Let’s talk about medication: concordance in rating medication adherence among multimorbid patients and their general practitioners

Dominik Ose
Cornelia Mahler
Ines Vogel
Sabine Ludt
Joachim Szecsenyi
Tobias Freund
University Hospital of Heidelberg, Department of General Practice and Health Services Research, Heidelberg, Germany

Background: Medication adherence can be essential for improving health outcomes. Patients with multiple chronic conditions, often receiving multiple medications, are at higher risk for medication nonadherence. Previous research has focused on concordance between patients and providers about which medication should be taken. However, the question of whether patients and providers are concordant in rating actual medication intake has not been answered as yet. This study aimed to explore the extent and predictors of patient – provider concordance in rating medication adherence in patients with multiple chronic conditions.

Methods: Overall medication adherence was measured by self-report (Medication Adherence Report Scale, MARS-D) in a sample of 92 patients with multiple chronic conditions. Twelve treating primary care physicians were asked to rate medication adherence in these patients using a mirrored version of the MARS-D. Concordance between external rating and self-reported medication adherence was analyzed descriptively. Predictors of concordance in rating medication adherence were explored in a multilevel analysis.

Results: Patients rate their medication adherence markedly higher than their general practitioner. Accordingly, the percentage of concordance ranges between 40% (forgot to take medication) and 61% (deliberately omitted a dose). In multilevel analysis, concordance in rating medication adherence was positively associated with being the single primary care provider (β = 2.24, P < 0.0001) and frequent questioning about medication use (β = 0.66, P = 0.0031). At the patient level, “not [being] married” (β = −0.81, P = 0.0064) and “number of prescribed medications” (β = −0.10, P = 0.0203) were negative predictors of patient – provider concordance in rating medication adherence.

Conclusion: Concordance for rating medication adherence between general practitioners and their patients was low. Talking about medication on a regular basis and better continuity of care may enhance patient – provider concordance in rating medication adherence as a prerequisite for shared decisions concerning medication in patients with multiple chronic conditions.

Keywords: patient – provider concordance, medication adherence, primary health care, multimorbidity, communication

Introduction

In primary care, the patient – physician relationship plays a pivotal role in optimal chronic care including the long-term management of risk factors, lifestyle interventions, and support of medication adherence.1-3 Patients with multiple chronic conditions in particular demand patient-centered care.4,5 However, these patients tend to be clinically complex and require extensive consultation time, and providers face the challenge of addressing these needs in brief patient encounters.6,7
Patient–provider concordance, ie, consent between patients and their doctors regarding health-related tasks, for example medication, is seen as an indicator of collaboration between patients and health care providers which requires communication and shared decision-making.\textsuperscript{9,10} and has previously been evaluated in different settings. Patient–provider concordance about the most relevant health conditions affecting patients with multimorbidity is seen as an indicator of a good patient–physician relationship.\textsuperscript{11} Agreement between patients and physicians regarding the diagnosis and treatment plan is associated with better health outcomes.\textsuperscript{12,13} In contrast, inadequate communication between patients and providers is an important cause of discordance, which can have serious consequences, including unsafe management of medication.\textsuperscript{14} Finally, a recent study suggests that patient–provider concordance is a relevant predictor of medication adherence.\textsuperscript{15}

Constant medication intake is a demanding issue, especially for patients with multiple chronic conditions. Commonly, this patient group receives multiple medications, which are associated with a higher risk for medication nonadherence.\textsuperscript{16} This could undermine quality of care and lead to poor health outcomes.\textsuperscript{17} Accordingly, improving medication adherence is an important task in primary care.\textsuperscript{18} In this context, it is essential that general practitioners know whether and to what extent patients actually take their prescribed medication.

However, previous research and discussion has focused on concordance between patients and providers about the “what” and “how” of a medication regime. The question of whether patients and providers are concordant in rating actual medication intake has not been answered as yet. To fill this void, our study aimed to explore how general practitioners rate medication adherence in patients with multiple chronic conditions and which factors influence concordance between externally rated and self-reported medication adherence. The results will contribute to a more comprehensive understanding of the complex process of improving medication adherence in patients with multiple chronic conditions.

Materials and methods

Study sample

This study was part of a set of exploratory studies aimed at developing a complex care management intervention for multimorbid patients at high risk for future hospitalization. The study was given ethical approval by the institutional review board of the University Hospital Heidelberg prior to beginning the study (S-052/2009). The study complied with the tenets of the Declaration of Helsinki. All participants gave their written informed consent.

