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ABSTRACT

Objective: To assess the relationship of patients' medication beliefs and treatment complexity with unintentional and intentional non-adherence for three therapeutic groups commonly used by patients with type 2 diabetes.
Methods: Survey data about adherence (Medication Adherence Report Scale) and beliefs about medicines (Beliefs about Medicines Questionnaire) were combined with prescription data from the Groningen Initiative to ANalyse Type 2 diabetes Treatment (GIANTT) database. Patients were classified as being adherent, mainly unintentional non-adherent, or partly intentional non-adherent per therapeutic group (glucose-, blood pressure-, and lipid-lowering drugs). Treatment complexity was measured using the Medication Regimen Complexity Index, which includes the dosage form, dosing frequency and additional directions of taking the drug. Analyses were performed using Kruskal–Wallis and Mann–Whitney U-tests.
Results: Of 257 contacted patients, 133 (52%) returned the questionnaire. The patients had a mean age of 66 years and 50% were females. Necessity beliefs were not significantly different between the adherers, mainly unintentional non-adherers, and partly intentional non-adherers (differences smaller than 5 points on a scale from 5 to 25). For blood pressure-lowering drugs, patients reporting intentional non-adherence had higher concern beliefs than adherers (8 point difference, $P = 0.01$). Treatment complexity scores were lower for adherers but similar for mainly unintentional and partly intentional non-adherers to glucose- and blood pressure-lowering drugs.
Conclusion: Treatment complexity was related to non-adherence in general. Beliefs about necessity were not strongly associated with non-adherence, while patients' concern beliefs may be associated with intentional non-adherence. However, the role of these determinants differs per therapeutic group.

Introduction

Although a drug should be taken as prescribed to achieve its intended effectiveness, adherence to drug therapy is a well-known problem in clinical practice [1–3]. Patients can be intentional as well as unintentional non-adherent to their drug treatment [4–6]. Intentional non-adherence is seen as a conscious decision for not taking the drug as prescribed after balancing the pros and cons, whereas unintentional non-adherence is a more passive behavior which is more strongly associated with demographics [3,6]. Non-adherence is influenced by many factors, including patient and treatment characteristics [3,7]. Of the modifiable factors, beliefs about a drug and treatment convenience or complexity are important predictors of non-adherence [7–10].

Within the belief domain it is relevant to distinguish between concern and necessity beliefs [11]. Concern beliefs are about the adverse consequences of taking a drug, whereas necessity beliefs are about the positive effects of a drug on someone's health [12]. Little is known about the influence of these different beliefs on unintentional versus intentional non-adherence. Two studies showed that concern and necessity beliefs were associated with intentional non-adherence, whereas only one study found that concern beliefs were associated with unintentional non-adherence [4,13]. In these studies, however, people using different therapeutic groups were combined. Another study showed that the association between beliefs and types of non-adherence can differ across therapeutic groups [7].

Focusing on different therapeutic groups also has implications for the treatment complexity. Treatment complexity includes the number of drugs that have to be taken, the route of drug administration, dosing frequency, and additional directions of taking the drug [14]. Higher treatment complexity is associated with lower rates of optimal

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adherence [10]. Previous studies showed for instance higher adherence to a once-daily than a twice-daily regime [15,16] and a study using a composite score of drug administration, dosing frequency and additional directions found that patients with low complexity scores were more often adherent than patients with high complexity scores [17]. At present, it is not known how this association varies for unintentional or intentional non-adherence.

Patients with type 2 diabetes are often treated with drugs from multiple therapeutic groups, including glucose-, blood pressure-, and lipid-lowering drugs [18]. Previously, it was shown that patients with type 2 diabetes reported more often unintentional non-adherence to the glucose-lowering drugs than the blood pressure- and lipid-lowering drugs, and that intentional non-adherence did not differ among the therapeutic groups [19]. The aim of the current study is to assess the role of different kinds of beliefs (necessity and concern) and treatment complexity on unintentional and intentional non-adherence, and whether this differs for glucose-, blood pressure-, and lipid-lowering drugs in patients with type 2 diabetes.

