

Trajectory of Disability in Older Adults With Newly Diagnosed Diabetes: Role of Elevated Depressive Symptoms

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OBJECTIVE

We examined whether the trajectory of disability differed between older adults with and without elevated depressive symptoms before and after the onset of diabetes mellitus (DM) over 10 years (2004–2014) and explored difficulties in basic and instrumental activities of daily living between the two groups.

RESEARCH DESIGN AND METHODS

A generalized linear mixed-model analysis was conducted using five waves (8th– 12th) of Health and Retirement Study (HRS) data. We included 419 older adults who self-reported new DM diagnosis within the previous 2 years and used the Center of Epidemiologic Studies Depression Scale to measure elevated depressive symptoms. Disability was measured by 10 items defined in the HRS data set.

RESULTS

The trajectory of disability differed between older adults with and without elevated depressive symptoms after newly diagnosed DM over time. Significant and clinically meaningful between-group differences were found in disability after the onset of DM (waves 10 and 11) but not before the onset of DM (waves 8 and 9). Among older adults with elevated depressive symptoms, disability at pre-DM waves (8 and 9) was significantly less than post-DM waves (10–12). Difficulties with shopping, walking, and dressing were mostly reported by older adults with elevated depressive symptoms.

CONCLUSIONS

Older adults with newly diagnosed DM and elevated depressive symptoms have a clinically meaningful and faster disablement trajectory than those without elevated depressive symptoms. Future interventions may take an indicated approach to disability prevention in older adults with newly diagnosed DM, especially in those with a change in depression severity.

The number of older adults will increase by an estimated threefold by 2050, and the number of older adults with diabetes mellitus (DM) is expected to increase by 4.5-fold (1). DM costs \$245 billion per year (\$176 billion in direct medical costs, \$69 billion in reduced productivity) in the U.S. and is well-known for its complications and association with disability (2,3).

Disability has been defined by the U.S. Census Bureau and National Institute on Disability, Independent Living, and Rehabilitation Research as the inability to perform ¹Department of Occupational Therapy, University of Pittsburgh School of Health and Rehabilitation Sciences, Pittsburgh, PA

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© 2018 by the American Diabetes Association. Readers may use this article as long as the work is properly cited, the use is educational and not for profit, and the work is not altered. More information is available at http://www.diabetesjournals .org/content/license. activities of daily living (ADL) and instrumental ADL (IADL) (4,5). ADL are important to sustain self-care (e.g., dressing, eating), whereas IADL are critical for independent living (e.g., shopping, preparing a meal). Emerging evidence suggests that the prevalence of disability is growing in older adults with DM (6). DM-related disability is problematic because it may lead to reduced quality of life, institutionalization, substantial health care costs, and early death (7,8). Identifying factors associated with DM-related disability early in the course of the disease may aid in the prevention of disability and save substantial health care costs

The examination of clinical factors common in late life may enhance our understanding of the disablement trajectory associated with DM. Elevated depressive symptoms comprise a common clinical factor that is comorbid with medical conditions in late life. Moreover, elevated depressive symptoms often are seen in older adults with newly diagnosed DM. Epidemiologic and clinical evidence suggests that 22-32% of older adults have DM (9,10), and 24-55% of these older adults have clinically significant depressive symptoms (11,12). Depressive symptoms and DM have a bidirectional and mutually exacerbating relationship (13) that may be mediated by behavioral and physiologic mechanisms (14). For example, after a new DM diagnosis, depressive symptoms may co-occur with metabolism dysregulation (15). The somatic features of depressive symptoms (e.g., lack of energy, sleep disturbance) often interfere with adopting necessary healthy behaviors (e.g., medication management, exercise) (16,17), worsening a vicious cycle of poor glucose control, inactivity, and low mood (13,18). Symptoms of acute hyperglycemia, including fatigue, nausea, frequent urination, and recurrent infections, also may cause or exacerbate depressive symptoms (14).

Although it is established that depressive symptoms are associated with chronic diseases and worse health outcomes over time, we have little understanding of the influence of elevated depressive symptoms on the disablement trajectory in older adults with newly diagnosed DM. Older adults who have a change in or elevated depressive symptoms after diagnosed medical conditions (e.g., the onset of DM) are at risk of further psychiatric complications (19,20) and deteriorated health over time (21). The understanding of the similarities or differences in the trajectories of disability between older adults with and without elevated depressive symptoms may aid in current research through early identification of older adults at risk for disability. The timing and design of future interventions may be tailored on the basis of this evidence.

