Impact of depression and anxiety disorders on adherence to oral hypoglycemics in older adults with diabetes mellitus in Canada

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Published online: 23 July 2016
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Abstract The prevalence of diabetes mellitus is increasing in Canada, and nonadherence to oral hypoglycemics is a common problem among older adults. This study aims to document the impact of depression and anxiety disorders on adherence to oral hypoglycemics in older adults with diabetes mellitus. Data used in this study came from the longitudinal Quebec survey on senior's health (Enquête sur la Santé des Aînés), using a representative sample of 2811 older adults aged 65 and over. The final sample for analysis consisted of 301 patients who received oral hypoglycemic pharmacotherapy. Medication adherence was measured with the medication possession ratio. An adapted version of Andersen's behavioral model was used to explain adherence to oral hypoglycemic medication while considering the following predisposing factors: age, gender, and level of education: enabling factors: marital status and income level: and need factors: physical and mental health status. Our explanatory model of oral hypoglycemic medication adherence was tested using a latent growth curve model. The results of the multiple-group analysis did not show any significant difference in oral hypoglycemic medication adherence ($p > 0.05$). Furthermore, individuals with higher levels of education were less adherent to oral hypoglycemics than those with lower levels of education ($p < 0.05$). Medication adherence to oral hypoglycemics

did not show any significant difference between participants with and without depression and anxiety disorders. Future studies with larger samples are needed to fully explore the association between mental disorders and oral hypoglycemic medication adherence in the older adult populations.

Keywords Type II diabetes · Oral hypoglycemic agent · Medication adherence · Older adult · Depression · Anxiety

Introduction

Diabetes mellitus affects over 20 % of Canadian seniors (Health Canada 2009). Diabetes is associated with a variety of complications and conditions such as cardiovascular disease, diabetic retinopathy, and diabetic nephropathy (Romero-Aroca et al. 2010). It has also been reported that patients with diabetes have higher rates of both mood and anxiety disorders than people without diabetes (Das-Munshi et al. 2007; Engum 2007).

Glycemic control remains the main therapeutic objective for prevention of organ damage and other complications arising from diabetes (Koro et al. 2004). Oral hypoglycemic agents (OHAs) are the main treatment for people with type II diabetes mellitus. However, poor adherence to these medications is a major contributor to poor glycemic control (Khatab et al. 2010).

Rates of medication adherence in seniors with diabetes vary widely. Estimates range from 36 to 93 % depending on whether the medication use is based on dispensing information or more rigorous electronic monitoring (Cramer 2004; Rubin 2005). In Canada, studies on adherence to diabetic medication in older adults are rare. An earlier study in older adults reported a mean refill rate of oral

Responsible editor: H.-W. Wahl.

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hypoglycemic medication reaching 86 % in patients taking the same drug type for 3 years, after controlling for age, gender, and category of oral antihyperglycemics (Morningstar et al. 2002). The majority of studies evaluated the prevalence of diabetes medication adherence across different classes of medication (Cramer 2004; Melikian et al. 2002), but few studies considered the effect of physical and mental health status as well as sociodemographic factors on patient's adherence to hypoglycemic medication.

A number of factors have been associated with nonadherence to medications in older adults (Hughes 2004). Some have highlighted the impact of sociodemographic factors on antidiabetic medication adherence (Vik et al. 2004) whereas others have not (Balkrishnan 1998). An increased number of comorbidities have also been associated with decreased medication adherence in diabetic patients (Balkrishnan et al. 2003). Depression and anxiety, which commonly coexist, affect 10 % of older adults (Preville et al. 2008). Studies have also shown that both these conditions are associated with a poor control of glycemia in diabetic populations (Kendzor et al. 2014; Anderson et al. 2002). Further, the presence of depression and anxiety has been associated with a decrease in metabolic control (Anderson et al. 2002; Ciechanowski et al. 2000; Collins et al. 2009), poor adherence (or compliance) to medication and diet regimens (Bouwman et al. 2010; Gonzalez et al. 2008; Lustman et al. 2000), and a reduction in the quality of life associated with diabetes complications. Among older adults, results on age have been contradictory (Balkrishnan 1998). Previous studies have also shown that women reporting a depressive or anxiety disorder were more likely to be adherent than men (Nau et al. 2007). Marital status and income level have also been identified as significant predictors of medication adherence (Jin et al. 2008). Understanding factors that contribute to medication adherence in older patients with diabetes is central to identifying at-risk individuals and providing more effective treatment.

