Journal of Diabetes and Its Complications 34 (2020) 107467

Contents lists available at ScienceDirect

Journal of Diabetes and Its Complications

journal homepage: WWW.JDCJOURNAL.COM

Changes in diabetes distress among people with type 2 diabetes during a risk screening programme for diabetic kidney disease – Longitudinal observations of the PRIORITY study

Lene Eide Joensen [a,*], Kristoffer Panduro Madsen [a], Marie Frimodt-Møller [a], Nete Tofte [a], Ingrid Willaing [a], Morten Lindhardt [a], Peter Rossing [a,b]

[a] Steno Diabetes Center Copenhagen, Niels Steensens Vej 2, 2820 Gentofte, Denmark
[b] Department of Clinical Medicine, University of Copenhagen, Blegdamsvej 3B, 2200 Copenhagen N, Denmark

ARTICLE INFO

Article history:
Received 3 July 2019
Received in revised form 4 October 2019
Accepted 5 October 2019
Available online 22 October 2019

Keywords:
Diabetes mellitus, type 2
Diabetes distress
Diabetic nephropathy
Risk screening

ABSTRACT

Aims: To investigate levels and changes in diabetes distress over the course of the PRIORITY (**P**roteomic prediction and **R**enin angiotensin aldosterone system **I**nhibition prevention **O**f early diabetic neph**R**opathy **I**n people with **TY**pe 2 diabetes and normoalbuminuria) randomised controlled trial of screening for diabetic kidney disease (DKD) risk among people with type 2 diabetes (T2D) at a specialist diabetes clinic in Denmark.
Methods: Of 436 trial participants with T2D, 216 were invited to complete the 17-item diabetes distress scale at the time of screening (T1, n = 180), immediately after receiving the screening results at 6–8 weeks (T2, n = 169), and at 12 months follow up (T3, n = 107). Linear mixed models were used to explore changes in diabetes distress.
Results: No significant changes in diabetes distress were observed between the time of screening, receiving results, and at 12 months. Changes in diabetes distress were not influenced by diabetes empowerment, sense of coherence, or perceived support for diabetes self-management.
Conclusions: In contrast to previous studies demonstrating that screening programmes can have negative psychological consequences, our findings indicate that participating in this screening programme for DKD does not influence emotional burden or physician-related distress among people with T2D.

1. Introduction

People with diabetes have increased mortality and morbidity. Diabetes-related complications include macrovascular complications such as cardiovascular disease and microvascular complications such as nephropathy, neuropathy, and retinopathy, which are associated with lower quality of life and high healthcare costs.[1] Identification and appropriate treatment of people with type 2 diabetes mellitus (T2D) at high risk of developing diabetes-related complications are core disease management activities.[2]

Identification of people at risk of diabetic kidney disease (DKD) typically occurs through screening for albuminuria and kidney function at routine visits when people are still without symptoms of DKD.[3] However, the urinary proteomics classifier CKD273 has been suggested as an improved marker for early identification of people at high risk of DKD compared to traditional methods.[4] The clinical multicentre intervention trial PRIORITY (**P**roteomic prediction and **R**enin angiotensin aldosterone system **I**nhibition prevention **O**f early diabetic neph**R**opathy **I**n people with **TY**pe 2 diabetes and normoalbuminuria) used this method to screen for future risk of DKD in people with T2D and normal kidney function.[5] Little is known about the effect of risk assessment for diabetes complications among people with T2D. Studies of psychological effects of screening often focus on reactions to screening results, rather than the effects of participating in a screening programme regardless of the results. Studies have shown that cancer screening programmes can have negative psychological consequences for participants, regardless of screening results.[6] However, other studies show that screening for melanoma, for example, does not worsen psychological well-being[7] and that screening for T2D does not cause increased anxiety levels.[8,9] A recent review including 22 studies concluded that psychological distress was low for participants in cancer screening programmes.[10] The psychological effects of screening for diabetes complications in people with existing disease may differ from the effects of screening for illness, such as cancer or T2D, among healthy people. But similarly, to the screening situation for cancer, screening for

* Corresponding author.
E-mail addresses: lene.eide.joensen@regionh.dk (L.E. Joensen), kristoffer.panduro.madsen@regionh.dk (K.P. Madsen), marie.frimodt-moeller@regionh.dk (M. Frimodt-Møller), nete.tofte@regionh.dk (N. Tofte), ingrid.willaing.tapager@regionh.dk (I. Willaing), morten.kofod.lindhardt@regionh.dk (M. Lindhardt), peter.rossing@regionh.dk (P. Rossing).

https://doi.org/10.1016/j.jdiacomp.2019.107467
1056-8727/

complications such as eye or kidney disease can reveal the complications at a stage where treatment is beneficial but where the individual has no symptoms of the complication. In addition, the psychological effect may depend on the specific screening context, such as information, guidance, and support provided during the screening process.