To identify patients likely to benefit from care management programs, insurance claims data for a systematic sample of all beneficiaries of the General Regional Health Fund in a region of Baden-Wuerttemberg, Germany, were obtained from 10 primary care practices in 2008 and 2009. The 10 primary care practices (six single practices and four group practices) were recruited from rural areas (five practices) and from urban areas (five practices). Within these practices, high-risk individuals for whom a hospitalization within the next 12 months was considered most likely were either identified by predictive modeling based on claims data or referred by their primary care physician (the general practitioner). The risk of future hospitalization was evaluated by subjective criteria determined by the general practitioner. For participants identified by the predictive model, a likelihood of hospitalization above the 90th percentile was set as the cutoff value for inclusion. Details on case finding and recruitment of participants for this study are published elsewhere.\textsuperscript{19} Additional inclusion criteria were concomitant type 2 diabetes, chronic obstructive pulmonary disease, chronic heart failure, late-life depression (age > 60 years), or any combination of these index conditions. Patients with the following conditions were excluded from participation: dementia, dialysis, active cancer disease under medical treatment, permanent nursing home residency, and being under palliative care. Minors (age < 18 years) were also excluded. Recruitment of patients was done between December 2009 and April 2010.

Study measures

All identified patients were asked to complete a paper-based questionnaire handed out by their general practitioner. After completion, it was sent back to the University Hospital Heidelberg for evaluation by surface mail in a stamped addressed envelope. The questionnaire included the Medication Adherence Report Scale (MARS-D)\textsuperscript{20} measuring self-reported overall medication adherence with five items on a five-step Likert-scale with values in the range of 5–25. Higher values indicate higher medication adherence. In addition to that, patients were asked to complete the Health Care Climate Questionnaire\textsuperscript{21} measuring perceived autonomy support by physicians as well as additional questions about sociodemographic characteristics (eg, age, gender, living with partner).\textsuperscript{22} The number of medicines taken by participants was measured as a mean of parallel refilled medications in four quarters in 2009 as documented in pharmacy claims.
At the practice level, the general practitioner completed a questionnaire including aspects to characterize the practice according to size, location, and number and roles of practice staff. Additionally, general practitioners were asked to fill out a questionnaire for every patient which included, among other variables, a rating of medication adherence. Therefore, the items of the MARS-D were rephrased to mirror the instrument as an external rating scale (MARS-GP).

Data analysis
In a first step, we descriptively measured concordance in rating medication adherence between patients and general practitioners by comparing scores on the MARS-D and the MARS-GP. By giving one point for each concordantly rated value, we calculated a sum score of overall concordance ranging from 0 (no concordantly rated item) to 5 (five concordantly rated items).

For multivariable prediction, a series of linear models was estimated to assess the effect of variables at the practice and patient level on sum scores of overall concordance. Because of the hierarchical data structure, multilevel analysis was performed to take into account dependence between patient outcomes (level 1) and primary care practices (level 2). Multilevel linear analysis started with a two-level null (empty) model with no predictor variables in the fixed part and only the intercepts in the random part of the model (M1). This model could be used as a reference for comparing the size of contextual variations in subsequent models. Next, practice-level characteristics were included as fixed effects (M2). Finally, we added patient-level variables in the fixed part of the third model (M3).

Descriptive statistics for practice-level and patient-level characteristics were calculated. Only patients with complete data for all explanatory variables considered in the final model were included in the analysis. The characteristics of these patients were compared with those for the patients who had to be excluded because of lack on information on explanatory variables. Continuous data were summarized using means and standard deviations. Categorical data are presented as frequency counts and percentages. Fixed-part results of the final two-level linear model (M3) followed by the random-part results of all three models (M1–M3) are reported. Variance partition coefficients in each level were calculated using the restricted maximum likelihood method; the corresponding intraclass correlations at the practice and country level are provided. Finally, the proportion of variance explained at each level is presented for models M2–M3.

Because this was an exploratory analysis, the significance level was set to 5% (two-sided) and no adjustment for multiple testing was performed. All descriptive analyses were carried out using IBM SPSS software version 19 (SPSS Inc, Chicago, IL). Multilevel analysis was done using SAS Enterprise Guide 4.2 (SAS Inc, Cary, NC).