To the best of our knowledge to date, no study has considered the effect of patient's mental and physical health status and sociodemographic characteristics on adherence to oral hypoglycemics in older adults with diabetes mellitus in Canada. The objective of this study was to document the impact of depression and anxiety on adherence to oral hypoglycemic therapy in older individuals with diabetes mellitus living in Quebec, Canada within a public managed healthcare system.

Conceptual framework

After conducting a review of the literature on various models on adherence (Bandura 1977; Becker 1974; Cummings et al. 1980; Floyd et al. 2000; Leventhal and

Cameron 1987; Prochaska and DiClemente 1982; Rosenstock 1974), an adaptation of Andersen's behavioral model of healthcare seeking behaviors, used in a wide range of research, was chosen to explain adherence to oral hypoglycemic medications in older patients with diabetes mellitus (Andersen and Newman 1973). The model, originally developed to predict healthcare service use, is based on predisposing, enabling, and need factors, which have also been used to predict medication adherence (De Smet et al. 2006; Murray et al. 2004).

The predisposing factors in the original model were included demographics, social structure, and health beliefs. Gender and level of education were also identified as significant predictors in explaining medication adherence (Vik et al. 2004). The enabling factors in the original model represented personal and community factors that should be present for healthcare service use to take place. We include marital status and income level as predictors of medication adherence (Jin et al. 2008). The need factors were perceived need and evaluated need. In this study, we included mental and physical status health (Charlson comorbidity index).

We hypothesized that patient adherence to oral hypoglycemic medications was determined by (1) predisposing factors such as gender and level of education, (2) enabling factors such as marital status and income level, and (3) need factors such as physical and mental health status (Fig. 1).

Methods

Data came from the longitudinal Quebec survey on seniors' health [Enquête sur la Santé des Aînés (ESA)] conducted between 2005 and 2008 ($n = 2811$) using a probabilistic sample of French-speaking community-dwelling older adults (94 % of the Quebec population speak French). Subjects living in remote regions of Quebec (Canada) were excluded on feasibility grounds. In 2005, 10 % of the older adult population resided in these regions. The sampling frame of the study included stratification by three geographical areas: metropolitan, urban, and rural. Subsequently, a proportional sample of households was constituted according to the 16 administrative regions of Quebec. A random sampling method was also used to select only one older adult (65 years or older) within the household. Participation rate in the ESA survey was 76.5 %. The research procedure was previously reviewed and authorized by the Ethics Committee of the Sherbrooke Geriatric University Institute.

Data were collected as follows. First, a health professional contacted the potential participants by phone to describe the objectives and length of the study, and asked

Fig. 1 An adaptation of Andersen's behavioral model was used to explain adherence to oral hypoglycemic medication

them to participate in an in-home interview and answer their questions. Next, a letter describing the study was sent to reassure potential respondents about the credibility of the investigation and the interviewer, namely a health professional working for a national polling firm. In preparation for the interviews, they were given a 2-day training course on the administration of the computer-assisted ESA-Q by the principal investigator. Respondents were offered \$15 compensation for their participation.

The in-home interviews were carried out within 2 weeks of first contact and lasted on average 1.5 h. A written consent was obtained at the beginning of the interview from all participants. As memory problems may affect the accuracy of the information given and performance on psychological questionnaires (Burke et al. 1989; Kafonek et al. 1989), individuals presenting severe or moderate cognitive problems based on the mini-mental state examination (MMSE) (score less than 22) (Crum et al. 1993; Folstein et al. 1975) were excluded at the beginning of the interview ($n = 27$). Additional analyses did not show a difference between those excluded on the basis of scores on the MMSE and those included with regard to the presence of anxiety and depression (Pearson coefficient = -0.42 ; $p = 0.19$), and with respect to the percentage of number of days supplied during the year (Pearson coefficient = 0.035 ; $p = 0.29$).