Method

In this study, cross-sectional survey data were collected in 2007, which were combined with prescription data collected in the Groningen Initiative to ANalyse Type 2 diabetes Treatment (GIANTT)-project [20]. The GIANTT-project is a regional initiative of health care professionals and researchers focusing on the primary care of patients with type 2 diabetes in the province of Groningen in The Netherlands. The study was carried out in accordance with the Code of Ethics of the World Medication Association (Declaration of Helsinki) for experiments involving humans. Ethical approval was not needed for this study, as determined by The Medical Ethics Committee of the University Medical Center Groningen in the Netherlands.

Participants

Of the 32 general practitioners (GPs) included in the GIANTT-project in 2006, 19 GPs (59%) agreed to recruit patients for this study. For these 19 GPs, we selected a total of 345 patients with type 2 diabetes from the GIANTT-database who had been prescribed an oral glucose-lowering drug in 2005. To recruit a balanced group of adherent and non-adherent participants, half of the patients were selected based on a medication possession ratio (MPR) <80% of their oral glucose-lowering drug indicating possible low adherence [21]. Of the 345 selected patients, 69 (20%) were excluded from the study by their GP because of: psychosocial problems (14), language issues (13), cognitive limitations (10), patient died (8), patient moved (6), GP expects unwillingness (4), serious comorbidity (3), admission to hospital or nursing home (3), or other reasons (8). The remaining 257 patients were contacted by mail, and those who gave informed consent received a survey composed of general questions and validated questionnaires assessing beliefs and adherence which were applied to glucose-, blood pressure-, and lipid-lowering drugs. Patients were asked to report the name of their glucose-lowering drugs, and when applicable, their blood pressure- and lipid-lowering drugs. In addition, patients were asked to indicate whether they self-measured their glucose levels, their blood pressure, and whether their lipid-levels had been measured without a GP order.

Beliefs

Patients' beliefs about the three therapeutic groups were assessed using the Beliefs about Medicines Questionnaire (BMQ) specific [12]. The BMQ contains 5 items about necessity beliefs (e.g. 'My health at present depends on my *glucose-lowering drugs*'), and 5 items about concern beliefs (e.g. 'I sometimes worry about becoming too dependent on the *glucose-lowering drugs*'). Participants indicate their agreement with each item on a 5-point Likert scale, ranging from totally disagree to totally agree. Scores on items per subscale were summed, ranging from 5 (totally agree) to 25 (totally disagree) for the necessity and concern subscales. Internal consistency was assessed using Cronbach's α. For those patients included in the analyses of glucose-lowering drugs, the internal consistency was .721 and .777 for the necessity and the concern subscales, respectively. These values were .834 and .823, and .779 and .828 for the patients included in the analyses of respectively blood pressure-, and lipid-lowering drugs. Besides the assessment of concern and necessity beliefs, the necessity–concern differential was measured. This differential gives an indication of which beliefs the patient weighs more heavily [4].

Treatment complexity

In the questionnaire, patients reported which glucose-, blood pressure-, and lipid-lowering drugs they had used in the previous 3 months. Dosing information on the drugs was derived from the GIANTT-database. A treatment complexity score was computed for each reported drug using the Medication Regimen Complexity Index [14]. For each patient using more than one drug within a therapeutic group, the scores of the Medication Regimen Complexity Index were combined resulting in one complexity score per therapeutic group. The Medication Regimen Complexity Index takes into account the dosage form, dosing frequency and additional directions of taking the drug. For the dosage form, the scores 1 and 3 were used for tablets and injections, respectively. The dosing frequency was registered in the GIANTT-database. The following additional directions were included in the complexity score based on additional dosing information in the GIANTT-database: break or crush a tablet, intake of multiple units at one time, variable dosing, and alternating dosing. Two researchers (SdV and PD) independently computed the complexity score for each patient. The researchers agreed on 96%, 100% and 99% of the scores for the patients using glucose-, blood pressure-, and lipid-lowering drugs, respectively. All disagreements were solved by discussion between the researchers.

Adherence

Adherence was assessed using the Medication Adherence Report Scale (MARS) [22]. The MARS contains one item that reflects unintentional non-adherence ('I forget to take my *glucose-lowering drugs*') and four items that largely reflect different forms of intentional non-adherence (e.g. 'I alter the dose of my *glucose-lowering drugs*') [4,22]. Participants indicate how often each statement applied to them in the last 3 months on a 5-point Likert scale ranging from always to never. Cronbach's α values were .715, .595 and .699 for intentional non-adherence to respectively glucose-, blood pressure-, and lipid-lowering drugs. The intentional non-adherence items were summed. Non-adherence was defined as a score of lower than the maximum of 5 for unintentional and lower than the maximum of 20 for intentional non-adherence, indicating any degree of non-adherence.