Results
Sample characteristics
Of 376 potentially eligible patients, 153 patients agreed to participate in the survey (40.7%). Patients not participating in the survey were in the same age group (71.0 versus 71.1 years, \( P = 0.90 \)) and had a similar gender distribution (59.7% versus 53.8% female, \( P = 0.28 \)) but suffered from higher comorbidity levels (Charlson Comorbidity Index 3.43 versus 2.80, \( P = 0.01 \)), resulting in a higher predicted risk of future hospitalization (1.80 versus 1.20, \( P < 0.01 \)) and costs (7616 € versus 5572 €, \( P < 0.01 \)).

After excluding patients with missing information, our cohort for multilevel analysis consisted of 92 patients (24.5%) from 10 practices staffed by 14 general practitioners (Figure 1). Compared with the patients actually included, responding but excluded patients did not differ significantly with respect to age, gender, marital status, number of medications, length of being a patient in a practice, and perceived autonomy support (Table 1). Of the 14 participating general practitioners, five were female (35.7%) and five were trained in general internal medicine (35.7%). The mean age was 55.3 ± 8.6 years and mean working experience as a general practitioner was 17.7 ± 9.7 years. Patient contacts per quarter in the ten participating practices were more than 1500 in six...
practices (60%), 1001–1500 in three practices (30%), and 500–1000 in one practice (10%).

Medication adherence
Patients rated their medication adherence higher in all five categories compared with their general practitioner. Accordingly, the percentage of concordance (Table 2) ranged between 40% (forgot to take medication) and 61% (deliberately omitted a dose). For calculation of overall concordance (sum score), 111 pairs of data (patient and their general practitioner) could be considered. Analysis of these pairs revealed a sum score of 5 in 20% of pairs, a sum score of 4 in 14%, a sum score of 3 in 13%, a sum score of 2 in 15%, and a sum score of 1 in 21%. In 17% of cases, we found no concordance between the patient and their general practitioner.

Multilevel analysis
The two-level linear regression analysis was based on 92 patients (level 1) nested within 10 practices (level 2), with up to 19 patients within each practice. Analysis showed that the sum score of overall concordance was associated with several variables. At the practice level, significant predictors of concordance were “single-handed practice” (yes) and “talk about use of medication” (always or often). At the patient level “marital status” (not married) and “number of concurrently prescribed medications” were predictors of nonconcordance for medication adherence. The variables “age of general practitioner”, “work experience of general practitioner” (practice level), “patient age”, “being patient in practice”, and “perceived autonomy support” (Health Care Climate Questionnaire, patient level) were not associated with the sum score for overall concordance (Table 3).

Analysis of the random part for all models showed that the greatest proportion of variance (intra-class coefficients and correlations) occurred at the patient level (68.1%). The proportion of variance at the practice level was estimated to be 39.0%. Including explanatory variables into the model at the practice level resulted in smaller proportions of variance, meaning that these variables explained the variance. Additional inclusion of explanatory variables at the patient level resulted in a final adjusted model that explained variance at the practice level by 87.5% and variance at the patient level by 9.6% (Table 4).

### Table 1 Patient characteristics

|                          | Complete sample (n = 153) | Included (n = 92) | Not included (n = 61) | P value |
|--------------------------|---------------------------|-------------------|-----------------------|---------|
| Patient age (years); mean (SD) | 70.6 (10.1)               | 70.9 (9.7)        | 70.1 (10.8)           | 0.649   |
| Patient gender (female); % (n) | 53.3 (80)                | 50.0 (46)         | 58.6 (34)             | 0.227   |
| Marital status (not married); % (n) | 38.0 (60)               | 33.7 (31)         | 44.8 (29)             | 0.319   |
| Patient in practice (years); mean (SD) | 14.5 (6.2)            | 14.8 (6.2)        | 14.2 (6.3)            | 0.567   |
| Number of medications; mean (SD) | 6.5 (3.4)               | 6.2 (3.0)         | 7.1 (4.1)             | 0.122   |
| Perceived autonomy support; mean (SD) | 5.9 (1.3)              | 5.8 (1.2)         | 5.9 (1.5)             | 0.832   |

Notes: *t*-test (included versus not included); *Chi-square (included versus not included).

Abbreviation: SD, standard deviation.

