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ORIGINAL RESEARCH

Incomplete medication adherence of chronically ill patients in German primary care

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Background: Incomplete medication adherence is a major problem in health care worldwide. Patients who adhere to medical treatment have a better prognosis and create fewer costs.

Objective: To assess the degree of incomplete adherence of chronically ill routine primary care patients in a German setting and analyze the association between incomplete medication adherence, as well as clinical and sociodemographic patient characteristics.

Methods: In a cross-sectional survey, chronically ill patients were asked to assess their adherence in primary care retrospectively using the Medication Adherence Report Scale (MARS-D) questionnaire. To investigate the association of incomplete adherence with sociodemographic and clinical data, univariate and multivariate analyses were conducted.

Results: In total, 62.1% of 190 patients were categorized as incompletely adherent. The mean MARS-D score was 23.5 (standard deviation = 2.7). Analyses revealed no statistically significant associations at $P < 0.05$ between degree of adherence and patient characteristics. The total explained variance amounted to 11.8% (Nagelkerke's $R^2 = 0.118$) in the multivariate analysis.

Conclusion: Previously reported results regarding associations of sociodemographic and clinical data with incomplete medication adherence could not be confirmed for this sample of chronically ill patients. In order to be able to provide guidelines for the reduction of incomplete medication adherence in German primary care, further research is needed.

Keywords: medication, adherence, chronic illness, primary care, Germany, MARS

Introduction

In all health care systems, prescribing medication represents a major part of medical treatment. Medications have been shown to improve health outcomes and reduce the utilization of health care resources.[1–5] Moreover, it has been shown that patients who are less likely to take their prescribed medication are more likely to suffer from secondary diseases,[6] and thus to be hospitalized or die.[7–10] The World Health Organization defines adherence as the extent to which a person's behavior (eg, taking medication, following a diet, and/or executing lifestyle changes) corresponds with agreed recommendations from a health care provider.[11] Therefore, incomplete adherence is the occurrence of a patient not completely following these recommendations.

Beyond the negative effects of incomplete adherence on a patient's health, it also represents a financial burden on health care systems. The estimated costs resulting from incomplete adherence in the United States in 2001 were up to 300 billion dollars.[12] This figure highlights the importance of comprehensive knowledge about incomplete adherence to minimize the problems that are subsequently incurred by patients and health care systems worldwide.

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Existing studies report various findings concerning the incomplete adherence of patients. Overall, incomplete adherence has been found to occur in 26% to 60% of all patients.[13–15] For Germany, the results range between 35% and 50%,[16,17] yet to this point, adherence has only been investigated in a few studies. In general, the findings vary depending on sample characteristics and applied measurement instruments.[18,19] Concerning measurement, these different results may be due to the lack of a consistent method for accurate measurement of incomplete adherence.[20] Adherence measures include pill count, physical tests, medical records, self-report, collateral report, or electronic monitoring.[12] Concerning sample characteristics, the following health-related variables have been found to be statistically significantly associated with incomplete adherence: disease (particularly low subjective severity of the disease to be treated, or low "disease threat";[12] also the occurrence of depression[21]); low objective severity of disease in patients with less serious conditions as well as a high objective severity of disease in patients with more serious conditions;[22] low perceived need for medication;[23] lack of social support (including emotional support, family cohesiveness, and marital status);[24] poor communication between patient and physician;[25] high complexity of a patient's medication regimen;[16,18,26] and low extent of medication information (in this context, medication information means the level to which patients feel they have received enough information about prescribed medication).[27,28] Unfortunately, these health-related factors are not always easy to assess in practice.