Statistical analyses

Analyses were conducted per therapeutic group, including data from those patients who reported the name of their drug in the correct therapeutic group, who completed all MARS-questions, who had no more than one missing value at the belief questions, and for whom drug dosing information was available in the database. For the patients with one missing value for the belief questions, the value was imputed using the median value of the other patients for that item. Since the median values are used to test for differences between groups (see below), this method does not affect the median value of the whole sample for that item.

Per therapeutic group, patients were divided into being fully adherent, mainly unintentional non-adherent, or in part intentional non-adherent.

This last group includes patients who report some form of intentional non-adherence but may also report to be unintentional non-adherent. Differences in patient characteristics between adherers, mainly unintentional non-adherers and partly intentional non-adherers were tested using Pearson χ^2-tests, one-way analyses of variance, and Kruskal–Wallis tests, depending on the distribution of the variables. Associations between beliefs and (un)intentional non-adherence, and treatment complexity and (un)intentional non-adherence were tested using Kruskal–Wallis tests. A P-value < 0.05 was considered statistically significant. Mann–Whitney U-tests with Bonferroni adjustment to correct for multiple testing (a P-value ≤ 0.01 was considered statistically significant) were used for subsequent testing for differences between two specific groups. All analyses were conducted using IBM SPSS Statistics version 20 (Armonk, New York, USA).

Results

Of the 257 contacted patients, 133 (52%) returned the questionnaire. Half of these patients were female, and the mean age was 66 years (Table 1). Patients included in the analyses with the glucose-lowering drugs had longer diabetes duration than those that were not included. No other differences were found between patients included in the analyses per therapeutic group and those that were not included in the analyses (Supplemental Table 1).

Of the patients reporting non-adherence to their drugs, almost all patients reported to be at least unintentional non-adherent (Fig. 1). Intentional non-adherers to glucose- or blood pressure-lowering drugs more often reported to alter their dose or take less than instructed than the intentional non-adherers to lipid-lowering drugs. Patients who were intentional non-adherent to their lipid-lowering drugs more often reported that they stopped taking the drug (Fig. 1).

We observed no significant differences between fully adherent, mainly unintentional non-adherent and partly intentional non-adherent patients in age, gender, education level, and diabetes duration. However, intentional non-adherers to glucose-lowering drugs more often self-measured their glucose levels than adherent patients (P < 0.01) (Supplemental Table 2). In addition, they had a higher body mass index than the unintentional non-adherers to these drugs (P < 0.01).

Beliefs and non-adherence

For all three therapeutic groups, no significant differences in necessity beliefs were found between the adherers and unintentional and intentional non-adherers (Table 2). For glucose-lowering drugs, the median necessity scores showed only 1 point difference, whereas this was 1.5 point for blood-pressure and 4 points for lipid-lowering drugs. In general, higher necessity beliefs were reported for the glucose-lowering drugs than for the blood pressure- and lipid-lowering drugs.

Intentional non-adherers to glucose- and blood pressure-lowering drugs had more concerns about these drugs than the adherers and unintentional non-adherers, which was only statistically significant for the blood pressure-lowering drugs (P < 0.05). The median concern scores showed differences of 2.5 points for glucose-lowering drugs, 8 points for blood pressure-lowering drugs, and 0 points for lipid-lowering drugs. The significant difference for the blood pressure-lowering drugs was mainly due to the difference between the adherers and intentional non-adherers (P = 0.01).

The adherent and the unintentional non-adherent patients weighed the necessity of their drug use heavier than their concerns about these drugs, as shown by the positive necessity–concern-differential (Table 2). This finding applied for the three therapeutic groups. For the intentional non-adherers to blood pressure- and lipid-lowering drugs, however, concerns weighed more heavily than necessity.