The current study examined whether the disablement trajectory before and after the diagnosis of DM is different between older adults with and without elevated depressive symptoms. The Health and Retirement Study (HRS) data set provided the opportunity to examine the longitudinal association between disability and elevated depressive symptoms over a 10-year period in older adults with newly diagnosed DM.

RESEARCH DESIGN AND METHODS

Data Set and Participants

The HRS is a longitudinal data set that was sponsored by the National Institute on Aging and was conducted by the University of Michigan (22). The HRS data set included a representative sample of \sim 20,000 people age >50 years. The HRS followed nationally representative samples of age-eligible respondents every 1-2 years. All the HRS survey data were collected by either phone or face-to-face interview by trained interviewers. The HRS survey data include demographics, work, health, functioning status, and disease conditions. The HRS data set also includes information about respondents' children and spouses.

We extracted survey data from the HRS cohorts from the 8th wave (2004-2006) to the 12th wave (2012-2014) because the 12th wave had the most recent survey data. The response rates ranged from 87.9 to 88.6% among waves 8 to 12. Respondents who 1) self-reported being newly diagnosed with DM between waves 9 and 10, 2) were \geq 55 years of age, and 3) had complete depressive symptoms and disability survey data were included in this study. In the HRS data set, we identified eligible respondents in wave 10 to examine disablement before (waves 8 and 9) and after (waves 10-12) the onset of DM. A total of 512 respondents who met the inclusion criteria were identified in the HRS data. We excluded 93 who had missing values for depressive symptoms; thus, 419 participants were included in the analyses.

Assessments Disability

Disability was measured by 5 ADL and 5 IADL tasks. Participants were asked whether they had difficulty with performing each task (yes/no). The total disability score ranged from 0 to 10, with a higher score indicating more disability. A cut point of 1 indicated the development of clinically meaningful, overt disability (23). In this study, separating two types of daily activities was important because ADL represent selfcare tasks (e.g., bathing, eating), whereas IADL represent more complex tasks required for successful independent living (e.g., shopping, preparing meals) in older adults.

Depressive Symptoms

Depressive symptoms were measured by the eight-item Center of Epidemiologic Studies Depression Scale (CESD) (24), a self-report questionnaire with total scores ranging from 0 to 8, with a higher score indicating more somatic and mood symptoms. We measured depressive symptoms with the CESD after participants received a diagnosis of DM and separated these individuals into two groups: those who had elevated depressive symptoms (elevated score on the CESD) from waves 9 to 10 and those who had the same or reduced depressive symptoms from waves 9 to 10. This approach would help to capture those with a tendency toward psychiatric complications and deteriorated health after the onset of DM (19,20).

Demographic Variables

We described the demographic and clinical characteristics of the sample by examining age, sex, years of education, race, ethnicity, marital status, comorbidity, BMI, and cognitive function. Comorbidity was measured by self-reported conditions (defined as high blood pressure, cancer or a malignant tumor, chronic lung disease, heart attack, stroke, psychiatric problems, or arthritis) before the onset of DM. Cognitive function was determined by survey questions that addressed several cognitive domains, including memory, recall, working memory, language, and vocabulary. Memory was self-rated, with item scores ranging from 1 (excellent) to 5 (poor). Recall was assessed by two word recall tests: immediate and delayed. The two test scores were added for a total score, which ranged from 0 to 20, with a higher score indicating better recall ability. Working memory was assessed by the serial sevens subtraction test. The total score ranged from 0 to 5, with a higher score indicating better working memory. Language was assessed by an eight-item date and object naming test (0 = incorrect and 1 = correct). Total scores were summed across items and ranged from 0 to 8, with a higher score indicating better language ability. Vocabulary was assessed by a defining words test. The total score ranged from 0 to 10, with a higher score indicating better-established knowledge (25). We did not include two cognitive domains (language and vocabulary), health behaviors (e.g., smoking cessation, physical activity), and income variables because of the amount of missing data for those variables.