Psychosocial problems are highly prevalent in people with diabetes.[11] They include mental health disorders and psychological distress specifically related to living with diabetes.[12] Diabetes distress reflects an emotional response to diabetes and refers to worries, concerns, and fears experienced by people with diabetes. A recent meta-analysis including 55 studies with >35,000 participants demonstrated that 36% of people with T2D experience diabetes distress.[13] Diabetes distress is defined by the context of diabetes and is linked to specific stressors such as worrying about complications.[14] Therefore, it is likely that screening for DKD and presenting screening results to participants may increase diabetes distress. Furthermore, diabetes distress is associated with difficulties in diabetes self-management and high HbA1c.[15–17] Studies have found that people with a high level of diabetes empowerment have lower diabetes distress than do those with a low level of diabetes empowerment.[18] How people with diabetes view their life in terms of their sense of coherence can also influence their psychological well-being.[19] In addition, high levels of social support are associated with reduced psychosocial problems in people with T2D,[20,21] including low levels of diabetes distress.[22] Thus, it is possible that any changes in diabetes distress following screening for DKD are influenced by diabetes empowerment, sense of coherence, and social support.

The aim of this study was to investigate levels and changes in diabetes distress in individuals with T2D undergoing a screening programme for future risk of DKD and to examine whether diabetes empowerment, sense of coherence, and social support moderate these changes. A second aim was to examine possible subgroup differences in changes in diabetes distress between participants with low versus high DKD risk, based on CKD273 score.

2. Methods

2.1. Study design and participants

The sample is a subsample of the Danish PRIORITY study population. The purpose and design of the PRIORITY study have been described in detail elsewhere.[5,23] PRIORITY inclusion criteria were: T2D, age 18–75 years, preserved kidney function (estimated glomerular filtration rate [eGFR] > 45 ml/min/1.73 m^2) and normoalbuminuria (2 of 3 urine samples with albumin to creatinine ratio [UACR] < 30 mg/g). Participants in the Danish part of the PRIORITY study were recruited from an outpatient clinic at a specialist diabetes clinic and from general practices near the specialist clinic. In the PRIORITY study, participants were randomised to a treatment group, a placebo comparator group or an observational group based on their CKD273 risk score. The treatment group (high risk) received 25 mg Spironolactone once daily and standard care, the placebo group (high risk) received a placebo tablet and standard care, and the observational group (low risk) received only standard care. All participants were provided an extra consultation at the specialist diabetes clinic as part of the screening study. The present study investigates levels and changes in diabetes distress among all Danish participants across the study period, but does not explore the effect of the PRIORITY intervention due to a low number of trial participants (people with a high risk score).

The sub study began while the PRIORITY trial was under way; half of Danish PRIORITY participants had already been screened for DKD risk and were not eligible for recruitment. Thus, 216 of 436 participants in the Danish PRIORITY study population were asked to participate. Timepoint T1 consisted of a screening visit at which urine samples were collected for CKD273 analysis, and one of the study investigators informed potential participants about the CKD273 risk score and the course of the study. Potential participants were invited to participate. Written consent was obtained, and participants were asked to fill out a questionnaire. Following CKD273 analysis, participants were categorised as at high or low risk of DKD. Six to eight weeks after T1, an investigator communicated the individual risk category to all participants, regardless of DKD risk group, at a second visit (T2), allowing ample time for questions and discussion of potential concerns in relation to the screening result. In addition, before using any medication included in the study, participants were asked to complete the questionnaire again. Twelve months later, they were asked to complete the questionnaire for the final time at a follow-up visit (T3). The study was approved by the local ethical committee and monitored in accordance with Good Clinical Practice.[23]