### Table 2 Description of concordance in rating medication adherence

|                          | n     | Concordance | Always | Often | At times | Rarely | Never |
|--------------------------|-------|-------------|--------|-------|---------|--------|-------|
| Forget to take medication| 147   | 40%         | 0.6    | 2.3   | 17.4    | 37.8   | 41.9  |
| PCP; %                   |       |             |        |       |         |        |       |
| Patient; %               | 4.1   |             | 0.0    |       | 6.8     | 24.3   | 64.9  |
| Change the doses         | 136   | 56%         | 0.0    | 3.5   | 10.5    | 31.0   | 55.0  |
| PCP; %                   |       |             |        |       |         |        |       |
| Patient; %               | 0.0   |             | 1.5    |       | 4.4     | 8.0    | 86.1  |
| Suspend for a while      | 137   | 57%         | 0.0    | 2.3   | 9.2     | 35.8   | 52.6  |
| PCP; %                   |       |             |        |       |         |        |       |
| Patient; %               | 0.0   |             | 0.7    |       | 2.9     | 7.3    | 89.1  |
| Deliberately omitted to take a dose | 137 | 61%         | 0.0    | 1.7   | 9.3     | 29.7   | 59.3  |
| PCP; %                   |       |             |        |       |         |        |       |
| Patient; %               | 0.0   |             | 0.7    |       | 2.2     | 8.7    | 88.4  |
| Take less than prescribed| 134   | 52%         | 0.6    | 2.4   | 10.0    | 38.2   | 48.8  |
| PCP; %                   |       |             |        |       |         |        |       |
| Patient; %               | 0.0   |             | 0.7    |       | 4.4     | 5.1    | 89.8  |

Abbreviation: PCP, primary care physician.
Table 3 Parameter estimates of the final multilevel model with overall concordance score as dependent variable (92 patients within 10 general practices)

|                      | Coeff | SE   | P value |
|----------------------|-------|------|---------|
| Intercept            | 4.29  | 2.71 | 0.1891  |
| Practice level       |       |      |         |
| PCP age (years)      | -0.12 | 0.09 | 0.1668  |
| PCP work experience (years) | 0.08  | 0.08 | 0.3272  |
| Single-handed practice (yes) | 2.24  | 0.34 | <0.0001 |
| Talk about use of medication (always or often) | 0.66  | 0.22 | 0.0031  |

Patient level

|                      | Coeff | SE   | P value |
|----------------------|-------|------|---------|
| Patient age (years)  | 0.02  | 0.01 | 0.1291  |
| Marital status (not married) | -0.81 | 0.29 | 0.0064  |
| Patient in practice (years) | 0.02  | 0.02 | 0.3745  |
| Number of medications | -0.10 | 0.04 | 0.0203  |
| Perceived autonomy support | 0.04  | 0.11 | 0.7264  |

Abbreviations: Coeff, regression coefficient; SE, standard error; PCP, primary care physician.

Discussion

To the best of our knowledge, this is the first study to compare rating of medication adherence between patients and their providers. Our analysis revealed three main findings. Firstly, in this sample, patients rated their medication adherence markedly higher than did their general practitioners. Only 20% of general practitioners rated medication adherence concordantly with the patient. Secondly, being a single general practitioner and making frequent enquiries about use of medication predicted concordance in rating medication adherence. Thirdly, at the patient level, “not [being] married” and a higher “number of currently prescribed medications” were negative predictors of concordance for rating medication adherence.

In previous research, more than 200 variables have been studied, but none of them, including socioeconomic and pathology-related factors, could be considered to predict medication adherence consistently.23 Characteristics that correlate with adherence vary across different types of medication and settings. Both patients and prescribers can influence adherence with medication.24 Patient – physician concordance seems to be essential in this context. Kerse et al showed that primary care consultations with higher levels of patient-reported concordance were associated with one-third greater medication adherence.18 However, patient – provider concordance cannot be reduced simply to a good patient – provider relationship as shown by Zulman et al, who found no correlation between patient – provider concordance and quality of the patient – provider relationship.31 Our finding that perceived autonomy support (Health Care Climate Questionnaire) does not impact patient – provider concordance in rating medication adherence probably reflects the same trend, although our results show that frequently talking about use of medication is the basis for patient – provider concordance in rating medication adherence. In addition, being the single primary care provider predicted patient – provider concordance. It is also known that personal continuity of care is associated with less discrepancy between the opinions of patients and physicians regarding meeting patient expectations.9 At the patient-level, previous research has shown that poor health status and a higher number of health conditions are associated with lower patient – provider concordance.31