Statistical Analyses

We used SPSS version 22 (IBM Corporation, Chicago, IL) and SAS 9.3 (SAS Institute, Cary, NC) statistical software for data analyses. All the analyses were considered significant at the 0.05 twotailed α -level. Disability was the dependent variable. Group (with or without elevated depressive symptoms after the onset of DM) and time (waves 8-12) were independent variables. We examined descriptive statistics, distribution plots, normality, and heterogeneity for the dependent variable (disability) over five waves to check the assumptions of the longitudinal linear mixed model (26). These assumptions were not met; therefore, we used the generalized linear mixed model with a Poisson distribution and an unstructured covariance matrix. The model included a group \times time interaction as well as group (older adults with and without elevated depressive symptoms) and time (waves 8-12) simple main effects. We treated the intercept of disability within participants as a random-effect variable. We controlled for wave 9 depressive symptoms in the model to take into account the severity of depressive symptoms before the onset of DM.

We conducted post hoc analyses and the Bonferroni correction for significance level adjustment after detecting a group \times time interaction. Effect sizes were computed between groups for the five waves to determine the clinical meaningfulness of group differences. The magnitude of effect sizes was followed by Cohen *d* (0.2 = small, 0.5 = moderate, 0.8 = large). The χ^2 test was used to examine whether there were group differences in percentages of participants who experienced difficulties with the 10 ADL and IADL tasks at wave 10.

Two steps were used to identify covariates in the model. First, group differences in demographic variables at wave 10 were examined by t and χ^2 statistics to identify potential covariates included in the model. Second, the relationships between disability and demographic variables were examined to identify variables with moderate associations (Pearson $r \ge 0.3$) to include as covariates in the model.

RESULTS

A total of 419 participants with 1,956 observations (time points of data) were included in the analyses. Statistically significant differences were found between the two groups in years of education, marital status, and working memory at wave 10 (Table 1). No variable was moderately associated with disability (age [r = 0.03], sex [r = 0.09], race [r = 0.10], ethnicity [r = 0.07], years of education [r = -0.19], marital status [r = 0.18], self-report memory [r = 0.18], recall memory [r = -0.20], working memory [r = -0.16], and BMI [r = 0.17]).

Generalized Linear Mixed Model

An interaction effect was found between time (waves) and group ($F_{4,4} = 3.52$; P = 0.01) after controlling for years of education, marital status, working memory, and wave 9 depressive symptoms. This result indicates that the change in disability differed by groups over time (Fig. 1).

Post Hoc Analyses Between Groups

We conducted post hoc tests for group differences from waves 8 to 12. Significant between-group differences were found in disability after the onset of DM at wave 10 ($t_{861.3} = -2.21$; P = 0.03) and wave 11 ($t_{829.6} = -2.53$; P = 0.01), but not at wave 12 ($t_{877.6} = -1.62$; P = 0.11). There was no significant

difference in disability between groups before the onset of DM at wave 8 ($t_{1,277} = -0.61$; P = 0.55) and wave 9 ($t_{1,275} = 0.56$; P = 0.58). Small to moderate effect sizes were found from waves 10 to 12 (d = 0.33-0.37), and negligible effect sizes were found at waves 8 and 9 (d = 0.13 and d = 0, respectively).

Within Groups

Among older adults with elevated depressive symptoms, post-DM diagnosis waves (10–12) had significantly more disability than pre-DM diagnosis wave 8 ([$t_{1,947} = -3.53$, P < 0.001; $t_{1,947} = -4.99$, P < 0.001; $t_{1,947} = -5.07$, P < 0.001]); and wave 9 ([$t_{1,947} = 4.21$, P < 0.001]); $t_{1,947} = 5.63$, P < 0.001; $t_{1,947} = 5.70$, P < 0.001]). Clinically overt disability was found after the diagnosis of DM (wave 11 mean disability score 1.19, wave 12 mean disability score 1.20) in those who had elevated depressive symptoms at the time of DM diagnosis (Table 2).

Among older adults with elevated depressive symptoms, no significant difference was found in disability between pre-DM diagnosis waves (8 and 9) ($t_{1,947}$ = 0.69; P = 0.49). There were no significant differences in disability among post-DM diagnosis waves (10 and 11 [$t_{1,947}$ = -1.70; P = 0.09], 10 and 12 [$t_{1,947}$ = 1.92; P = 0.05], 11 and 12 [$t_{1,947}$ = 0.31; P = 0.76]).