2.2. Measures

The full Diabetes Distress Scale (DDS17) was administered to participants; however, for the purpose of this study, only the emotional burden (5 items) and physician-related distress (4 items) subscales were analysed. The emotional burden domain includes questions related to emotions such as “feeling that diabetes controls my life”. Furthermore, emotional burden includes the item “Feeling that I will end up with serious long-term complications, no matter what I do”, which was explored as a single item due to the study's focus on risk of complications. The physician-related distress domain was selected as an outcome measure to explore whether the screening programme affected the relationship with the health care professional. Physician-related distress includes, for example, “feeling that my doctor does not give me clear enough directions on how to manage my diabetes”. Possible scores on each item range from 1 (‘not a problem’) to 6 (‘a very serious problem’). The diabetes distress subscale scores were calculated by dividing the total domain score by the number of items in the domain, with scores ranging from 1 (no distress) to 6 (high distress). Scores ≥2 indicate moderate to high distress.

Diabetes empowerment was measured by the Diabetes Empowerment Scale-Short Form (DES-SF).[24] The DES-SF contains eight questions designed to assess psychosocial self-efficacy among people with diabetes. The total score was calculated as the average of the total sum of the eight items and ranged from 1 (low diabetes empowerment) to 5 (high diabetes empowerment). Sense of coherence (SOC) was measured using a 13-item questionnaire focusing on meaningfulness, comprehensibility, and manageability.[25] The total score was calculated as the average of the total sum of the scale items and ranged from 1 (low sense of coherence) to 7 (strong sense of coherence). Social support was measured by the DAWN Support for Diabetes Self-Management Profile (DSDSP).[26,27] It explored how supportive four potential support providers had been in helping the respondent manage diabetes over the past 12 months, with scores ranging from 1 to 12 (least to maximum support). Missing data on the DDS17, DES-SF, SOC, and DSDSP scales were imputed using individual mean imputation.[28] Four participants did not answer any item on the DSDSP scale at T1, and scores were not imputable. In addition to the questionnaires obtained at T1, T2, and T3, information on age, gender, diabetes duration, body mass index (BMI), haemoglobin A1c (HbA1c), systolic and diastolic blood pressure (BP), ischemic heart disease, history of stroke, and smoking status were obtained during a clinical interview at T2. UACR was measured between T1 and T2 and eGFR at T1.

2.3. Statistical methods

Study variables were examined with descriptive statistics. Histograms were used to examine distributions of key variables. Differences between PRIORITY participants who were invited and not invited to participate and differences between respondents and non-respondents at T1, T2, and T3 were explored using Chi-squared tests for categorical variables, Student's two-sided *t*-tests for continuous

normally distributed variables, and Mann-Whitney tests for continuous non-normally distributed variables.

Multivariate linear regression models were used to examine baseline associations between mean scores on the emotional burden and physician-related distress subscales, the single item on worry about future complications, and other study variables (patient characteristics and questionnaire data). Backward model selection was used to identify the best model fit.

Linear mixed-effects models (LMMs) using restricted maximum likelihood estimation were used to explore changes in diabetes distress over time. LMMs allow analysis of changes in the dependent variable based on the full range of data while taking into account that repeated measurements within the same individual are not independent.[29] Two models were constructed for each diabetes distress outcome variable of interest: 1) a crude model including timepoint adjusted for individual-specific intercepts and slopes and 2) an adjusted model that included baseline values of variables found to be significantly correlated with diabetes distress domains in the cross-sectional analyses as fixed effects alongside the intercept and timepoint. Interactions between timepoint and low/medium versus high levels of diabetes empowerment, sense of coherence and perceived support for diabetes self-management were subsequently included to test for between-group changes and effect modification. An unstructured covariance structure for the random parameters provided the best model fit. P values <0.05 were considered statistically significant. All analyses were performed in Stata 15.