The subjects presenting no moderate or severe cognitive problems were invited to respond to the ESA-Q ($n = 2784$). At the end of the interview, respondents were asked to give written consent allowing access to their health and pharmaceutical service use from the Régie d'Assurance-Maladie du Québec (RAMQ) (agency responsible for Quebec's health insurance plan). Using the

participant's medical insurance number, it was possible to link the ESA survey and individual level information from the RAMQ's medical and pharmaceutical service databases and the health ministry's MED-ECHO database on hospitalizations. Information on pharmaceutical services included the dispensed drug's code, quantity, dosage, and length of treatment, and the date the drug was dispensed. A success rate of 99.6 % ($n = 2494$) was obtained in the matching of the data. Participants with private drug insurance were excluded ($n = 208$).

Study sample

Participants in the ESA study with diabetes were identified based on criteria from the national diabetes surveillance system (NDSS) (Health Canada 2009). According to the NDSS, the minimum requirement for a diagnosis was at least one hospitalization or two physician claims, with diabetes specific code(s), over a 2-year period. In this study, 358 patients were diagnosed with type II diabetes mellitus. Patients taking oral hypoglycemic medication alone during the 2 years of follow-up were included ($n = 313$). Patients who did not have at least two consecutive prescriptions of oral hypoglycemic drugs were excluded from this study ($n = 4$). Patients initially treated with OHAs who switched to insulin were excluded ($n = 8$) because the multiple-interval measure of medication availability (adherence measure used in this study) could not account for the variability of insulin regimens. The final sample for analysis consisted of 301 patients who received oral hypoglycemic pharmacotherapy (Fig. 2). The preliminary analysis showed that participants with

Fig. 2 Sample characteristics

probable depression and anxiety disorders were not associated with switching of medication or use of hypoglycemic polytherapy (Fisher's test $p > 0.05$).

Measures

Medication adherence was measured using the medication possession ratio (MPR) that estimated the proportion (or percentage) of days of supply obtained during a specified time period or over a period of multiple-interval refills. The MPR is the day's supply of medication dispensed during a specified follow-up period divided by the number of days from the first dispensing to the end of the follow-up period (Steiner and Prochazka 1997). The index date of the study was the date when the first hypoglycemic medication was filled in the study period. The total exposure period was 2 years with four 6-month period measurements taken to examine the change in medication adherence. The number of days a patient was hospitalized was subtracted from the denominator due to the fact that medications dispensed in the hospital are not included in the RAMQ database.

Mental health status was assessed using the diagnostic component of the "ESA Questionnaire (ESA-Q)," which was based on DSM-IV criteria (Erdman et al. 1992; Wittchen et al. 1991). The ESA-Q is similar to the diagnostic interview schedule and the composite international

diagnostic interview, which demonstrates good reliability and validity (Bucholz et al. 1996). In this study, a 12-month period DSM-IV diagnosis was made for the following mental disorders: major depression, minor depression, mania, specific phobia, social phobia, agoraphobia, panic disorder, obsessive-compulsive disorder, and generalized anxiety disorder (Preville et al. 2008). Major depression was defined as the presence of the essential features of depression, that is, either depressed mood or loss of interest or pleasure in usual daily activities nearly every day and most of the day during at least two consecutive weeks, who also report impairment in at least one area of social functioning, and who report at least five of the seven associated symptoms. In addition, individuals who showed the essential features of depression and reported between two and four of the seven associated symptoms of depression were classified as having minor depression (Preville et al. 2008). Finally, individuals who were told by their doctor that their symptoms were attributable to a physical disease, a drug or to grief were excluded from the major and minor depression category (Preville et al. 2008). The presence of an anxiety disorder was based on individuals presenting DSM-IV criteria for panic disorder, agoraphobia, generalized anxiety disorder, obsessive compulsive disorder, social and specific phobia during the preceding 12-month period and who report impairment in at least one area of social functioning were

classified as having anxiety. Individuals attributing their symptoms to a physical health disease were considered to not have the diagnosis. The complete definition of the disorders studied in the ESA survey has been reported previously (Preville et al. 2008). For the analysis, the participants were classified as having (1) at least one probable DSM-IV disorder (depressive or anxiety disorders), or (2) absence of a probable DSM-IV disorder (depressive or anxiety disorders) during the 2-year study period.