ADL and IADL Disability Between Groups

No between-group differences were found in ADL or IADL disability over time ($F_{4,4} = 2.08$ [P = 0.08], $F_{4,4} = 1.66$ [P = 0.16], respectively) after controlling for years of education, marital status, working memory, and wave 9 depressive symptoms. There were significant group differences in the percentages of participants who experienced difficulties with eating [$\chi^2_{(1)} = 4.36$; P = 0.04], getting in/out of bed [$\chi^2_{(1)} = 4.79$; P = 0.03], managing medication [$\chi^2_{(1)} = 5.99$; P =0.01], preparing meals [$\chi^2_{(1)} = 5.65$; P = 0.02] at wave 10 (Fig. 2).

The percentages of participants reporting difficulties with 10 ADL and IADL tasks were higher in those with elevated depressive symptoms (5.3–15%) than in those without elevated depressive symptoms (1.6–8.5%) at wave 10. Among those with elevated depressive

Characteristic	All	With elevated depressive symptoms	Without elevated depressive symptoms	t statistic or χ^2 statistic	P value
Participants, n (%)	419 (100)	113 (27)	306 (73)		
Age, mean (SD)	70.30 (8.62)	71.05 (8.52)	70.02 (8.65)	$t_{417} = -1.09$	0.28
Sex <i>, n</i> (%) Male Female	199 (47.5) 220 (52.5)	46 (40.7) 67 (59.3)	153 (50) 153 (50)	$\chi^2_{(1)} = 2.50$	0.11
Race, <i>n</i> (%) White Black Other	329 (87.1) 62 (14.8) 28 (6.7)	80 (70.8) 23 (20.4) 10 (8.8)	249 (81.4) 39 (12.7) 18 (5.9)	$\chi^2_{(2)} = 5.49$	0.06
Ethnicity, <i>n</i> (%) Hispanic Non-Hispanic	54 (12.9) 365 (87.1)	21 (18.6) 92 (81.4)	33 (10.8) 273 (89.2)	$\chi^2_{(1)} = 3.80$	0.05
Years of education, mean (SD)	12.48 (3.20)	11.85 (3.35)	12.71 (3.12)	$t_{416} = 2.46$	0.01*
Marital status, <i>n</i> (%) Married Not married	250 (59.7) 169 (40.3)	54 (47.8) 59 (52.2)	196 (64.1) 110 (35.9)	$\chi^2_{(1)} = 8.41$	<0.01*
Comorbidities, n (%) High blood pressure Cancer Lung disease Heart problems Stroke Arthritis Psychiatric condition	316 (73) 87 (20.8) 52 (12.4) 142 (33.9) 30 (7.2) 288 (68.7) 73 (17.4)	91 (80.5) 26 (23.0) 16 (12.4) 39 (34.5) 10 (8.8) 83 (73.5) 25 (22.1)	225 (73.5) 61 (19.9) 36 (11.8) 103 (33.7) 20 (6.6) 205 (67.0) 48 (15.7)	$\begin{array}{l} \chi^2_{(1)} = 1.82 \\ \chi^2_{(1)} = 0.31 \\ \chi^2_{(1)} = 0.24 \\ \chi^2_{(1)} < 0.01 \\ \chi^2_{(1)} = 0.35 \\ \chi^2_{(1)} = 1.32 \\ \chi^2_{(1)} = 1.95 \end{array}$	0.18 0.58 0.62 0.96 0.55 0.25 0.16
BMI (kg/m ²), mean (SD)	29.83 (6.01)	29.80 (5.91)	29.84 (6.05)	$t_{412} = 0.05$	0.96
Cognitive function, mean (SD) Self-report memory Recall [†] Working memory [†]	3.11 (0.94) 9.57 (3.44) 3.44 (1.70)	3.25 (0.95) 9.43 (3.46) 3.02 (1.87)	3.07 (0.94) 9.62 (3.44) 3.60 (1.61)	$t_{417} = -1.76$ $t_{417} = 0.49$ $t_{417} = 3.14$	0.08 0.63 0.02*
Depressive symptoms, mean (SD)	1.39 (1.89)	3.14 (2.10)	0.75 (1.31)	$t_{417} = -13.93$	<0.01*
Acquired disability, n (%)	102 (24.3)	39 (34.5)	63 (20.6)	$\chi^{2}_{(1)} = 7.95$	<0.01*

Table 1-Descriptive statistics in older adults with n	newly diagnosed DM at wave 10
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*P < 0.05. †Higher scores indicate better cognitive function.

symptoms, 1 in 7 older adults (15%) reported difficulties in dressing and shopping, and 1 in 10 older adults (10%) reported difficulties in walking and meal preparation (Fig. 2).