3. Results

3.1. Sample characteristics and retention

Of 216 PRIORITY participants invited to participate in this sub study, 180 (83%) agreed and completed the questionnaire at T1. Significant differences existed between individuals enrolled in the PRIORITY trial who were invited to participate in this study and those who were not (Table 1). Individuals invited to participate had shorter mean diabetes duration and higher mean diastolic blood pressure, compared to those who were not invited, and more women and fewer people with high DKD risk were invited to participate. No differences were found in HbA1c, UACR, or eGFR. There were no significant differences between invited participants who completed the questionnaire at T1 (n = 180) and those who did not (n = 36), nor were there differences between respondents and non-respondents across the study period (results not shown). At T2 and T3, 169 and 107 respondents, respectively, completed the questionnaire. Attrition was 6% (n = 11) from T1 to T2 and 37% (n = 62) from T2 to T3. At T1, T2, and T3, five (3%), seven (4%) and one (1%) respondents, respectively, had single missing items on the emotional burden subscale that were imputed, and one (1%) respondent had four missing items at T1. For the physician-related distress subscale, four (2%), three (2%) and seven (4%) respondents respectively had one, two, and three missing items at T1 that were imputed. At T2, three (2%) respondents had three missing observations on the physician-related distress subscale, while, at T3, two (2%) and one (1%) respondent had one and three missing items, respectively. Excluding respondents with more than one missing scale item from the analysis did not significantly change the results.

Total scores on the emotional burden subscale, the physician-related distress subscale, and the item on worry about future complications were 1–4.6 (median = 1.6, IQR = 1.2–2.4), 1–4 (median = 1.4, IQR = 1.0–1.5) and 1–6 (median = 2.0, IQR = 1.0–3.0), respectively. The proportion of respondents with elevated levels (mean score ≥ 2) of emotional burden and physician-related distress was 39% (n = 70) and 16% (n = 28), respectively. With respect to worrying about future complications, 68% (n = 122) of respondents reported it was a moderate to very serious problem. The proportion of overall moderate to high distress (full DDS17) was 29% (n = 52).

3.2. Associations between diabetes distress scores and other study variables

Table 2 shows beta coefficients for cross-sectional baseline associations between mean diabetes distress scores and the study variables

Table 1
Characteristics of PRIORITY trial and substudy participants.

	PRIORITY trial participants (n = 436)	Not invited to participate in substudy (n = 220)	Invited to participate in substudy (n = 216)	P value of difference	Substudy respondents at T1 (n = 180)[a]
Age (years)	60.4 (9.4)	60.1 (9.3)	60.8 (9.5)	0.403	61.2 (9.4)
Women, n (%)	152 (34.9)	62 (28.2)	90 (41.7)	0.003	73 (40.6)
Diabetes duration (years)	11.7 (7.5)	12.7 (7.9)	10.6 (6.9)	0.003	10.3 (7.0)
BMI (kg/m^2)	30.6 (5.6)	30.2 (5.4)	31.0 (5.7)	0.095	31.0 (5.8)
HbA1c (mmol/mol)	57 (12)	58.1 (12)	56.1 (12)	0.094	56 (11)
Systolic BP (mmHg)	133.0 (11.9)	133.7 (11.5)	132.3 (12.3)	0.222	132.5 (12.2)
Diastolic BP (mmHg)	80.4 (9.4)	78.3 (9.2)	82.4 (9.3)	<0.001	82.4 (9.4)
eGFR	87.5 (16.2)	87.3 (15.6)	87.6 (16.8)	0.879	86.8 (16.1)
UACR (mg/g)	5.9 (3.7, 9.8)	5.8 (4.0, 8.5)	5.9 (3.8, 8.7)	0.017	6.0 (3.9, 8.6)
High risk for DKD, n (%)	64 (14.7)	41 (18.6)	23 (10.7)	0.018	20 (11.1)
Ischemic heart disease, n (%)	53 (12.2)	29 (13.2)	24 (11.1)	0.508	19 (10.6)
Stroke, n (%)	24 (5.5)	14 (6.4)	10 (4.6)	0.427	10 (5.6)
Smoking status, n (%)	–	–	–	0.183	–
Never smoker	216 (49.7)	100 (45.5)	116 (54.0)	–	97 (54.2)
Previous smoker	160 (36.8)	86 (39.1)	74 (34.4)	–	63 (35.2)
Smoker	59 (13.6)	34 (15.4)	25 (11.6)	–	19 (10.6)
Emotional burden	–	–	–	–	1.86 (0.8)
Physician-related distress	–	–	–	–	1.36 (0.6)
Worries about future complications	–	–	–	–	2.20 (1.1)
DES score	–	–	–	–	3.8 (0.7)
SOC score	–	–	–	–	4.9 (1.0)
DSDSP score	–	–	–	–	2.0 (0.7)

Data are given as mean (SD) or median (IQR) unless other is stated.
Note: Diabetes duration, HbA1c, blood pressure, eGFR, and smoking status each had one missing observation. Social support had four completely missing observations and was not imputable.
Abbreviations: BMI, body mass index; BP, blood pressure; DES, Diabetes Empowerment Scale; DKD, diabetic kidney disease; DSDSP, DAWN Support for Diabetes Self-Management Profile; SD, standard deviation; SOC, sense of coherence; UACR, urinary albumin to creatinine ratio.
[a] Respondents at T1 did not vary on any study variable from those who did not participate, and there were no differences between respondents and non-respondents at T1, T2, and T3.