Demographic data are usually more feasible to acquire; however, according to a meta-analysis by DiMatteo,[12] demographic effects on adherence are small and moderated by sample, regimen, and measurement issues. The only sociodemographic factors found to be associated with incomplete adherence seem to be age below 50 and above 75 years,[13,23] low income,[12,23] and college education.[23] Yet, all these results were found to be affected by the population under study.[12] Most relevant studies have been conducted in the USA,[21] whereas empirical evidence on incomplete medication adherence in Germany is still rare and should be amended by additional data.[16] Accordingly, we aimed to assess the degree of incomplete medication adherence in a sample of chronically ill patients in German primary care. Furthermore, we examined if incomplete medication adherence is associated with certain health-related and/or sociodemographic characteristics. The following health-related variables were considered to potentially be associated with incomplete medication adherence: medication information, medication complexity (consisting of dosage form, dosage frequency, and additional instructions), health-related quality of life (HRQoL, consisting of physical and mental health), and treated condition(s). Investigated sociodemographic data included age, sex, education, and employment status.

This analysis was conducted to clarify which of these potential associations should be taken into consideration in clinical care of chronically ill outpatients in German primary care. Once incomplete adherence is understood better, guidelines for screening procedures in clinical routine could be developed and ultimately lead to more favorable clinical outcomes and savings of health care costs.

Methods

Design

Data were collected in a prospective controlled trial that examined medication complexity, prescription behavior, and patient adherence at the interface between outpatient and inpatient medical care.[29] The data used for the presented analysis were obtained cross-sectionally at the time of admission during an inpatient stay for the treatment of at least one of the patient's chronic cardiovascular and/or metabolic conditions. Patients were recruited between March 2010 and October 2011 from two internal medicine and two urology departments at the University Medical Center in Hamburg-Eppendorf, Germany. Patients were asked to assess their medication adherence in primary care treatment prior to admission retrospectively. Inclusion criteria for participation included age (>18 years), treatment for cardiovascular and/or metabolic diseases, sufficient knowledge of the German language, and the absence of cognitive impairment. To be included in the presented secondary analyses, a filled out German version of the Medication Adherence Report Scale (MARS-D) acquired from the patients was required to ensure that information on adherence was available.[17]

Measures

To measure incomplete medication adherence, the German version of the MARS-D was used.[17] The MARS-D is considered to be an adequate tool for the detection of the frequency of patients' incompletely adherent behavior. Internal consistency (Cronbach's alpha: 0.60–0.69) and test–retest reliability (Pearson's r: 0.61–0.63) of the MARS-D are satisfactory.[17] The MARS-D consists of five items assessing the frequency of incompletely adherent behavior, each featuring a five-level Likert scale (from 1 = always to 5 = never) based on self-reports. Sum scores can vary between 5 and 25 points, with lower scores corresponding to incompletely

adherent behavior. There is no gold standard for dichotomizing the MARS-D and opinions differ concerning acceptable cut-off points,[17] ranging from 20 to 25.[31,32] In this study, patients were categorized as incompletely adherent if they scored less than 25 points on the MARS-D questionnaire. A high cut-off score (as used in this study) is recommended, as social desirability bias needs to be considered and any report of incomplete adherence should be taken into account.[14,33] Additionally, we conducted sensitivity analyses with a cut-off of 23 (representing the lowest quartile of our distribution).

To measure medication information, the 17-item German version of the Satisfaction with Information about Medicines Scale (SIMS-D) was used.[27,34] Total scores vary between 0 and 17 points, quantifying the patient's satisfaction with the information they received about their medication. The SIMS-D consists of two subscales: satisfaction with information received about medication usage (items 1–9) and satisfaction with information received about potential problems of the medication (items 10–17).

Medication complexity was obtained using the German version of the Medication Regimen Complexity Index (MRCI-D).[7,35] The MRCI-D shows good interrater and test–retest reliability (intraclass correlation coefficients > 0.80) quantifying medication complexity concerning the total number of medications, the number of dosage units to be taken at a time, the dosage frequency, and specific directions concerning administration from clinical documentation.[7]

To measure HRQoL, the Short Form Health Survey Questionnaire-12, an indicator of physical and mental health, which was developed as a shorter version of the Short Form Health Survey Questionnaire-36, was utilized.[36,37]

Patients also provided information on their sex, age, education, and employment status. Patients' diagnoses were acquired from their clinical records.