Respondent physical health status was measured using the Charlson comorbidity index (1987). In this index, each medical condition has a weight assigned from 1 to 6, which is derived from relative risk estimates of proportional hazard regression models using clinical data. This index has been shown to have a strong monotonic association of approximately a 2-fold increase in mortality per increment in the index level. This index was calculated using medical claims from the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes for the 12-month period before the interview date and excluded diagnoses related to diabetes mellitus.

The predisposing and enabling factors examined in this study were as follows: age (65–74 and ≥ 75 years), gender (female/male), education (less than 10, 10 years and over), marital status (married or living in a couple or single/separated/divorced/widowed), and family annual income (less than \$15,000, and \$15,000 and over).

Analysis

The method of imputation for missing categorical data proposed by Van Buuren and Van Rijckevorsel was used to estimate missing data on the income variable (Van Buuren and Van Rijckevorsel 1992). Group sample sizes of 47 and 254 achieve 86 % power to detect a difference of 20 % in adherence rates between the two groups with known group standard deviations of 46.2 % and with a significance level α of 0.05 using a one-sided two-sample t test.

A latent growth curve model was used to test our explanatory model of the impact of depression and anxiety disorders on oral hypoglycemic medication adherence illustrated in Fig. 3 (Duncan et al. 1999). In this model, the ξ_i (K_{sis}) ($i = 1-3$) are latent constructs representing observed enabling, predisposing, and need factors. The y_i ($i = 1-4$) represent adherence to the oral medications observed at four consecutive 6-month periods, where ε_j (theta-epsilons) ($i = 1-4$) are measurement errors of medication adherence. The dependent latent variables are represented by η_1 (eta) ($i = 1, 2$). The first factor (η_1) that represents the initial level (intercept) of medication adherence at Time 1 was specified by fixing all four of the

loadings ($\lambda_{i,1}$) (lambdas) ($i = 1-4$) between y_i and η at 1.0 according to the procedure proposed by Duncan et al. (1999). The second factor (η_2) that represents the linear slope of the growth curve (rate of change over the four time points) was defined by fixing the first loading ($\lambda_{1,2}$) at 0, the second loading ($\lambda_{2,2}$) at 1, the third loading ($\lambda_{3,2}$) at 2, and the fourth loading ($\lambda_{4,2}$) at 3, which correspond to the time interval scale between the four adherence measures. Parameter α (alpha) refers to the intercept (α_1) that represents the mean level of adherence at the beginning of the study, and the slope (α_2) that represents the average rate of change in the level of medication adherence during the 24 months of follow-up. The γ (gamma) coefficients represent the effect of the predisposing and facilitating factors on the intercept (η_1) and slope (η_2) of medication adherence. The ϕ (phi) coefficients represent the associations between the exogenous factors. Finally, ζ (zetas) represent variance in the latent constructs explained by external causes not measured in the study.

The covariates studied were added to the model to test the effect of the exogenous factors on the baseline and change in adherence to medication observed regressing the latent intercept (η_1) and slope (η_2) factors on covariates studied (Fig. 3). Our explanatory model was tested using LISREL 8.80 (Jöreskog and Sörbom 1993). When the variables are categorical or their distribution is strongly asymmetrical, as was the case here, the use of a polychoric correlation matrix and its asymptotic covariance matrix and the column vector of means is recommended. The robust maximum likelihood (ML) method was used to estimate the model's parameters. The χ^2 statistic, adjusted goodness-of-fit index (AGFI), root mean square error of approximation (RMSEA), and RMRS indexes were used to guide the overall assessment of the model. The 95 % statistical threshold was employed for our analyses. The AGFI estimates the proportion of variances and covariances explained by the model adjusted for degrees of freedom (df). This index varies from 0 to 1 with 1 indicating a perfect fit. The RMSEA index measures the discrepancy between the observed and estimated covariance matrices per df. This index varies from 0 to 1. A value lower than 0.05 indicates a close fit. The RMRS index represents the average of the residuals between the observed variances and covariances and the predicted values obtained under the model's constraints. An RMRS value of 0 indicates a perfect adjustment.