Table 2
Associations between diabetes distress subscales and study variables at baseline.

Variable	Emotional burden	Physician-related distress	Worries about future complications
Age	−0.017* (0.006)	–	−0.025* (0.008)
Female gender	0.269* (0.111)	–	0.331* (0.156)
HbA1c, mmol/mol	0.011* (0.005)	–	0.015* (0.007)
DES score	–	−0.191* (0.065)	−0.284* (0.769)
SOC score	−0.277** (0.059)	–	–
Constant	3.278** (0.534)	2.080** (0.250)	3.490** (0.769)
Adjusted r-squared	0.227	0.040	0.133
Observations, n	179	180	179

Note: Standard errors are in parentheses.
* $P < 0.05$.
** $P < 0.01$.

as predicted in backward selected multiple linear regression models. When adjusting for the other variables in the model, lower age, lower SOC, being female, and higher HbA1c were associated with higher emotional burden. Only higher DES was found to be associated with lower physician-related distress. Experiencing worries about future complications was associated with lower age, lower DES, being female and higher HbA1c.

3.3. Longitudinal analysis

Table 3 shows mean DDS and subscale scores at T2 and T3 relative to T1, as estimated by the LMMs. No significant changes were found on mean emotional burden and physician-related distress scores or the single item on worry about future complications at T2 and T3 compared to T1 for crude and adjusted models. Adjusting for combinations of age, gender, HbA1c, DES, and SOC as defined separately for each outcome only had a small effect on the results. No significant changes in any of the diabetes distress outcome variables were found at T2 and T3, relative to T1, when stratifying the study sample on low/medium versus high levels of DES, SOC, and DSDSP. In addition, there were no significant differences in between-group changes (results not shown). Due to the low number of respondents with high risk of DKD in this sub study (n = 20 [T1], n = 20 [T2], n = 9 [T3]) and a risk of selection bias compared to the total PRIORITY study population, stratified analyses were not performed on diabetes distress changes between low and high DKD risk groups as well as intervention vs. placebo groups.

4. Discussion

The rationale behind screening for diabetes complications in people with T2D is to identify individuals at risk, usually before there are any symptoms due to the complication and provide appropriate treatment to optimise physical health and quality of life. Annual screening for most complications is recommended in most diabetes care guidelines.[30] A potential risk related to screening for complications is to induce and/or increase diabetes distress, including worry about diabetes complications. Overall, the results of this study showed that screening for DKD did not induce or increase diabetes distress in this particular context.

A recent review showed that risk perception of diabetes-related complications in people with T2D is often characterised by low awareness of risk.[31] Thus, it is likely that participation in this screening study may have increased participants' awareness of the risk of complications and related concerns. Other studies have reported unrealistic pessimism and overestimation of personal risk of complications among people with T2D.[31] If participants in this study experienced unrealistic concern at the beginning of the screening programme, the ample time given to discussing accurate personal risks of complications postscreening might have decreased worry about complications. The recent meta-analysis of the prevalence of overall diabetes distress among people with T2D found that 38% experience diabetes distress; studies using the DDS17 found an average prevalence of diabetes distress of 42%.[13] One of the studies in the meta-analysis also reported 63% prevalence of emotional burden and 25% prevalence of physician distress. In contrast, the prevalence we observed at T1 was lower at 29% for overall distress, 39% for emotional burden, and 16% for physician distress. Although participants' distress level was low, they did not become more

Table 3
Predicted mean diabetes distress scores at T2 and T3, relative to T1.