Statistical analyses

Descriptive analyses were used to describe the degree of incomplete adherence in this sample of chronically ill patients. Chi-squared/Fisher's exact tests were used to evaluate the relationship between categorical variables sex, education, employment status, diagnosis of hypertension/type two diabetes/hyperlipidemia/obesity/malignant tumor, and incomplete adherence, respectively. We used *t*-tests to assess differences between adherent and incompletely adherent patients regarding metric variables (age, medication information, medication complexity, HRQoL). To assess clinical significance, we report the respective effect sizes for all univariate results by calculating Cohen's d for all metric and categorical variables. For the latter, we converted the respective odds ratios into Cohen's d.[38]

To examine multivariate associations of sociodemographic and clinical information with incomplete adherence, we conducted a multiple logistic regression analysis. All variables were entered into the same model (entry method). In order to preclude collinearity problems, we entered total scores of instruments with highly correlating dimensions (SIMS-D, MRCI-D) instead of the subscales in the regression equation. The statistical analyses were performed with the software PASW/SPSS Statistics 18 (IBM Corp, Armonk, NY, USA).

Results

Descriptive analyses

A total of 190 patients met the inclusion criteria and took part in the study, providing an analysis sample of 142 male and 48 female participants. Of the 190 patients, 72 patients were recruited at urology departments. One hundred and fourteen patients were recruited at internal medicine departments. For four patients, this information was not available. Patients' age ranged from 23 to 92 years (mean = 62.9 years, standard deviation (SD) = 13.8). The mean MARS-D score was 23.5 (SD = 2.7). Forty-seven of the patients were employed, and 37 of them had an academic education (at least college). The patients' physical quality of life ranged from 15.8 to 61.5 (mean = 38.9, SD = 11.4). The patients' mental quality of life ranged from 18.2 to 64.2 (mean = 46.2, SD = 10.7). On average, patients reported being better informed about "action and usage of medication" (mean = 6.6, SD = 2.5) than about "potential problems of medication" (mean = 3.6, SD = 2.9). Overall, the patients scored an average 10.1 (SD = 4.8) points on the SIMS-D. Medication complexity was rather high with an average score of 15.2 (SD = 10.5) in the MRCI-D. Records of the patients' diseases were available for 186 of the initial 190 patients. The most common diseases were arterial hypertension (prevalence: 89.8%), type two diabetes (33.3%), malignant tumors (18.4%), obesity (13.4%), and hyperlipidemia (6.5%). In total, 62.1% (n = 118) of the patients were categorized as incompletely adherent.

Univariate analyses

Univariate analysis revealed no statistically significant differences at $P < 0.05$ between adherent and incompletely adherent patients regarding sex, age, employment status, academic education, medication information, medication complexity, physical and mental quality of life, hypertension, type two diabetes, obesity, or malignant tumors (Table 1).

Table 1 Associations between patient characteristics and medication adherence in univariate analysis