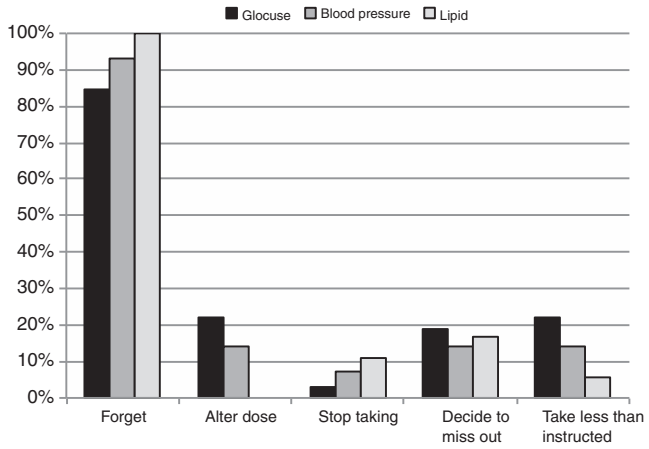

Fig. 1. Percentage of patients reporting different types of non-adherence per therapeutic group.

Treatment complexity and non-adherence

Treatment complexity scores were lower for adherers than non-adherers to glucose- (P < 0.05) and blood pressure-lowering drugs (P < 0.05) (Table 2). For all three therapeutic groups, no differences in complexity scores were seen between the unintentional and intentional non-adherers (Table 2).

Discussion

This study shows that treatment complexity is related with non-adherence to glucose- and blood pressure-lowering drugs, which is similar for patients reporting mainly unintentional or partly intentional non-adherence. Patient beliefs have a more complex association with non-adherence. Concerns were higher in case of intentional non-adherence for blood pressure-lowering and glucose-lowering drugs but this finding was only significant for the blood pressure-lowering drugs. Beliefs about necessity did not show much difference among the adherence groups for glucose-lowering and blood pressure-lowering drugs. For lipid-lowering drugs, the difference in necessity beliefs among the adherence groups was larger but also non-significant. Concerns were more heavily weighed than necessity by intentional non-adherers to blood pressure- and lipid-lowering drugs, whereas necessity was more heavily weighed by intentional non-adherers to glucose-lowering drugs. Previous studies showed inconsistent associations between beliefs and (un)intentional non-adherence [4,13]. The current data suggests that this inconsistency may be due to differences across therapeutic groups.

Patients with type 2 diabetes differ in their concerns and beliefs about necessity across the three therapeutic groups. As has been observed before, necessity is believed to be higher for glucose-lowering drugs (median score 20) than for blood pressure-lowering

Table 1
Patient characteristics per therapeutic group.

	Total (N = 133)	Glucose-lowering drugs (N = 85)	Blood pressure-lowering drugs (N = 67)	Lipid-lowering drugs (N = 85)
Females (%)	66 (49.6)	38 (44.7)	34 (50.7)	39 (45.9)
Mean age in years (SD)	66.3 (9.6)	65.8 (9.5)	65.9 (10.1)	65.7 (9.9)
Education (%)				
Low education	70 (53.0)	41 (48.8)	32 (48.5)	42 (50.0)
Middle education	29 (22.0)	23 (27.4)	17 (25.8)	22 (26.2)
High education	25 (18.9)	15 (17.9)	13 (19.7)	14 (16.7)
Other	8 (6.1)	5 (6.0)	4 (6.1)	6 (7.1)
Mean BMI (SD)	29.3 (4.3)	29.0 (4.0)	29.7 (4.7)	29.2 (4.3)
Median diabetes duration (IQR)	7 (4.0–10.0)	7 (5.0–11.0)	7 (5.0–11.0)	7 (3.0–10.0)
Measurement outside GPs office				
Yes (%)		22 (27.2)	18 (26.9)	8 (9.4)

GPs = General practitioners; BMI = Body mass index; SD = Standard deviation; IQR = Interquartile range.

Table 2
Beliefs and treatment complexity for glucose-, blood pressure-, and lipid-lowering drugs according to adherence.