	T1 (n = 180)	Mean change, T1 to T2 (n = 169)	Mean change, T1 to T3 (n = 107)
Emotional burden			
Crude	1.86 (0.06)	−0.02 (0.04)	−0.02 (0.06)
	[1.74–1.99]	[−0.10–0.06]	[−0.14–0.10]
Adjusted[a]	1.85 (0.05)	−0.002 (0.04)	0.006 (0.06)
	[1.75–1.96]	[−0.08–0.08]	[−0.11–0.13]
Physician-related distress			
Crude	1.36 (0.04)	−0.04 (0.04)	−0.11 (0.06)
	[1.28–1.45]	[−0.11–0.03]	[−0.23–0.01]
Adjusted[b]	1.35 (0.44)	−0.02 (0.04)	−0.09 (0.06)
	[1.26–1.44]	[−0.09–0.05]	[−0.21–0.03]
Worries about future complications			
Crude	2.17 (0.08)	−0.11 (0.07)	−0.05 (0.09)
	[2.00–2.33]	[−0.25–0.04]	[−0.22–0.13]
Adjusted[c]	2.16 (0.08)	−0.10 (0.07)	−0.02 (0.09)
	[2.01–2.34]	[−0.24–0.05]	[−0.20–0.16]

Note: Standard errors are in parentheses; 95% confidence intervals are in brackets. Coefficients for fixed effect covariates not shown.
[a] Adjusted for age, gender, HbA1c, and SOC.
[b] Adjusted for DES.
[c] Adjusted for age, HbA1c, and SOC.

worried after participation in the screening study. The information and support provided by the health care professionals during the screening programme may have prevented increases in distress.

Consistent with previous studies, younger age, being female, higher HbA1c, and lower DES scores were found to be strongly associated with higher diabetes distress in the cross-sectional analyses.[18,32] However, the meta-analysis noted above demonstrated an association only between higher distress and being female; younger age and having a high HbA1c were not related to distress.[13] We also found an association between SOC and emotional burden that has not been previously reported and indicates an association between experienced sense of coherence and emotional distress. Despite the findings of our cross-sectional analysis, age, gender, HbA1c, diabetes empowerment, sense of coherence, and social support did not substantially influence the longitudinal results. Future studies should investigate factors that facilitate maintaining low levels of distress when assessing and discussing risk with people with diabetes.

Strengths of our study include the fact that validated scales were used to measure diabetes distress, diabetes empowerment, sense of coherence, and social support, a high response rate and a thorough description of participant characteristics. Some baseline characteristics were self-reported; however, they were monitored in accordance with Good Clinical Practice.[23] Although there were no differences in measured characteristics between respondents and non-respondents at T2 and T3, those invited to participate differed from those who were not invited to participate. People who were invited to participate in our study had shorter mean diabetes duration and higher mean diastolic blood pressure and included more women and fewer people with high risk of DKD. This might reflect the fact that participants were initially recruited from the outpatient clinic at the specialist diabetes clinic. After the diabetes distress study was under way, participants with less complicated diabetes from general practices near the specialist clinic were also recruited. Few study participants were at high risk of DKD, which precluded the possibility of analysing differences in changes in diabetes distress among people at high versus low risk of DKD. Similarly, the overall diabetes distress level in the study population was relatively low. Finally, this study took place at a single diabetes specialist clinic, and the results may not be generalisable to other types of settings or other types of risk screening consultations.

Future studies related to how screening processes affect people with T2D would benefit from larger sample sizes that include more people at high risk of DKD or other complications, such as retinopathy. Future studies could also benefit from investigating the effect of screening of diabetes complications in populations with higher levels of diabetes distress, as well as populations with a larger variation in diabetes distress levels. This study was conducted in a trial setting with time allocated by dedicated staff to inform participants about screening and results, which may assist in maintaining low initial diabetes distress levels. Screening as part of routine clinical activities with less dedicated time might have a different effect, such as an increased diabetes distress, and should be investigated in future studies.

4.1. Conclusions

This study suggests that this way of screening for diabetic kidney disease does not negatively influence emotional or physician-related distress among people with T2D. Future studies could benefit from investigating screening of complications in larger populations with greater variation in diabetes distress as well as screening for other diabetes related complications. Comparing distress changes between people who do and do not participate in a complications screening study would also contribute to knowledge about possible effects of screening for diabetes complications.

Funding

This work was supported by the European Union Seventh Framework Programme (FP7/2007–2013) [grant number 279277].