Variable	Complete adherence; N (%) 72 (37.9)	Incomplete adherence; N (%) 118 (62.1)	N (total) = 190	Test (df)	*P*	d
Sex; N (%)			190	$\chi^2 = 2.741$ (1)	0.098	0.307
Male	49 (25.8)	93 (48.9)				
Female	23 (12.1)	25 (13.2)				
Age; M (SD)	63.7 (14.8)	62.6 (13.2)	183	$t = -0.491$ (181)	0.624	0.08
Employment status; N (%)			189	$\chi^2 = 0.554$ (1)	0.457	0.144
Employed	16 (8.5)	31 (16.4)				
Unemployed	57 (30.2)	85 (44.9)				
Education; N (%)			183	$\chi^2 = 0.437$ (1)	0.508	0.140
Academic	13 (7.1)	24 (13.1)				
Not academic	60 (32.8)	86 (47)				
Patient information; M (SD)	11 (4.7)	9.6 (4.8)	178	$t = -1.922$ (176)	0.056	0.292
Action and usage	6.9 (2.4)	6.3 (2.5)	178	$t = -1.647$ (176)	0.101	
Potential problems	4 (2.9)	3.3 (2.9)	177	$t = -1.724$ (175)	0.086	
Medication complexity; M (SD)	16.5 (10.7)	14.4 (10.4)	175	$t = -1.301$ (173)	0.195	0.199
Physical QoL; M (SD)	39.6 (11.8)	38.6 (11.2)	174	$t = -0.541$ (172)	0.589	0.088
Mental QoL; M (SD)	46.2 (10.6)	46.1 (10.8)	174	$t = -0.056$ (172)	0.955	0.009
Hypertension; N (%)			186	$\chi^2 = 0.001$ (1)	0.981	0.007
Yes	62 (33.3)	105 (56.5)				
No	7 (3.8)	12 (6.4)				
DM type 2; N (%)			186	$\chi^2 = 0.104$ (1)	0.747	0.057
Yes	22 (11.8)	40 (21.5)				
No	47 (25.3)	77 (41.4)				
Hyperlipidemia; N (%)			186	FET	0.131	0.511
Yes	7 (3.8)	5 (2.7)				
No	62 (33.3)	112 (60.2)				
Obesity; N (%)			186	$\chi^2 = 2.123$ (1)	0.145	0.392
Yes	6 (3.2)	19 (10.2)				
No	63 (33.9)	98 (52.7)				
Malignant tumor; N (%)			190	$\chi^2 = 1.585$ (1)	0.208	0.282
Yes	10 (5.3)	25 (13.2)				
No	62 (32.6)	93 (48.9)				

Notes: Patient information is the patients' satisfaction with the information they received about their medication (SIMS-D score); medication complexity is the MRCI-D (Medication Regimen Complexity Index) Score.

Abbreviations: N, number; df, degrees of freedom; d, effect size; M, mean; SD, standard deviation; QoL, quality of life; FET, Fisher's exact test; DM Type 2, diabetes mellitus type two; SIMS-D, Satisfaction with Information about Medicines Scale; MRCI-D, Medication Regimen Complexity Index.

Conducting the identical univariate analysis using the alternative cut-off value (MARS-D score of 23) as part of the sensitivity analysis did not show any statistically significant results either. Most standardized effect sizes were negligible with a few, but still not statistically significant, moderate values.

Multivariate analyses

No strong multicollinearities between the variables were detected (Table 2); therefore, we conducted a multivariate analysis to determine if any of the variables were associated with incomplete medication adherence (Table 3). None of the variables were found to be statistically significantly associated with incomplete medication adherence. Conducting the identical multivariate analysis using the alternative cut-off value (MARS-D score of 23) as part of the sensitivity analysis did not show any statistically significant results either. The total explained variance amounted to 11.8% (Nagelkerke's $R^2 = 0.118$).

Discussion

Due to the cross-sectional design of the study, the conducted analyses allowed us to investigate possible associations between incomplete medication adherence and the patients' sociodemographic and clinical data. However, cross-sectional studies are not appropriate for testing causal relationships between dependent and independent variables, and our findings should be interpreted accordingly. We found a rate of 62.1% of incomplete medication adherence in chronically ill patients. Neither univariate nor multivariate analysis showed

