibility of a standardized medication plan. Eur J Clin Pharmacol 72: 1229–1237.

Brown MT, Bussell JK (2011) Medication adherence. WHO cares? Mayo Clin Proc 86: 304–314.

Budnitz DS, Shehab N, Kegler SR, Richards CL (2007) Medication use leading to emergency department visits for adverse drug events in older adults. Ann Intern Med 147: 755–765.

Bundesministerium für Gesundheit (2013) Aktionsplan 2013 - 2015 des Bundesministeriums für Gesundheit zur Verbesserung der Arzneimitteltherapiesicherheit in Deutschland. Aktionsplan AMTS 2013 - 2015, http://www.akdae.de/AMTS/Aktionsplan/Aktionsplan-AMTS-2013-2015.pdf.

Bundesministerium für Gesundheit (2015) Gesetz für sichere digitale Kommunikation und Anwendungen im Gesundheitswesen. E-Health-Gesetz, http://www.bgbl.de/xaver/bgbl/start.xav?startbk=Bundesanzeiger_BGBl&jumpTo=bgbl115s2408.pdf.

Committee on Identifying and Preventing Medication Errors (2006) What can you do to avoid medication errors. fact sheet, http://www.nationalacademies.org/hmd/~/media/Files/Report%20Files/2006/Preventing-Medication-Errors-Quality-Chasm-Series/medicationerrorsfactsheet.pdf.

European Commission (2009) Guideline on the readability of the labelling and package leaflet of medicinal products for human use, http://ec.europa.eu/health/files/eudralex/vol-2/c/2009_01_12_readability_guideline_final_en.pdf.

Ewen S, Baumgarten T, Rettig-Ewen V, Mahfoud F, Griese-Mammen N, Schulz M, Bohm M, Laufs U (2015) Analyses of drugs stored at home by elderly patients with chronic heart failure. Clin Res Cardiol 104: 320–327.

Fitzgerald AA, Powers JD, Ho PM, Maddox TM, Peterson PN, Allen LA, Masoudi FA, Magid DJ, Havranek EP (2011) Impact of medication nonadherence on hospitalizations and mortality in heart failure. J Card Fail 17: 664–669.

Freigofas J, Seidling HM, Quinzler R, Schottker B, Saum K-U, Brenner H, Haefeli WE (2015) Characteristics of medication schedules used by elderly ambulatory patients. Eur J Clin Pharmacol 71: 1109–1120.

Gehi A, Haas D, Pipkin S, Whooley MA (2005) Depression and medication adherence in outpatients with coronary heart disease. Findings from the Heart and Soul Study. Arch Int Med 165: 2508–2513.

Gurwitz JH, Field TS, Harrold LR, Rothschild J, Debellis K, Seger AC, Cadoret C, Fish LS, Garber L, Kelleher M, Bates DW (2003) Incidence and preventability of adverse drug events among older persons in the ambulatory setting. JAMA 289:1107–1116.

Hartholt KA, van der Velde N, Looman CWN, Panneman MJM, van Beeck EF, Patka P, van der Cammen TJM (2010) Adverse drug reactions related hospital admissions in persons aged 60 years and over, The Netherlands, 1981-2007. Less rapid increase, different drugs. PloS one 5: e13977.

Hussein MA, Chapman RH, Benner JS, Tang SSK, Solomon HA, Joyce A, Foody JM (2010) Does a single-pill antihypertensive/lipid-lowering regimen improve adherence in US managed care enrolees? A non-randomized, observational, retrospective study. Am J Cardiovasc Drugs 10: 193–202.

Hutchinson TA, Flegel KM, Kramer MS, Leduc DG, Kong HH (1986) Frequency, severity and risk factors for adverse drug reactions in adult out-patients. A prospective study. J Chronic Dis 39: 533–542.

Jaarsma T, Arestedt KF, Martensson J, Dracup K, Stromberg A (2009) The European Heart Failure Self-care Behaviour scale revised into a nine-item scale (EHFScB-9). A reliable and valid international instrument. Eur J Heart Fail 11: 99–105.

Koberich S, Glattacker M, Jaarsma T, Lohrmann C, Dassen T (2013) Validity and reliability of the German version of the 9-item European Heart Failure Self-care Behaviour Scale. Eur J Cardiovasc Nurs 12: 150–158.

Koordinierungsgruppe zur Umsetzung und Fortschreibung des Aktionsplanes zur Verbesserung der Arzneimitteltherapiesicherheit in Deutschland (2013) Spezifikation für einen patientenbezogenen Medikationsplan. Version 2.0 - für Modellvorhaben, http://www.akdae.de/AMTS/Medikationsplan/docs/Medikationsplan.pdf.

Kroenke K, Spitzer RL, Williams JB (2001) The PHQ-9: validity of a brief depression severity measure. Gen Intern Med 16: 606–613.