Declaration of competing interest

M.L. has equity interest in Novo Nordisk A/S. P.R. reports having given lectures for Astra Zeneca, Bayer, Boehringer Ingelheim, MSD and Mundi Pharma, and has served as a consultant for AbbVie, Astra Zeneca, Bayer, Eli Lilly, Boehringer Ingelheim, Astellas, Janssen and Novo Nordisk, with all fees given to the Steno Diabetes Centre Copenhagen, and has equity interest in Novo Nordisk. LJ, KPM, NT, MFM and IW have no competing interests to declare.

Acknowledgements

The authors gratefully acknowledge all participants in the study. We would also like to thank sub-investigators, laboratory technicians and study nurses for their valuable contribution.

References

1. World Health Organization. *Global report on diabetes*. Geneva, Switzerland: WHO. 2016.
2. Inzucchi SE, Bergenstal RM, Buse JB, et al. Management of hyperglycemia in type 2 diabetes: a patient-centered approach: position statement of the american diabetes association (ADA) and the european association for the study of diabetes (EASD). Diabetes Care 2012;35:1364-79. https://doi.org/10.2337/dc12-0413.
3. Parving HH, Persson F, Rossing P. Microalbuminuria: a parameter that has changed diabetes care. Diabetes Res Clin Pract 2015;107:1-8. https://doi.org/10.1016/j.diabres.2014.10.014.
4. Lindhardt M, Persson F, Zurbig P, et al. Urinary proteomics predict onset of microalbuminuria in normoalbuminuric type 2 diabetic patients, a sub-study of the DIRECT-Protect 2 study. Nephrol Dial Transplant 2017;32:1866-73. https://doi.org/10.1093/ndt/gfw292.
5. Lindhardt M, Persson F, Currie G, et al. Proteomic prediction and renin angiotensin aldosterone system inhibition prevention of early diabetic nephropathy in type 2 diabetic patients with normoalbuminuria (PRIORITY): essential study design and rationale of a randomised clinical multicentre trial. BMJ Open 2016;6, e010310. https://doi.org/10.1136/bmjopen-2015-010310.
6. Wardle J, Pope R. The psychological costs of screening for cancer. J Psychosom Res 1992;36:609-24.
7. Risica PM, Matthews NH, Dionne L, et al. Psychosocial consequences of skin cancer screening. Prev Med Rep 2018;10:310-6. https://doi.org/10.1016/j.pmedr.2018.04.011.
8. Skinner T, Davies M, Farooqit AM, Jarvis J, Tringham JR, Khunti K. Diabetes screening anxiety and beliefs. Diabet Med 2005;22:1497-502. https://doi.org/10.1111/j.1464-5491.2005.01680.x.
9. Eborall HC, Griffin SJ, Prevost AT, Kinmonth AL, French DP, Sutton S. Psychological impact of screening for type 2 diabetes: controlled trial and comparative study embedded in the ADDITION (Cambridge) randomised controlled trial. BMJ 2007;335:486. https://doi.org/10.1136/bmj.39303.723449.55.
10. Chad-Friedman E, Coleman S, Traeger LN, et al. Psychological distress associated with cancer screening: a systematic review. Cancer 2017;123:3882-94. https://doi.org/10.1002/cncr.30904.
11. Peyrot M, Rubin RR, Lauritzen T, Snoek FJ, Matthews DR, Skovlund SE. Psychosocial problems and barriers to improved diabetes management: results of the cross-cational diabetes attitudes, wishes and needs (DAWN) study. Diabet Med 2005;22:1379-85. https://doi.org/10.1111/j.1464-5491.2005.01644.x.
12. Egede LE, Dismuke CE. Serious psychological distress and diabetes: a review of the literature. Curr Psychiatry Rep 2012;14:15-22. https://doi.org/10.1007/s11920-011-0240-0.
13. Perrin NE, Davies MJ, Robertson N, Snoek FJ, Khunti K. The prevalence of diabetes-specific emotional distress in people with type 2 diabetes: a systematic review and meta-analysis. Diabet Med 2017;34:1508-20. https://doi.org/10.1111/dme.13448.
14. Fisher L, Gonzalez JS, Polonsky WH. The confusing tale of depression and distress in patients with diabetes: a call for greater clarity and precision. Diabet Med 2014;31:764-72. https://doi.org/10.1111/dme.12428.
15. Aikens JE. Prospective associations between emotional distress and poor outcomes in type 2 diabetes. Diabetes Care 2012;35:2472-8. https://doi.org/10.2337/dc12-0181.
16. Fisher L, Mullan JT, Arean P, Glasgow RE, Hessler D, Masharani U. Diabetes distress but not clinical depression or depressive symptoms is associated with glycemic control in both cross-sectional and longitudinal analyses. Diabetes Care 2010;33:23-8. https://doi.org/10.2337/dc09-1238.
17. Strandberg RB, Graue M, Wentzel-Larsen T, Peyrot M, Rokne B. Relationships of diabetes-specific emotional distress, depression, anxiety, and overall well-being with HbA1c in adult persons with type 1 diabetes. J Psychosom Res 2014;77:174-9. https://doi.org/10.1016/j.jpsychores.2014.06.015.
18. Wang R, Wu L, Hsu H. A path model of health-related quality of life in type 2 diabetic patients: a cross-sectional study in Taiwan. J Adv Nurs 2011;67:2658-67. https://doi.org/10.1111/j.1365-2648.2011.05701.x.