Our finding that a greater number of medications is correlated with lower concordance could be interpreted in a similar manner. However, this finding underscores the fact that, with an increasing number of medications, it becomes more difficult to achieve patient – provider concordance. This is a dilemma particularly for multimorbid patients with a high number of medicines, for whom patient – provider concordance is relevant for adherence to medication. Previous research has shown that nonadherence in these patients is linked with potentially avoidable hospitalization and emergency department use.25

Moreover, patient beliefs about medication, especially perceived concerns, are associated with more nonadherence26 and are therefore important to ensure patient – provider concordance. Regular enquiries from general practitioners about how patients tolerate their medication and which medicines they are taking are indicators of patient satisfaction with information on medicines being associated with higher medication adherence.27 Therefore, frequently talking about medications may be essential for multimorbid patients taking multiple medicines to ensure patient – provider concordance.

Table 4 Random part of all random intercept models with overall concordance score as dependent variable (92 patients within 10 general practices)

|                     | VC    | SE   | EV    | ICC   |
|---------------------|-------|------|-------|-------|
| M1: Null model      | 1.3110| 0.7978| 0.39  |       |
| Practices (random)  | 2.0557| 0.2864| 0.61  |       |
| M2: Practice level covariates added | 0.2661| 0.2894| 0.7970| 0.11  |
| Practices (random)  | 2.1161| 0.3026| -2.94%| 0.89  |
| M3: Patient level covariates added | 0.1640| 0.2328| 87.49%| 0.08  |
| Practices (random)  | 1.8578| 0.2958| 9.63% | 0.92  |

Abbreviations: VC, variance component; SE, standard error; EV, explained variance; ICC, intra-class coefficient.
Strengths and limitations

We used multilevel modeling to account for the hierarchical data structure and to identify predictors of patient–provider concordance, while adjusting for all other variables. Hierarchical models combine information across units to produce accurate and well-calibrated prediction of outcomes. This analytic approach has been seen to be highly relevant in health services research because patient data are similarly clustered at more than one level.

Due to the fact that we focused our research on highly vulnerable patients at risk for (avoidable) hospitalizations, the sample size of this analysis was modest. However, modest sample size is not a problem for multilevel analysis. Multilevel methods are particularly robust for small sample sizes. Analyses have shown that for sample sizes over 50, estimates of regression coefficients, components of variance, and standard errors are unbiased and accurate.28

Another limitation is the low participation rate in this survey. We included a relatively small sample of multimorbid patients at high risk for future hospitalizations, with an even smaller number of participants who could be included in the final model. Otherwise, our analysis of characteristics did not suggest systematic bias between included and not included patients. However, patients not included were more frequently female, not married, and took a higher number of medicines. Given that marital status and the number of other conditions had a negative impact on patient–provider concordance, lower scores for this group could be expected.

Finally, due to the retrospective, cross-sectional design of this study, no causal relationship between the variables can be drawn from the results of multilevel analysis. However, our exploratory results may encourage further research in this field.

Conclusion

Concordance in rating medication adherence between general practitioners and their patients was low. Talking about medication on a regular basis and higher continuity of care may enhance patient–provider concordance in rating medication adherence as a prerequisite for shared decisions about medication in patients with multiple chronic conditions.

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Disclosure

Under the contract between the sponsor and the University of Heidelberg, full responsibility for the scientific work, the management of data and analysis, and publication rests with the investigators, who have no conflicts of interest to declare.