Results

In this older adult population sample, the prevalence of oral hypoglycemic medication use was 13.2 %. Our sample included more women (64.8 %) than men (35.2 %). Close to 58 % of

Fig. 3 Explanatory model of medication adherence. The $(\lambda_{i,1})$ (λ mbdas) ($i = 1-4$) represents the initial level (intercept) of medication adherence at *Time 1* and represents the linear slope of the growth curve (rate of change over the four *time points*). The ξ_i (K_{sis}) ($i = 1-5$) are latent constructs representing observed predisposing (gender and education level), enabling (marital status and income), and need factors (Charlson comorbidity index). The γ_i (gamma) ($i = 1-5$) coefficients represent the effect of gender and education level, marital status, income, and Charlson comorbidity index on the intercept (η_1) and slope (η_2) of medication adherence. The ε_j (theta-epsilons) ($j = 1-4$) are measurement errors of medication adherence. The ζ (zetas) represent variance in the latent constructs explained by external causes not measured in the study. The ϕ (phi) coefficients represent the associations between the exogenous factors (predisposing: gender and education level, enabling: marital status and income, and need factors: Charlson comorbidity index)

participants were aged less than 75 years and 45 % were married, and 69.8 % of the respondents had had less than 10 years of education. Finally, 15.6 % of the respondents reported a probable DSM-IV depression and anxiety disorders (Table 1).

The model tested (M0) corresponds to the latent growth curve model illustrated in Fig. 3. As indicated by all of the goodness-of-fit indexes, this model satisfactorily fits the observed data ($\chi^2_{ML} = 21.31$, $df = 23$, $p = 0.56$, AGFI = 0.97, RMSR = 0.03). The findings demonstrate that a change in medication adherence over 2 years was linear. Complementary analyses did not show evidence that a nonlinear slope fits the data better. The presence of depression and anxiety disorders was not associated with the level of initial medication adherence ($\gamma_{1,1} = 0.01$, $p > 0.05$) but was significantly associated with the rate of change ($\gamma_{2,1} = -0.07$, $p > 0.001$). Respondents classified

as having a probable depression and anxiety showed a significant decrease in their adherence level over time. The results also indicated that education level was not associated with initial level of medication adherence ($\gamma_{1,4} = 0.08$, $p > 0.05$) but was significantly associated with the rate of change ($\gamma_{2,4} = -0.06$, $p < 0.001$). Individuals with a higher level of education had a significantly greater decrease in the rate of change than those with lower levels of education. Furthermore, marital status was associated with the initial level of medication adherence ($\gamma_{1,3} = -0.12$, $p < 0.05$) but was not significantly associated with the rate of change ($\gamma_{2,3} = 0.03$, $p > 0.05$).

To examine potential differences in the latent growth trajectories between respondents having a probable DSM-IV depression and anxiety disorders (group 1) and those without a probable DSM-IV depression and anxiety

Table 1 Sociodemographic and health characteristics of the population

	<i>n</i> = 301	%	95 % CI
Age			
65–74	173	57.5	52.0–63.0
≥75	128	42.5	37.0–48.0
Gender			
Male	106	35.2	30.0–41.0
Female	195	64.8	59.0–70.0
Marital status			
Married	135	44.9	39.2–50.5
Separated/divorced/widowed/single	166	55.1	49.5–60.8
Education			
<10 years	216	71.8	65.0–75.0
≥10 years	85	28.2	25.0–35.0
Missing			
Depression and/or anxiety disorders (DSM)			
Yes	47	15.6	11.0–20.0
No	254	84.4	80.0–89.0
Charlson comorbidity index			
0	204	67.8	62.5–73.0
1–2	79	26.2	21.0–31.0
3–5	11	3.6	2.0–6.0
≥6	7	2.4	1.0–4.0
Income			
<\$15,000	66	23.4	18.8–28.4
≥\$15,000	216	76.6	71.6–81.2
Missing	19	–	–
	Mean	SD	95 % CI
Charlson comorbidity index (0–11)	0.65	1.2	0.50–0.80

disorders (group 2), a multiple-group analysis was conducted. Multiple-group analysis in structural equation modeling is very useful to ensure the invariance of latent construct measurements and the validity of theoretical models across different subpopulations.