19. Cohen M, Kanter Y. Relation between sense of coherence and glycemic control in type 1 and type 2 diabetes. Behav Med 2004;29:175-83. https://doi.org/10.3200/BMED.29.4.175-185.
20. Strom JL, Egede LE. The impact of social support on outcomes in adult patients with type 2 diabetes: a systematic review. Curr Diab Rep 2012;12:769-81. https://doi.org/10.1007/s11892-012-0317-0.
21. Rogvi S, Tapager I, Almdal TP, Schiotz ML, Willaing I. Patient factors and glycaemic control—associations and explanatory power. Diabet Med 2012;29:e382-9. https://doi.org/10.1111/j.1464-5491.2012.03703.x.
22. Baek RN, Tanenbaum ML, Gonzalez JS. Diabetes burden and diabetes distress: the buffering effect of social support. Ann Behav Med 2014;48:145-55. https://doi.org/10.1007/s12160-013-9585-4.
23. Tofte N, Lindhardt M, Adamova K, et al. Characteristics of high- and low-risk individuals in the PRIORITY study: urinary proteomics and mineralocorticoid receptor antagonism for prevention of diabetic nephropathy in type 2 diabetes. Diabet Med 2018. https://doi.org/10.1111/dme.13669.
24. Anderson RM, Fitzgerald JT, Gruppen LD, Funnell MM, Oh MS. The diabetes empowerment scale-short form (DES-SF). Diabetes Care 2003;26:1641-2. https://doi.org/10.2337/diacare.26.5.1641-a.
25. Antonovsky A. *Appendix: the sense of coherence questionnaire. Unraveling the mystery of health: how people manage stress and stay well. 1 ed.* San Francisco: Jossey-Bass. 1987:189-95.
26. Nicolucci A, Kovacs Burns K, Holt RI, et al. Diabetes attitudes, wishes and needs second study (DAWN2): cross-national benchmarking of diabetes-related psychosocial outcomes for people with diabetes. Diabet Med 2013;30:767-77. https://doi.org/10.1111/dme.12245.
27. Peyrot M, Burns KK, Davies M, et al. Diabetes attitudes wishes and needs 2 (DAWN2): a multinational, multi-stakeholder study of psychosocial issues in diabetes and person-centred diabetes care. Diabetes Res Clin Pract 2013;99:174-84. https://doi.org/10.1016/j.diabres.2012.11.016.
28. Shrive FM, Stuart H, Quan H, Ghali WA. Dealing with missing data in a multi-question depression scale: a comparison of imputation methods. BMC Med Res Methodol 2006;6. https://doi.org/10.1186/1471-2288-6-57.
29. West BT, Welch KB, Gałecki AT, Gillespie BW. *Linear mixed models: a practical guide using statistical software. 2nd ed.* Boca Raton: CRC Press. 2015.
30. American Diabetes Association. Standards of medical care in diabetes-2019. Diabetes Care 2019;42.
31. Rouyard T, Kent S, Baskerville R, Leal J, Gray A. Perceptions of risks for diabetes-related complications in type 2 diabetes populations: a systematic review. Diabet Med 2017;34:467-77. https://doi.org/10.1111/dme.13285.
32. Fisher L, Skaff MM, Mullan JT, Arean P, Glasgow R, Masharani U. A longitudinal study of affective and anxiety disorders, depressive affect and diabetes distress in adults with type 2 diabetes. Diabet Med 2008;25:1096-101. https://doi.org/10.1111/j.1464-5491.2008.02533.x.