	All	Adherent	Unintentionally non-adherent	Intentionally non-adherent	P-value[a]
Glucose-lowering drugs	N = 85	N = 53	N = 22	N = 10	
Differential median (IQR)	8.0 (4.0–13.0)	8.0 (3.0–11.0)	8.5 (5.8–15.0)	8.0 (0.5–13.8)	.370
Median (IQR) of necessity beliefs (scale 5–25)	20.0 (17.0–22.0)	20.0 (16.5–22.0)	21.0 (18.8–23.0)	20.0 (15.8–24.0)	.152
Median (IQR) of concern beliefs (scale 5–25)	11.0 (9.0–14.0)	11.0 (9.0–14.0)	10.5 (8.8–13.3)	13.0 (7.8–16.5)	.516
Median (IQR) of treatment complexity scores	6 (3.0–7.5)	4 (3.0–7.0)	7 (5.5–7.3)	7.5 (2.8–13.0)	.126**
Blood pressure-lowering drugs	N = 67	N = 53	N = 10	N = 4	
Differential median (IQR)	5.0 (2.0–9.0)	5.0 (2.0–10.0)	7.0 (1.8–9.5)	−0.5 (−4.8–5.3)	.152
Median (IQR) of necessity beliefs (scale 5–25)	17.0 (14.0–20.0)	17.0 (14.5–20.0)	15.5 (13.0–22.3)	17.0 (12.0–21.3)	.855
Median (IQR) of concern beliefs (scale 5–25)	11.0 (9.0–14.0)	11.0 (9.0–13.0)	9.0 (7.8–14.3)	17.0 (13.5–19.8)	.037*
Median (IQR) of treatment complexity scores	3 (2.0–5.0)	3 (2.0–4.0)	4 (3.8–6.0)	4 (4.0–4.8)	.050***
Lipid-lowering drugs	N = 85	N = 67	N = 15	N = 3	
Differential median (IQR)	3.0 (0.0–7.0)	4.0 (0.0–7.0)	2.0 (0.0–7.0)	−1.0[b]	.459
Median (IQR) of necessity beliefs (scale 5–25)	15.0 (11.5–18.0)	15.0 (12.0–18.0)	14.0 (10.0–18.0)	11.0[b]	.347
Median (IQR) of concern beliefs (scale 5–25)	11.0 (9.0–14.0)	11.0 (9.0–14.0)	11.0 (8.0–14.0)	11.0[b]	.779
Median (IQR) of treatment complexity scores	2 (2.0–2.0)	2 (2.0–2.0)	2 (2.0–2.0)	2 (2.0–2.0)	.884

IQR = Interquartile range.
[a] Kruskal–Wallis test.
[b] No IQR due to low numbers.
* Significance due to difference between adherers and intentional non-adherers (P = 0.01).
** Significant difference between adherers and non-adherers (P = 0.04).
*** Significant difference between adherers and non-adherers (P = 0.01).

drugs (median score 17) and lipid-lowering drugs (median score 15), whereas no differences are seen across the therapeutic groups for concerns, with median scores of 11 for all three groups [23]. These differences in necessity beliefs among the therapeutic groups may be explained using Leventhal's self-regulatory model of illness cognitions [24]. Patients perceive more (personal) control, symptoms, and emotional distress in type 2 diabetes than either hypertension or hyperlipidemia [23].

Previously, it was found that for intentional non-adherers, concerns play a more important role than beliefs about the necessity of the drug [4]. This result was confirmed in the current study for the blood pressure-lowering drugs, where a negative necessity–concern differential corresponded with strong concern beliefs in the group of intentional non-adherers. For glucose-lowering drugs, our findings indicate a different mechanism with a positive necessity–concern differential and less strong concern beliefs in intentional non-adherers. This finding may be explained by a different type of intentional non-adherence for these drugs. We found that these patients often altered doses or took less than instructed, which could be driven by self-management. Self-measurement of glucose-levels was significantly related to intentional non-adherence to glucose-lowering drugs. One may doubt whether we should talk here of non-adherence, since the changes in drug use may be the result of the self-management. Consequently, intentional non-adherence to glucose-lowering drugs might be overestimated when self-management is not taken into account. For lipid-lowering drugs, a negative necessity–concern differential was found for the intentional non-adherers. Concern beliefs were, however, similar in all adherence groups. Previously, it has been concluded that concerns about or experiences with adverse events are the most common reason for statin discontinuation [25]. Our findings suggest that also people who continue statin treatment may have similar concerns.

The current study confirms previous results that treatment complexity is related to non-adherence in general [10,17]. We did not observe any difference between patients who reported mainly unintentional non-adherence and those reporting partly intentional non-adherence. For lipid-lowering drugs, treatment complexity was not associated with non-adherence in general since complexity scores were low in all three groups.