Table 2 Pairwise correlations between analyzed patient characteristics

	Sex	Age	Employment status	Education	SIMS-D score	MRCI-D score	Physical QoL	Mental QoL	Arterial hypertension	DM 2	Hyperlipidemia	Obesity	Malignant tumor
Sex	1	0.09	−0.12	−0.15*	−0.05	0.19*	−0.08	−0.12	0.08	−0.03	0.17*	−0.03	−0.15*
Age	0.09	1	−0.47*	0.00	0.09	0.04	−0.23*	0.02	0.07	0.13	−0.01	−0.10	0.15*
Employment status	−0.12	−0.47*	1	0.12	−0.06	−0.14	0.24*	−0.01	−0.01	−0.03	0.01	0.04	0.02
Education	−0.15*	0.00	0.12	1	0.01	−0.04	0.12	0.19*	−0.01	−0.01	0.04	−0.03	−0.05
Patient information	−0.05	0.09	−0.06	0.01	1	0.07	0.04	0.17*	−0.11	0.02	0.02	−0.13	−0.09
Medication complexity	0.19*	0.04	−0.14	−0.04	0.07	1	−0.3*	−0.26*	−0.04	0.33*	0.07	−0.01	−0.23
Physical QoL	−0.08	−0.23*	0.24*	0.12	0.04	−0.29*	1	0.22*	0.06	−0.20*	−0.09	0.00	0.07
Mental QoL	−0.12	0.02	−0.01	0.19*	0.17*	−0.26*	0.2*	1	0.01	−0.14	−0.06	−0.09	−0.09
Arterial hypertension	0.08	0.07	−0.01	−0.01	−0.11	−0.04	0.06	0.01	1	0.04	0.09	0.02	−0.09
DM 2	−0.03	0.13	−0.03	−0.01	0.02	0.33*	−0.20*	−0.14	0.04	1	0.17*	0.02	−0.15*
Hyperlipidemia	0.17*	−0.01	0.01	0.04	0.02	0.07	−0.09	−0.06	0.09	0.17*	1	−0.04	−0.13*
Obesity	−0.03	−0.10	0.04	−0.03	−0.13	−0.01	0.00	−0.09	0.02	0.02	−0.04	1	0.07
Malignant tumor	−0.15*	0.15*	0.02	−0.05	−0.09	−0.23	0.07	−0.09	−0.09	−0.15*	−0.13*	0.07	1

Notes: *Level of significance < 0.05. Patient information represents the patients' satisfaction with the information they received about their medication (SIMS-D score). Medication complexity indicates the MRCI score.
Abbreviations: R, Pearson product–moment correlation coefficient; SIMS-D, Satisfaction with Information about Medicines Scale; MRCI-D, Medication Regimen Complexity Index; QoL, quality of life; DM 2, diabetes mellitus type two.

Table 3 Associations of incomplete medication adherence in multivariate analysis

Variable	OR	95% CI	*P*
Female sex	1.38	0.55; 3.47	0.493
Lower age	0.99	0.96; 1.02	0.534
Unemployment	0.92	0.35; 2.40	0.859
Lower education	0.38	0.13; 1.11	0.076
Lower information (SIMS-D score)	0.94	0.87; 1.02	0.143
Lower medication complexity (MRCI-D score)	0.98	0.94; 1.02	0.211
Lower physical QoL	0.97	0.94; 1.01	0.108
Lower mental QoL	0.99	0.96; 1.03	0.756
Absence of arterial hypertension	0.56	0.17; 1.92	0.359
Absence of DM 2	0.78	0.31; 1.97	0.598
Hyperlipidemia	2.33	0.49; 11.11	0.288
Absence of obesity	0.82	0.28; 2.40	0.717
Absence of malignant tumor	0.96	0.35; 2.63	0.929

Note: Nagelkerke's $R^2 = 0.118$.
Abbreviations: OR, odds ratio; CI, confidence interval; SIMS-D, Satisfaction with Information about Medicines Scale; MRCI-D, Medication Regimen Complexity Index; QoL, quality of life; DM 2, diabetes mellitus type two.

evidence for significant associations between incomplete medication adherence and the patients' sociodemographic or clinical characteristics. Our findings conflict with preceding studies from other countries. Discrepancies between results of this study and other reported results regarding the associations of incomplete adherence could be due to several reasons, of which some include measurement of adherence, publication bias, low generalizability, and power.