The results presented in Table 2 showed that model (M1) with a complete invariance hypothesis between both groups was plausible ($\chi^2 = 78.57$; $p = 0.59$). Furthermore, model (M2) that specified the same pattern of free and fixed parameters and invariance of the psi matrix in probable DSM-IV depression and anxiety disorders (group 1) and those without a probable DSM-IV depression and anxiety disorders (group 2) was plausible ($\chi^2 = 57.73$; $p = 0.70$). Our results showed that model (M3) specifying invariance and that adding equality constraints of the γ matrix in both groups (M3) was also plausible ($\chi^2 = 65.54$; $p = 0.69$). Finally, our results showed that a model (M4) specifying invariance and that

adding equality constraints of the α matrix in both groups (M4) was also plausible ($\chi^2 = 70.72$; $p = 0.59$). These findings indicate that the change trajectories of medication adherence were similar in participants having a probable DSM-IV depression and anxiety disorders (group 1) and those without a probable DSM-IV depression and anxiety disorders (group 2).

According to the model (M4), a significant mean of the intercept factor ($\alpha_1 = 0.97$, $p < 0.05$) indicated that at baseline the patients presented an average level of adherence to oral hypoglycemic medication of 97 % (Table 2). The mean slope, however, was not significant ($\alpha_2 = -0.09$, $p > 0.05$), indicating that medication adherence remained constant during the follow-up period for both DSM-IV depression and anxiety disorders (group 1) and those without a probable DSM-IV depression and anxiety disorders (group 2). Furthermore, the final model (M4) showed a significant variance of the intercept factor ($\zeta_{1,1} = 0.50$, $p < 0.05$), reflecting individual variability around the group mean of medication adherence at baseline. In addition, the variance of the slope factor (η_2) ($\zeta_{2,2} = 0.13$, $p < 0.05$) indicated a small individual variability in the rate of change during the 24 months of follow-up. Finally, the correlation between the variance of the intercept and slope factors was significant ($\zeta_{1,2} = -0.12$, $p < 0.05$), indicating that a higher initial level of medication adherence was not associated with lower level medication adherence at the end of the follow-up period.

As indicated in Table 3, the Charlson comorbidity index, income, age, and marital status were not associated with either initial medication adherence at baseline or rate of change in medication adherence. The results also showed that gender was not significantly associated with the initial level of medication adherence ($\gamma_{1,4} = 0.00$, $p > 0.05$) or rate of change ($\gamma_{2,4} = -0.01$, $p > 0.05$) in the study sample. Finally, the results also indicated that the education level was not associated with the initial level of medication adherence ($\gamma_{1,3} = 0.09$, $p > 0.05$) at baseline but was significantly associated with the rate of change ($\gamma_{2,3} = -0.06$, $p < 0.05$). Individuals with a higher level of education had slightly steeper decreases in adherence levels over time.

Discussion

The prevalence rate of type II diabetes observed in this study (13.2 %) was lower in comparison to other Canadian (22.8 %) and Quebec (22.2 %) estimates in older adults (Health Canada 2009). The differences could be explained by the fact that the ESA study was restricted to a representative sample of French-speaking older adults in the province of Quebec and excluded the Inuit

Table 2 Estimates for latent growth curves of medication adherence and depression and anxiety disorders

	χ^2	df	α	p	RMSEA	CFI	$\Delta\chi^2$	p
M1 (LY = IN, TE = IN, PS = IN, AL = IN, GA = IN)	78.51	82	0.94	0.59	0.0	1	0	
M2 (LY = IN, TE = IN, PS = IN, AL = SP, GA = SP)	57.73	64	0.74	0.70	0.0	1	20.78	0.05
M3 (LY = IN, TE = IN, PS = IN, AL = IN, GA = SP)	65.54	72	0.97	0.69	0.0	1	7.81	0.09
M4 (LY = IN, TE = IN, PS = IN, AL = SP, GA = IN)	70.72	74	0.97	0.59	0.0	1	5.18	0.04