CONCLUSIONS

Among older adults with newly diagnosed DM, those with elevated depressive symptoms had a clinically relevant and faster disablement trajectory than those without elevated depressive symptoms. A disability score ≥ 1 is a threshold that suggests overt difficulties in performing ADL and IADL. The disability threshold was not crossed when disablement was examined across all the participants (n = 419) or in those with DM only (Table 2). However, clinically overt disability emerged soon, by 2 years (wave 11), and still presented at 4 years (wave 12) if elevated depressive symptoms were present at the time of DM diagnosis.

The different trajectories of disability between groups may be explained by the emergence of disability before clinically overt disability (27). Usually, older adults with the emergence of disability are found to adjust their daily tasks or spend more time to complete daily tasks (27). For example, older adults with new-onset DM may carry fewer items than previously while shopping. Another example is that older adults may take a longer time to prepare meals than previously. These changes, although subtle, potentially suggest the emergence of disability. The emergence of disability may soon shift to overt disability, which is the incapability to complete ADL or IADL independently. In this study, we found that older adults with new-onset DM showed signs of emerging disability. Furthermore, older adults with both DM and elevated depressive symptoms progressed to clinically overt disability within 2 years.

The current findings suggest that the group differences in disability were statistically reliable at waves 10 and 11 but not at wave 12. The differences in significance may be due to participant attrition from wave 10 to wave 12. The group with elevated depressive symptoms had a 23% attrition rate from wave 10 to wave 12, which was higher than the group without elevated depressive symptoms (16.6%). Those who dropped out might have experienced more disability, which may have contributed to the insignificant between-group differences observed at wave 12. Of note, the small to moderate effect sizes throughout the post-DM diagnosis waves (10-12) were detected. These early distinct differences may be the determinant of long-term disability and high health care costs. For example, Fried et al. (28) found that older adults with disabilities spent \$2,700 more per person on health care than those without disabilities.



Trajectory of disability, with and without elevated depressive symptoms

Figure 1—Trajectory of disability between groups.

In addition, older adults with both DM and depressive symptoms had 4.5 times more health expenditures to manage their disability than those with DM only (29).

Many possible mechanisms may explain why elevated depressive symptoms were associated with a faster disability trajectory (30). The literature indicates that older adults with depressive symptoms experience subtle changes in their daily activities. Possibly related to anhedonia and apathy, these older adults may develop sedentary behaviors, give up social activities and healthy lifestyle practices (e.g., adherence to medication management, healthy meal preparation) (31,32). More time spent being sedentary, socially isolated, and practicing unhealthy lifestyle behaviors is associated with an increased risk of incident disability among community-dwelling older adults (33). Elevated depressive symptoms also may be associated with biologic dysregulation (e.g., hormones, neurotransmitters) that leads to disability, especially when DM is newly diagnosed (34). Elevated depressive symptoms may coexist with declines in memory and executive function, further decreasing the ability to perform IADL (35), including medication management, meal preparation, and shopping. Another possibility is that older adults with elevated depressive symptoms may sense a greater degree of disability than they actually experience (30).

In the current study, the change in disability differed by groups over time. However, when we separated disability into ADL and IADL disabilities, no significant between-group differences were found, suggesting that elevated depressive symptoms may be associated with disability in the spectrum of daily activities from basic (e.g., ambulation, eating) to complex (e.g., shopping) rather than with a specific type of daily activity. This finding may contribute to elevated depressive symptoms being associated with slower gait speed and movements, causing difficulties in ambulation and dressing (36). Elevated depressive symptoms also may be associated with cognitive impairments that contribute to difficulties in shopping and meal preparation, although cognitive impairments may not always be the primary clinical manifestation of new-onset DM (37). These activities are self-management tasks critical to stabilizing DM disease courses (17). The inability to go shopping, prepare meals, walk, and dress may lead to poor nutrition, an inactive life, and poor skin care, which may potentially deteriorate DM disease control and create a vicious cycle toward long-term disability (38).