References

1. Street RL Jr, Makoul G, Arora NK, Epstein RM. How does communication heal? Pathways linking clinician-patient communication to health outcomes. Patient Educ Couns. 2009;74:295–301.
2. Simons-Morton DG, Blair SN, King AC, et al. Effects of physical activity counseling in primary care: the Activity Counseling Trial: a randomized controlled trial. JAMA. 2001;286:677–687.
3. Eriksson MK, Hagberg L, Lindholm L, Malmgren-Ohlsson EB, Osterlind J, Eliasson M. Quality of life and cost-effectiveness of a 3-year trial of lifestyle intervention in primary health care. Arch Intern Med. 2010;170:1470–1479.
4. Weiss KB. Managing complexity in chronic care: an overview of the VA state-of-the-art (SOTA) conference. J Gen Intern Med. 2007;22 Suppl 3:374–378.
5. Adler HM. Toward a biopsychosocial understanding of the patient–physician relationship: an emerging dialogue. J Gen Intern Med. 2007;22:280–285.
6. Boyd CM, Darer J, Boult C, Fried LP, Boul t L, Wu AW. Clinical practice guidelines and quality of care for older patients with multiple comorbid diseases – implications for pay for performance. JAMA. 2005;294:716–724.
7. Abbo ED, Zhang Q, Zelder M, Huang ES. The increasing number of clinical items addressed during the time of adult primary care visits. J Gen Intern Med. 2008;23:2058–2065.
8. Fung CH, Setodji CM, Kung FY, et al. The relationship between multimorbidity and patients’ ratings of communication. J Gen Intern Med. 2008;23:788–793.
9. Zebi ne E, Svab I, Sapoka V, et al. Agreement in patient–physician communication in primary care: a study from Central and Eastern Europe. Patient Educ Couns. 2008;73:246–250.
10. Bell RA, Kravitz RL, Thom D, Krupat E, Azari R. Unmet expectations for care and the patient–physician relationship. J Gen Intern Med. 2002;17:817–824.
11. Zulman DM, Kerr EA, Hofer TP, Heisler M, Zikmund-Fisher BJ. Patient–provider concordance in the prioritization of health conditions among hypertensive diabetes patients. J Gen Intern Med. 2010;25:408–414.
12. Staiger TO, Jarvik JG, Deyo RA, Martin B, Braddock CH 3rd. Brief report: patient–physician agreement as a predictor of outcomes in patients with back pain. J Gen Intern Med. 2005;20:935–937.
13. Starfield B, Wray C, Hess K, Gross R, Birk PS, D’Lugoff BC. The influence of patient-practitioner agreement on outcome of care. Am J Public Health. 1981;71:127–131.
14. Schillinger D, Wang F, Rodriguez M, Bindman A, Macht ingen EL. The importance of establishing regimen concordance in preventing medication errors in anticoagulant care. J Health Commun. 2006;11:555–567.
15. Christensen AJ, Howren MB, Hillis SL, et al. Patient and physician beliefs about control over health: association of symmetrical beliefs with medication regimen adherence. J Gen Intern Med. 2010;25:397–402.
16. Hughes CM. Medication non-adherence in the elderly: how big is the problem? Drugs Aging. 2004;21:793–811.
17. DiMatteo MR, Giordani PJ, Lepper HS, Croghan TW. Patient adherence and medical treatment outcomes: a meta-analysis. Med Care. 2002;40:794–811.
18. Kerse N, Buetow S, Mainous AG 3rd, Young G, Coster G, Arroll B. Physician–patient relationship and medication compliance: a primary care investigation. Ann Fam Med. 2004;2:455–461.
19. Freund T, Mahler C, Erler A, et al. Identification of patients likely to benefit from care management programs. *Am J Manag Care*. 2011;17:345–352.

20. Mahler C, Hermann K, Horne R, et al. Assessing reported adherence to pharmacological treatment recommendations. *Transl and evaluation of the Medication Adherence Report Scale (MARS) in Germany. J Eval Clin Pract*. 2010;16:574–579.

21. Schmidt K, Gensichen J, Petersen JJ, et al. Autonomy support in primary care – validation of the German version of the Health Care Climate Questionnaire. *J Clin Epidemiol*. 2012;65:206–211.

22. Freund T, Wensing M, Mahler C, et al. Development of a primary care-based complex care management intervention for chronically ill patients at high risk for hospitalization: a study protocol. *Implement Sci*. 2010;5:70.

23. Vermeire E, Hearnshaw H, Van Royen P, Denekens J. Patient adherence to treatment: three decades of research. *A comprehensive review. J Clin Pharm Ther*. 2001;26:331–342.

24. van Dijk L, Heerdink ER, Somai D, et al. Patient risk profiles and practice variation in nonadherence to antidepressants, antihypertensives and oral hypoglycemics. *BMC Health Serv Res*. 2007;7:51.

25. Stuart B, Briesacher B. Medication decisions – right and wrong. *Med Care Res Rev*. 2002;59:123–145.

26. Mahler C, Hermann K, Horne R, Jank S, Haefeli WE, Szecsenyi J. Patients’ beliefs about medicines in a primary care setting in Germany. *J Eval Clin Pract*. 2012;18:409–413.

27. Mahler C, Jank S, Hermann K, Haefeli WE, Szecsenyi J. Information on medications – How do chronically ill patients assess counselling on drugs in general practice? *Dtsch Med Wochenschr*. 2009;134:1620–1624. German.

28. Maas CJM, Hox JJ. Robustness issues in multilevel regression analysis. *Stat Neerl*. 2004;58:127–137.