Some limitations of this study need to be acknowledged. First of all, this is a cross-sectional study, which makes it impossible to draw causal inferences. Medication beliefs and treatment complexity can be expected to influence adherence but may also change in patients after they have become non-adherent. A self-report measure of adherence was used because self-report is the only method that can be used to distinguish between intentional and unintentional non-adherence [26,27]. Only the item on forgetting to take the drug is considered to reflect mainly unintentional non-adherence, whereas all other items are considered as reflecting largely intentional non-adherence [4,22]. The internal consistency of the intentional non-adherence items ranged from 0.6 to 0.7, indicating the need for better measures of intentional non-adherence. Currently, however, we lack better self-reported medication adherence measures [27]. The use of self-reported adherence measurement may lead to underestimations of non-adherence especially intentional non-adherence, because of socially desirable answering and recall bias when completing the questionnaire [26,28]. A study that compared self-reports of adherence with more objective instruments (e.g. pill counts, electronic monitors) found moderate to high agreement in adherence rates among the measures [29]. Although intentional non-adherence was assessed using four different types of non-adherence, only a small number of patients reported to be intentional non-adherent to the blood pressure- and lipid-lowering drugs. This low number limited the power to detect differences of less than 3 to 4 points on the belief scales for glucose- and blood pressure-lowering drugs and less than 5 points for lipid-lowering drugs as being significant. In addition, the results of intentional non-adherers should be interpreted with caution since patients who reported both unintentional and intentional non-adherence were classified as being intentional non-adherent. The low number of patients in this study made it impossible to classify this behavior in a separate group. Possible selection bias of patients due to the moderate response rate could be another limitation of this study. Participating patients were, however, comparable in general patient characteristics to other patients with type 2 diabetes in Dutch primary care [30]. Patients with inadequate survey or prescription data had to be excluded from the analyses. These patients did not differ from the other patients in age, gender, education level and body mass index, but for the glucose-lowering drugs included patients had longer diabetes duration. Furthermore, the use of other drugs then diabetes and cardiovascular risk management related drugs were not taken into account in the treatment complexity scores.

The strength of our study is that we evaluated the association between determinants and types of non-adherence for different therapeutic groups within the same population of patients. This approach prevents that differences in determinants are influenced by other differences in the patient population.

To conclude, addressing concerns about drugs appears to be more important than stressing the necessity of treatment in patients with diabetes. Concerns seem to be associated with intentional non-adherence to especially blood pressure-lowering drugs but not with unintentional non-adherence. Beliefs about necessity showed no clear association with either type of non-adherence. Treatment complexity was relevant for any non-adherence to glucose- and blood pressure-lowering drugs, and health care professionals should thus try to avoid complex regimens as much as possible. Finally, our study indicates that determinants do not only differ among types of non-adherence, but also differ across therapeutic groups. Fighting non-adherence asks for more than a one-size fits all approach.

Competing interests

S.T.d.V., J.C.K, R.V., F.M.H.R., J.V. and P.D. have no competing interests to report. D.d.Z. has been/is a consultant (honoraria to institution) for Astra Zeneca, Abbott, Amgen, BMS, Hemocue, J&J, MSD, Novartis, and REATA.