SP same pattern, IN invariant, *lambda Y* (LY) path coefficients between latent η variables and manifest y variables, *theta-epsilon* (TE) correlation matrix for each observed variable, *PS* (psi) variances/covariances of the residual variables ζ in the structural model, α (alpha) specifies the intercepts of the structural model for the eta (η) variables (dependent latent) and the KSI (ξ) (independent latent) variables, *GA* (gamma) path coefficients between ε - and η -variables in the structural model, α (alpha 1), *RMSEA* root mean square error of approximation, *CFI* comparative fit index, p p value, $\Delta\chi^2$ chi-squared test difference

Table 3 Parameter estimates (standard error) for the latent growth curve model

Parameters	Estimates (SE)	Parameters	Estimates (SE)	Parameters	Estimates (SE)
$\lambda_{y1,1}$	1	$\gamma_{1,1}$	0.01 (0.06)	$\zeta_{1,1}$	0.50 (0.10)*
$\lambda_{y2,1}$	1	$\gamma_{1,2}$	-0.12 (0.06)	$\zeta_{2,2}$	0.13 (0.02)*
$\lambda_{y3,1}$	1	$\gamma_{1,3}$	0.09 (0.06)	$\zeta_{1,2}$	-0.12 (0.04)
$\lambda_{y4,1}$	1	$\gamma_{1,4}$	0.00 (0.05)	$\phi_{1,1}$	1 (0.06)
$\lambda_{y1,2}$	0	$\gamma_{1,5}$	0.05 (0.06)	$\phi_{2,2}$	1 (0.06)
$\lambda_{y2,2}$	1	$\gamma_{1,6}$	0.01 (0.02)	$\phi_{3,3}$	1 (0.06)
$\lambda_{y2,3}$	2	$\gamma_{2,1}$	-0.01 (0.02)	$\phi_{4,4}$	1 (0.06)
$\lambda_{y2,4}$	3	$\gamma_{2,2}$	-0.03 (0.03)	$\phi_{5,5}$	1 (0.06)
$\varepsilon_{1,1}$	0.47 (0.12)*	$\gamma_{2,3}$	-0.06 (0.03)*	$\phi_{6,6}$	1 (0.06)
$\varepsilon_{2,2}$	0.61 (0.08)*	$\gamma_{2,4}$	-0.01 (0.02)	$\phi_{1,1}$	1 (0.06)
$\varepsilon_{3,3}$	0.46 (0.08)*	$\gamma_{2,5}$	0.00 (0.03)		
$\varepsilon_{4,4}$	0.06 (0.14)	$\gamma_{2,6}$	0.01 (0.02)		
$\varepsilon_{1,2}$	0.16 (0.07)*				
$\varepsilon_{2,3}$	0.12 (0.03)*				
$\varepsilon_{3,4}$	0.09 (0.08)				

The ($\lambda_{i,1}$) (lambdas) ($i = 1-4$) represents the initial level (intercept) of medication adherence at Time 1 and represents the linear slope of the growth curve (rate of change over the four time points). The ζ_i (K_{sis}) ($i = 1-5$) are latent constructs representing observed predisposing (gender and education level), enabling (marital status and income), and need factors (Charlson comorbidity index). The γ_i (gamma) ($i = 1-5$) coefficients represent the effect of gender and education level, marital status, income, and Charlson comorbidity index on the intercept (η_1) and slope (η_2) of medication adherence. The ε_j (theta-epsilons) ($i = 1-4$) are measurement errors of medication adherence. The ζ (zetas) represent variance in the latent constructs explained by external causes not measured in the study. The ϕ (phi) coefficients represent the associations between the exogenous factors (predisposing: gender and education level, enabling: marital status and income, and need factors: Charlson comorbidity index)

* $p < 0.05$

and Cree populations and those living in northern regions of Quebec, whose prevalence rates of diabetes are three–five times those of the general population (Horn et al. 2007). In addition, the lower prevalence rate observed is also due to the fact that the study population included individuals with type II diabetes using oral hypoglycemics, which excluded patients using other drugs or those who are not using antidiabetic drugs.

In this 2-year follow-up study, the average medication adherence was 88 %, which falls in the range of other studies reporting adherence rates in older adult patients varying between 36 % and 93 % (Cramer 2004; Cramer

et al. 2008; DiMatteo 2004). The majority of studies in the literature however have shown average adherence rates to medication regimens reaching less than 0.50 (Dailey et al. 2001). We hypothesize that the presence of an obligatory (public or private) drug insurance program in Quebec (Canada) may be responsible for the medication adherence rate observed in this study since other studies have shown that older adults with no drug insurance are less likely to adhere to their treatment (Lynch 2006).