Krueger KP, Berger BA, Felkey B (2005) Medication adherence and persistence. A comprehensive review. Adv Ther 22: 313–356.

Kuske S, Lessing C, Lux R, Schmitz A, Schrappe M (2012) Patient safety indicators for medication safety (AMTS-PSI). International status, transferability and validation. Gesundheitswesen 74: 79–86.

Laufs U, Rettig-Ewen V, Böhm M (2011) Strategies to improve drug adherence. Eur Heart J 32: 264–268.

Leendertse AJ, Egberts ACG, Stoker LJ, van den Bemt PMLA (2008) Frequency of and risk factors for preventable medication-related hospital admissions in the Netherlands. Arch Intern Med 168: 1890–1896.

Manea L, Gilbody S, McMillan D (2012) Optimal cut-off score for diagnosing depression with the Patient Health Questionnaire (PHQ-9): a meta-analysis. CMAJ 184: E191-196.

Martin LR, Williams SL, Haskard KB, Dimatteo MR (2005) The challenge of patient adherence. Ther Clin Risk Manag 1: 189–199.

Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, Falk V, Gonzalez-Juanatey JR, Harjola V-P, Jankowska EA, Jessup M, Linde C, Nihoyannopoulos P, Parissis JT, Pieske B, Riley JP, Rosano GMC, Ruilope LM, Ruschitzka F, Rutten FH, van der Meer P (2016) 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur Heart J 18: 891–975.

Rieckmann N, Gerin W, Kronish IM, Burg MM, Chaplin WF, Kong G, Lesperance F, Davidson KW (2006) Course of depressive symptoms and medication adherence after acute coronary syndromes. An electronic medication monitoring study. J Am Coll Cardiol 48: 2218–2222.

Rose AJ, Fischer SH, Paasche-Orlow MK (2017) Beyond medication reconciliation. The correct medication list. JAMA 317: 2057–2058.

San-Jose A, Agusti A, Vidal X, Formiga F, Lopez-Soto A, Fernandez-Moyano A, Garcia J, Ramirez-Duque N, Torres OH, Barbe J (2014) Inappropriate prescribing to older patients admitted to hospital. A comparison of different tools of misprescribing and underprescribing. Eur J Intern Med 25: 710–716.

Sapkota S, Brien J-AE, Greenfield JR, Aslani P (2015) A systematic review of interventions addressing adherence to anti-diabetic medications in patients with type 2 diabetes--components of interventions. PloS one 10: e0128581.

Schulz M (2014) Grundlegende Voraussetzungen für die elektronische Abbildung von Arzneimitteldaten im Hinblick auf den Medikationsplan. Aktionsplan Arzneimitteltherapiesicherheit (AMTS) des Bundesministeriums für Gesundheit (BMG). Abschlussbericht, https://www.bundesgesundheitsministerium.de/fileadmin/dateien/Publikationen/Gesundheit/Forschungsberichte/Abschlussbericht_Grundlegende_Voraussetzungen_fuer_die_elektronische_Abbildung.pdf.

Scrutinio D, Passantino A, Guida P, Ammirati E, Oliva F, Braga SS, La Rovere MT, Lagioia R, Frigerio M (2016) Prognostic impact of comorbidities in hospitalized patients with acute exacerbation of chronic heart failure. Eur J Intern Med 34: 63–67.

Sokol MC, McGuigan KA, Verbrugge RR, Epstein RS (2005) Impact of medication adherence on hospitalization risk and healthcare cost. Med Care 43: 521–530.

Steinman MA (2016) Polypharmacy - time to get beyond numbers. JAMA Intern Med 176: 482–483.

Stratton IM, Adler AI, Neil HA, Matthews DR, Manley SE, Cull CA, Hadden D, Turner RC, Holman RR (2000) Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. BMJ 321: 405–412.

van der Hooft CS, Dieleman JP, Siemes C, Aarnoudse A-JLHJ, Verhamme KMC, Stricker BHCH, Sturkenboom MCJM (2008) Adverse drug reaction-related hospitalisations. A population-based cohort study. Pharmacoepidemiol Drug Saf 17: 365–371.

Waltering I, Schwalbe O, Hempel G (2015) Discrepancies on medication plans detected in German community pharmacies. J Eval Clin Pract 21: 886–892.

Wang PS, Bohn RL, Knight E, Glynn RJ, Mogun H, Avorn J (2002) Noncompliance with antihypertensive medications. The impact of depressive symptoms and psychosocial factors. J Gen Intern Med 17: 504–511.

Wenger NS, Young RT (2007) Quality indicators for continuity and coordination of care in vulnerable elders. J Am Geriatr Soc 55 Suppl 2: S285-92.

Wolf MS, Davis TC, Curtis LM, Bailey SC, Knox JP, Bergeron A, Abbet M, Shrank WH, Parker RM, Wood AJJ (2016) A patient-centered prescription drug label to promote appropriate medication use and adherence. J Gen Intern Med 31:1482–1489.