Among all the participants, one in four (24.3%) had disability. The risk of disability was higher when older adults had relapsing or remitting mood changes; one in three older adults (34.5%) acquired disability if they had elevated depressive symptoms. In addition, nearly 15% of older adults with elevated depressive symptoms reported difficulties in dressing and shopping, which matched the results from other studies that recruited older adults with longterm DM (13.5–31.5%) (39). This finding suggests that older adults with newonset DM and elevated depressive

Table 2- The level of disability at five waves									
	Wave 8	Wave 9	Wave 10	Wave 11	Wave 12				
Disability level	(2004–2006)	(2006–2008)	(2008–2010)	(2010–2012)	(2012–2014)				
ADL, mean (SD)									
All participants	0.25 (0.72)	0.26 (0.76)	0.31 (0.83)	0.39 (0.96)	0.42 (0.99)				
With elevated depressive symptoms	0.32 (0.81)	0.28 (0.82)	0.50 (1.05)	0.63 (1.22)	0.68 (1.29)				
Without elevated depressive symptoms	0.22 (0.68)	0.25 (0.73)	0.25 (0.72)	0.31 (0.83)	0.33 (0.85)				
IADL, mean (SD)									
All participants	0.15 (0.57)	0.17 (0.54)	0.27 (0.75)	0.30 (0.88)	0.32 (0.87)				
With elevated depressive symptoms	0.20 (0.53)	0.18 (0.50)	0.44 (0.99)	0.55 (1.22)	0.52 (1.08)				
Without elevated depressive symptoms	0.14 (0.59)	0.17 (0.55)	0.21 (0.63)	0.21 (0.70)	0.26 (0.78)				
ADL + IADL, mean (SD)									
All participants	0.40 (1.18)	0.43 (1.15)	0.59 (1.33)	0.69 (1.65)	0.74 (1.65)				
With elevated depressive symptoms	0.53 (1.20)	0.46 (1.14)	0.94 (1.72)	1.19 (2.16)	1.20 (2.21)				
Without elevated depressive symptoms	0.35 (1.17)	0.42 (1.15)	0.46 (1.13)	0.51 (1.38)	0.58 (1.38)				

Table 2—The level of disability at five waves

Values in boldface type suggest that there was an overt disability observed at waves 11 and 12 in older adults with elevated depressive symptoms.





symptoms may have an accelerated path to disability that older adults with longterm DM had already experienced. This suggests an indicated approach to disability prevention for older adults with newly diagnosed DM.

We acknowledge limitations in this study. Because of the nature of secondary data analysis, we included older adults who self-reported that they were diagnosed with DM since their last study interview. We do not know the exact dates of the DM diagnosis or specific times of diagnosis to follow-up interviews of depressive symptoms. Our disability measurement was self-reported and may be influenced by the perceptions of participants instead of objective measures. We did not have a measure of DM severity in the data set, especially fasting glucose or hemoglobin A_{1c}, which may be associated with comorbidity and further complicate the relationship between elevated depressive symptoms and disablement trajectory. Plausibly, the trajectory of disability between groups may be driven by demographic characteristics (e.g., race, ethnicity), cognition, or comorbidity. We controlled for years of education, marital status, working memory, and wave 9 depressive symptoms as covariates in our analyses, but no other variables met criteria for covariates.

This study had many strengths. First, we included five waves of data to examine a 10-year disablement trajectory in older adults with newly diagnosed DM. Often, the disablement trajectory is subtle and hard to identify within just a few years. These longitudinal data provide the opportunity to detect the transition of disability before and after DM diagnosis in older adults. Second, we found that elevated depressive symptoms were a determinant of steeper disablement in older adults with newly diagnosed DM. In this study, we conceptualized depressive symptoms as a relapsing and remitting syndrome in influencing health over time. We took a different approach to capture severity change in depressive symptoms, which is different from a traditional approach that assesses a categorical diagnosis. Third, the time points when disability emerged (2 years from new onset of DM) and remained (2-4 years from new onset of DM) also were captured through these longitudinal data, suggesting the need for early interventions for older adults with both new-onset DM and depression. Future interventions should take an indicated approach to disability prevention in older adults with newly diagnosed DM, especially for those with a change in depression severity during

the window before and after diagnosis of DM.

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