First, a well-known problem when investigating incomplete medication adherence is measurement. A gold standard has not been developed, neither for the method of measurement, nor for the interpretation of results. Although direct measurements of medication ingestion, such as determining blood levels of pharmacological agents or medication event monitoring systems (a medication container with a special closure that records the time and date of each time the container is opened and closed), are more precise, questionnaires about the patient's adherence (self-reports) are usually used because they are cheaper, noninvasive, and easier to conduct. However, the adherence rates assessed through questionnaires depend on the patient's honesty and social desirability bias. While generally providing moderate-to-high concordance with objective measures, self-reports have been shown to provide higher adherence rates compared to nonself-reports (for example 13% higher than medication event monitoring systems, and 3% higher than pill counts).[13,17,39,40] In this study the MARS-D (self-report) was used. While some researchers refer to the MARS as an appropriate measure to detect incomplete medication adherence,[17] others do not recommend it, for it lacks sensitivity.[33] In order to increase sensitivity,

we decided to measure complete medication adherence (MARS-D score of 25) versus incomplete medication adherence (MARS-D score of less than 25). The measured incomplete adherence rate of 62.1% was rather high,[12] yet still in accordance with previous findings.[15,32] However, sensitivity analyses with a broader MARS-D cut-off did not indicate any statistically significant associations between incomplete medication adherence and the patients' data. The findings suggest that the results are unlikely to be attributable to the strict cut-off that was chosen. However, additional investigation is needed to examine whether associations between adherence rates and patient characteristics depend on the type of measurement.

Secondly, a further explanation for contrary results could possibly be an underestimated publication bias in the field of adherence. Publication bias is a common problem in other fields of research.[41] Since previous results on the associations of incomplete medication adherence have reported inconsistent findings with generally small effect sizes,[20] the extent of a possible publication bias should be explored through future meta-analyses. However, existing meta-analyses concluded that the possible risk of publication bias due to unpublished nonsignificant findings is rather low.[21,24]

Thirdly, a limitation of our study is the convenient sample that was examined. However, participants were recruited consecutively without any selection, which makes the findings fairly generalizable to a population of patients admitted to inpatient treatment. This sample was heterogeneous, yet fairly representative of chronically ill patients treated with antihypertensive medication.[29] Differences regarding the patients' diseases in previous studies and this study could have influenced the results (and therefore limited this study), as (for example) depression and other diseases are shown to affect adherence.[12,21] Nevertheless, multimorbidity is found in most samples of chronically ill patients and represents the same problem in research and practice. The majority (74.7%) of all participants were male; 38.7% of the patients were recruited from urology wards. However, since gender has not been found to influence adherence,[12] this should not reduce the generalizability of our findings. The relatively high average age of 62.9 years and the low percentage of patients being currently employed (24.9%) can be expected in a sample of chronically ill patients. Lastly, 79.8% of the participants were without an academic education. This finding is also expected in a sample of chronically ill patients because a low socioeconomic status is more likely to be accompanied by disease.[42,43] The high clinical heterogeneity of the analyzed sample provides a meaningful, even if negative, result on possible associations of adherence and medication. Based on the sufficient power of the analyses, it is probable that this negative finding contributes substantially to the existing knowledge by showing us that we are likely to know less than we sometimes suppose.

Finally, featuring a sample size of 190 patients, the power of this study allowed for the detection of any small- to medium-sized association (Cohen's d of 0.4) with a power above 80% (two-tailed at $P = 0.05$). Thus, it is to be expected that clinically relevant associations would have become visible. The total explained variance of 11.8% in the multivariate analysis indicates that even though combining information from all tested variables may explain a moderate amount of the observed variation in adherence behavior, the contribution of each single variable remains negligible.

In conclusion, we could not find sociodemographic or clinical variables that are associated with incomplete medication adherence. Variables associated with incomplete medication adherence found in previous research from other countries (and only one study regarding Germany) could not be confirmed. Further research is needed to find predictors of incomplete adherence in German settings. The focus should lie on primary care since inpatients exhibit almost complete medication adherence leading to more favorable clinical outcomes.[13] Studies that explore medication adherence beyond individual patient characteristics are needed to fully understand adherence as an interactive construct shaped by the relationship between patients and their health care providers.[44]

Disclosure

The authors report no conflicts of interest in this work.

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