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Incremental predictive value of screening for anxiety and depression beyond current type 2 diabetes risk models: a prospective cohort study

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ABSTRACT

Objectives We sought to determine whether screening for anxiety and depression, an emerging risk factor for type 2 diabetes (T2D), adds clinically meaningful information beyond current T2D risk assessment tools.

Design Prospective cohort.

Participants and setting The 45 and Up Study is a large-scale prospective cohort of men and women aged 45 years and over, randomly sampled from the general population of New South Wales, Australia. 51 588 participants without self-reported diabetes at baseline (2006–2009) were followed up for approximately 3 years (2010).

Methods T2D status was determined by self-reported doctor who diagnosed diabetes after the age of 30 years, and/or current use of metformin. Current symptoms of anxiety and/or depression were measured by the 10-item Kessler Psychological Distress Scale (K10). We determined the optimal cut-off point for K10 for predicting T2D using Tjur's R^2 and tested risk models with and without the K10 using logistic regression. We assessed performance measures for the incremental value of the K10 using the area under the receiver operating characteristic (AROC), net reclassification improvement (NRI) and net benefit (NB) decision analytics with sensitivity analyses.

Results T2D developed in 1076 individuals (52.4% men). A K10 score of ≥19 (prevalence 8.97%), adjusted for age and gender, was optimal for predicting incident T2D (sensitivity 77%, specificity 53% and positive predictive value 3%; OR 1.70 (95% CI 1.41 to 2.03, P<0.001). K10 score predicted incident T2D independent of current risk models, but did not improve corresponding AROC, NRI and NB statistics. Sensitivity analyses showed that this was partially explained by the baseline model and the small effect size of the K10 that was similar compared with other risk factors.

Conclusions Anxiety and depressing screening with the K10 adds no meaningful incremental value in addition to current T2D risk assessments. The clinical importance of anxiety and depression screening in preventing T2D requires ongoing consideration.

Strengths and limitations of this study

► We considered various approaches beyond statistical analyses to assess the incremental predictive value of screening for anxiety and depression to current type 2 diabetes (T2D) risk models.
► We determined the optimal cut-off point on the K10 for predicting T2D risk.
► Other strengths of this study include the recruitment of a large (over 250 000 participants) population-based sample at baseline, and the high (over 60%) response rate achieved in the subsample at follow-up.
► Study weaknesses include the low incidence of T2D observed in the cohort, reliance on self-report measures, low (less than 18%) response rate achieved at baseline, residual confounding and misclassification of variables potentially resulting in bias.

INTRODUCTION

Type 2 diabetes (T2D) is the most common type of diabetes and accounts for at least 90% of all cases.[1] The Global Burden of Disease Study ranked diabetes the 14th leading cause of global disease burden in 2010, moving up several places since 1990.[2] This trend is likely to continue increasing in coming decades since it is estimated that over 415 million people worldwide have diabetes, and by 2040 this figure is projected to rise to 642 million.[1] Effective prevention of T2D is urgently needed in high-income countries, where healthcare expenditure for diabetes is among the highest in the world,[1] to realise significant population health and economic benefits.[3]

People with diagnosed T2D are likely to have progressed from an intermediate stage of hyperglycaemia called 'prediabetes'. Prediabetes is defined as impaired fasting glucose and/or impaired glucose tolerance.[4] It is estimated that the prevalence of pre-diabetes may have reached 20%–30% in high-income countries such as Australia and the USA.[5 6] Hyperglycaemia and consequent progression to T2D is partially explained by sociodemographics[7] as well as obesity and lifestyle risk factors.[8–11] Thus, diabetes prevention

programmes targeting high-risk individuals could effectively delay their progression from prediabetes to diagnosed T2D.

Indeed, national[12] and international[11] guidelines recommend lifestyle intervention that focuses on achieving a healthy body weight for the primary prevention of T2D, based on large randomised controlled trials (RCTs) in people with prediabetes.[13] However, diabetes is a chronic physical health condition that is often comorbid with clinically relevant symptoms of depression and anxiety.[14–16] Comorbid mental disorders worsen the self-care,[17] health[18–20] and economic burden of diabetes,[21] and predict non-completion of exercise-based intervention.[22 23] Similarly, depression, anxiety and eating disorders are often present in people with diabetes and obesity (40%–70%),[24–28] which adversely affects weight loss,[29–31] sleep quality,[32] health-related quality of life and health service use.[33] Therefore, people with depression and anxiety present with barriers to weight loss and sustainable healthy lifestyle changes (especially diet and exercise behaviours); this suggests that preventing T2D in this high-risk population group would be challenging.

Observational studies show that clinically significant depression (defined by diagnostic criteria or elevated number and/or severity of depressive symptoms) is consistently associated with a twofold increased risk of diabetes.[34–36] More recently, we showed that having a current depressive and/or anxiety disorder more than doubles the risk of developing diabetes over 2 years in a large cohort study, the Netherlands Study of Depression and Anxiety.[37] Thus, having current symptoms of anxiety and/or depression could be a novel risk factor for T2D in addition to being a major barrier to achieving sustained healthy lifestyle changes (especially diet and exercise behaviours).

Effective prevention of T2D requires early identification of high-risk individuals who might benefit from targeted intervention.[38] There is evidence suggesting that screening for T2D risk factors is cost-effective in high-risk individuals and with appropriate intervention.[39] There are several diabetes risk models or scoring systems (often called 'risk assessment tools') with potential adaptation for use in routine clinical practice.[40] Variants of these T2D risk tests are currently used in national diabetes prevention programmes worldwide, and typically include questions on demographics (age, gender, ethnicity), medical history (self and family), body weight and waist circumference, lifestyle (physical inactivity, diet) and pathology results (eg, glucose, triglycerides). However, these diabetes risk models may need to be updated as novel risk factors have since emerged. Therefore, the aim of this study was to determine whether screening for anxiety and/or depression adds clinically meaningful information beyond current T2D risk models, to inform guidelines, consumers and clinical practice.

METHODS

Study design and setting

The 45 and Up Study is a large prospective cohort study of men and women aged 45 years and older from the general population of New South Wales (NSW), Australia.[41] Participants were randomly sampled from the Medicare Australia enrolment database held by the Department for Human Services. Eligible individuals were invited to participate by mail, which included participant information, study questionnaire, consent form and a reply paid envelope. Recruitment into the 45 and Up Study was from 2006 through 2009, and had an overall response rate of 18%, comprising approximately 11% of target population. Although the response rate was low and participants from favourable socioeconomic groups (more people in the highest household income group) were likely to enrol, previous work has shown that findings based on internal comparisons for estimates of exposure-outcome relationships, such as ORs, are generalisable and comparable to those derived from the NSW Population Health Survey.[42] Also, the 45 and Up cohort was generally healthier: the prevalence of smoking, high/very high psychological distress, ever diagnosed with hypertension, diabetes and asthma was lower than participants in the NSW Population Health Survey.

The Social, Economic and Environmental Factors (SEEF) study was conducted in 2010 as the first follow-up of a subsample of the 45 and Up Study. The SEEF questionnaire, which extended the original 45 and Up Study questionnaire, was distributed to the first 100 000 of the 45 and Up Study participants, of whom 60 404 returned completed questionnaires yielding a response rate of 60.4%. After excluding baseline participants with known diabetes (n=4653), and incomplete data for one or more of the following variables: body mass index (BMI; n=3395), K10 score (n=1343) and country of birth (n=575), the final cohort sample studied consisted of 51 588 participants.

Primary endpoint

Diabetes at baseline and follow-up was defined by self-reported medically diagnosed diabetes, and use of metformin (diabex, diaformin) in the baseline and follow-up questionnaire.[43]

Predictor variables

As done previously,[38] we selected predictor variables from risk models that could be used in routine clinical practice including the Australian type 2 diabetes risk assessment tool (AUSDRISK),[44] Atherosclerosis Risk in Communities,[45] Cambridge risk score,[46] Finnish Diabetes Risk Score (FINDRISC),[47] Framingham Offspring Study,[48] San Antonio Heart Study[49] and QDScore.[50] All risk factor variables were collected through a self-administered questionnaire from the 45 and Up Study Baseline Questionnaire.[51] