More work is needed to better understand diabetes distress as a predictor of all-cause mortality in type 2 diabetes

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Abbreviation

PAID Problem Areas in Diabetes

To the Editor: With interest, we read a recently published article in *Diabetologia*, by Hayashino et al, which focused on the association between diabetes distress and all-cause mortality in a prospective cohort study among 3305 Japanese individuals with type 2 diabetes [1]. Diabetes distress and all-cause mortality were measured once a year during the median follow-up period of 6.1 years. Interestingly, Hayashino et al found a significant positive association between high baseline diabetes distress and all-cause mortality (HR 1.56 [95% CI 1.17, 2.08]; $p = 0.002$) in the individuals with type 2 diabetes (after controlling for possible confounders) compared with those without diabetes distress. We believe that several aspects of this interesting paper need further discussion.

The authors conducted several subgroup analyses, investigating whether the association between baseline diabetes distress and all-cause mortality was different for men vs women, participants with different HbA_{1c} levels, different age groups or different diabetes therapy. The association between high baseline diabetes distress (measured using the Problem Areas in Diabetes [PAID] questionnaire) and higher all-cause mortality was found in men (HR 1.76 [95% CI 1.26, 2.46]) but not in women (HR 1.09 [95% CI 0.60, 2.00]), with

a significant interaction between diabetes distress and sex ($p = 0.0336$) [1].

This raises the question: why did a high level of diabetes distress predict mortality in the male participants but not in the female participants with diabetes? The final Cox proportional hazards models in the whole sample were adjusted for several potential confounders (age, sex, BMI, HbA_{1c}, types of diabetes therapy, urinary albumin/creatinine ratio, history of any diabetes retinopathy, symptomatic diabetic neuropathy and past medical history [acute myocardial infarction, chronic stable angina, peripheral artery disease, leg ulceration, ischaemic stroke and haemorrhagic stroke]) [1]. Yet, in order to understand why the association was different for men and women, it would be relevant to provide data on socio-demographic and clinical characteristics for both sexes. In addition, information regarding the mortality rates for men and women (separately) is not reported [1], while this is needed to interpret the results.

Furthermore, Hayashino et al measured diabetes distress using the total 20-item scale of PAID. They used a Japanese translation of PAID, reporting that this has shown good consistency and validity [1]. However, earlier research has shown that the sources of diabetes distress can be regarded as a multidimensional construct. In a study in Dutch and American individuals with diabetes, in which the cross-cultural validity of PAID was assessed, the latent structure of the 20-item PAID was best described with a 4-factor structure [2]. Four subscales are frequently used for PAID: emotional burden, physician-related distress, regimen-related distress and diabetes-related interpersonal distress [2]. The validation study for the Japanese translation of PAID is written in Japanese [3] and it is unclear whether the factor structure has been investigated. Repeating the original analyses from Hayashino et al using the subscales of PAID instead of the total score might lead to much more detailed insight into the associations

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between different forms of diabetes distress and all-cause mortality. For example, it may help to reveal the elements of diabetes distress that contribute to increased mortality rates, and whether elevated blood glucose levels or hypoglycaemic events play a role. A more specific focus on the PAID subscales might also give us a better understanding of potential mechanisms underlying the association between diabetes distress and all-cause mortality.

Finally, we respectfully wish to disagree with one statement by Hayashino et al in their discussion of the limitations of the study. The authors state that, despite the fact that they have not adjusted for depression, they do not expect this to influence their results as they highlight depression and diabetes distress as two different constructs. Even though we agree that depression and diabetes distress are two different constructs, it is clear that both constructs are also largely overlapping [4]. Items of PAID with considerable resemblance with some of the symptoms of depression include: ‘feeling depressed when you think about living with diabetes?’, ‘not knowing if your mood or feelings are related to your diabetes?’ and ‘feeling that diabetes is taking up too much of your mental and physical energy every day?’ [4]. Recent papers have highlighted the importance of measuring both diabetes distress and depression constructs to create a comprehensive picture [5, 6]. Furthermore, a systematic review and meta-analysis by van Dooren et al concluded that depression is associated with an almost 1.5-fold increased risk of mortality in individuals with diabetes, which illustrates why inclusion of depression in the original analyses by Hayashino et al seems relevant [7].

Duality of interest The authors declare that there is no duality of interest associated with the manuscript.

Contribution statement Both authors were responsible for drafting the article and revising it critically for important intellectual content. Furthermore, both authors approved the version to be published.

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