In this study, the mean of the slope factor was not significant, indicating that medication adherence did not change during the follow-up period ($\alpha_2 = -0.09$, $p > 0.05$). With

regard to the predictive variables studied, baseline and rate of change in medication adherence levels were not significantly associated with the respondent's age, gender, marital status, or income. These findings are consistent with other studies that suggested that these variables may have no impact on medication adherence (Vik et al. 2004). Previous studies have shown the association between depression and medication adherence to be stronger in men than women (Nau et al. 2007). Others have also shown that the effect of income is inconsistent mainly due to variations in the study design and sample populations (Mann et al. 2009). A recent review similarly did not report a significant association between age, gender, and marital status and medication adherence in diabetic patients (Krass et al. 2015). We did however observe a significant effect of education level on the rate of change in medication adherence ($\gamma_{2,2} = -0.06, p < 0.05$). This result is consistent with previous findings showing that people with lower education had better adherence. It has been hypothesized that educated patients might have less trust in advice coming from physicians than patients with less education (Senior et al. 2004). Furthermore, the results indicated that physical health status as measured by Charlson comorbidity index was not associated with initial level or rate of change in adherence to medication use over time as has been previously reported (Balkrishnan 1998).

Finally, the presence of depression and anxiety disorders was not associated with medication adherence to OHAs. The depression was associated with nonadherence to therapy in older adult patients with diabetes (Kilbourne et al. 2005; Lin et al. 2004).

Study limitations

First, our measure of adherence depended on pharmacy records. Although this method has been shown to be reliable, refill measures may overestimate medication consumption because it assumes that medications are taken as directed (Choo et al. 1999; Tamblyn et al. 1995). Second, the administrative databases do not contain information on blood glucose level and glycated hemoglobin, it is therefore possible that some of the participants characterized as totally adherent did not take their medications despite filling their prescriptions, leading to an overestimation of adherence in this study. In addition, due to the lack of glucose level and glycated hemoglobin, the exact severity of the patients was not known. Further, information on at-home assistance by nurses and other potential care-givers such as family or household members with activities in daily living were not available. This may have biased the association between medication adherence and mental health status if individuals with depression and anxiety

were also more likely to receive at-home nurse services than those without. Third, mental health status in this study was based on self-reported data which can be subject to recall and social desirability bias. Fourth, 41 participants using insulin therapy were excluded because pharmacy records do not contain information for the variability of insulin regimens on a day-to-day basis. Fifth, studies have shown that cognitive and memory problems may play an important role in medication adherence (Salas et al. 2001; Park et al. 1992) and therefore it is possible that medication adherence may have been overestimated as we excluded individuals with moderate and severe cognitive problems. However, this bias is limited given that our analyses did not show a difference between the total number of medication days supplied during the study period between those with less than 22 versus those with 22 and above on the MMSE. Sixth, the severity of the symptoms associated with depression and anxiety disorders was not considered in this study which may have had a more important impact on medication adherence. Further, given the small sample size ($n = 301$), we were not able to assess medication adherence rates for depression and anxiety specifically. Finally the Inuit and Cree populations, those living in the northern regions of Quebec and older adults institutionalized were excluded populations, and the results therefore may not apply to these groups who have higher prevalence rates of diabetes.

Conclusion

To the best of our knowledge, this is one of the first studies to explore the link between mental health status and subsequent oral hypoglycemic medication adherence using survey and administrative databases in Quebec. There is a lack of understanding of how patient-specific factors influence low medication adherence and how effective interventions can be targeted to overcome these factors and improve adherence in older adults. We observed that respondents with depression and anxiety disorders did not show a decrease in medication adherence compared to those without depression and anxiety disorders on average over a 24-month period. Given the impact of depression and anxiety on diabetes outcomes, strategies need to be implemented by primary care provider teams to address these mental health issues such as depression and anxiety. This might include more intensive efforts to recognize and treat depression and in older adult patients with diabetes in the primary care. Future studies with larger samples are needed to fully explore the effect between mental health status and medication adherence in older adults in Canada.

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