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References

[1] 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;26:331–42.
[2] Delamater AM. Improving patient adherence. Clin Diabetes 2006;24:71–7.
[3] Lehane E, McCarthy G. Intentional and unintentional medication non-adherence: a comprehensive framework for clinical research and practice? A discussion paper. Int J Nurs Stud 2007;44:1468–77.
[4] Clifford S, Barber N, Horne R. Understanding different beliefs held by adherers, unintentional nonadherers, and intentional nonadherers: application of the Necessity–Concerns Framework. J Psychosom Res 2008;64:41–6.
[5] Schuz B, Marx C, Wurm S, Warner LM, Ziegelmann JP, Schwarzer R, et al. Medication beliefs predict medication adherence in older adults with multiple illnesses. J Psychosom Res 2011;70:179–87.
[6] Wroe AL. Intentional and unintentional nonadherence: a study of decision making. J Behav Med 2002;25:355–72.
[7] Unni E, Farris KB. Determinants of different types of medication non-adherence in cholesterol lowering and asthma maintenance medications: a theoretical approach. Patient Educ Couns 2011;83:382–90.
[8] Mann DM, Ponieman D, Leventhal H, Halm EA. Predictors of adherence to diabetes medications: the role of disease and medication beliefs. J Behav Med 2009;32:278–84.
[9] Rubin RR. Adherence to pharmacologic therapy in patients with type 2 diabetes mellitus. Am J Med 2005;118:27S–34S.
[10] Ingersoll KS, Cohen J. The impact of medication regimen factors on adherence to chronic treatment: a review of literature. J Behav Med 2008;31:213–24.
[11] Phatak HM, Thomas III J. Relationships between beliefs about medications and nonadherence to prescribed chronic medications. Ann Pharmacother 2006;40:1737–42.
[12] Horne R, Weinman J, Hankins M. The Beliefs about Medicines Questionnaire: the development and evaluation of a new method for assessing the cognitive representation of medication. Psychol Health 1999;14:1–24.
[13] Unni EJ, Farris KB. Unintentional non-adherence and belief in medicines in older adults. Patient Educ Couns 2011;83:265–8.
[14] George J, Phun YT, Bailey MJ, Kong DC, Stewart K. Development and validation of the Medication Regimen Complexity Index. Ann Pharmacother 2004;38:1369–76.
[15] Malmenas M, Bouchard JR, Langer J. Retrospective real-world adherence in patients with type 2 diabetes initiating once-daily liraglutide 1.8 mg or twice-daily exenatide 10 mug. Clin Ther 2013;35:795–807.
[16] Dezii CM, Kawabata H, Tran M. Effects of once-daily and twice-daily dosing on adherence with prescribed glipizide oral therapy for type 2 diabetes. South Med J 2002;95:68–71.
[17] Pollack M, Chastek B, Williams SA, Moran J. Impact of treatment complexity on adherence and glycemic control: an analysis of oral antidiabetic agents. 2010;17:257–65.
[18] American Diabetes Association. Standards of medical care in diabetes—2013. Diabetes Care 2013;36:S11–66.
[19] Stack RJ, Bundy CE, Elliott RA, New JP, Gibson M, Noyce PR. Intentional and unintentional non-adherence in community dwelling people with type 2 diabetes: the effect of varying numbers of medicines. Br J Diabetes Vasc Dis 2010;10:148–52.
[20] Voorham J, Denig P. Computerized extraction of information on the quality of diabetes care from free text in electronic patient records of general practitioners. J Am Med Inform Assoc 2007;14:349–54.
[21] Vink NM, Klungel OH, Stolk RP, Denig P. Comparison of various measures for assessing medication refill adherence using prescription data. Pharmacoepidemiol Drug Saf 2009;18:159–65.
[22] Horne R. The Medication Adherence Report Scale (MARS): a new measurement tool for eliciting patients' reports of non-adherence. Unpublished working paper.
[23] Stack RJ, Bundy C, Elliott RA, New JP, Gibson JM, Noyce PR. Patient perceptions of treatment and illness when prescribed multiple medicines for co-morbid type 2 diabetes. Diabetes Metab Syndr Obes 2011;4:127–35.
[24] Leventhal H, Diefenbach M, Leventhal EA. Illness cognition: using common sense to understand treatment adherence and affect cognition interactions. Cogn Ther Res 1992;16:143–63.
[25] Maningat P, Gordon BR, Breslow JL. How do we improve patient compliance and adherence to long-term statin therapy? Curr Atheroscler Rep 2013 Jan;15:291–8.
[26] Rees G, Leong O, Crowston JG, Lamoureux EL. Intentional and unintentional nonadherence to ocular hypotensive treatment in patients with glaucoma. Ophthalmology 2010;117:903–8.
[27] Garfield S, Clifford S, Eliasson L, Barber N, Willson A. Suitability of measures of self-reported medication adherence for routine clinical use: a systematic review. BMC Med Res Methodol 2011;11:149–57.
[28] Holt EW, Muntner P, Joyce C, Morisky DE, Webber LS, Krousel-Wood M. Life events, coping, and antihypertensive medication adherence among older adults: the cohort study of medication adherence among older adults. Am J Epidemiol 2012;176:S64–71.
[29] Garber MC, Nau DP, Erickson SR, Aikens JE, Lawrence JB. The concordance of self-report with other measures of medication adherence: a summary of the literature. Med Care 2004;42:649–52.
[30] Sidorenkov G, Haaijer-Ruskamp FM, de Zeeuw D, Denig P. A longitudinal study examining adherence to guidelines in diabetes care according to different definitions of adequacy and timeliness. PLoS One 2011;6:e24278.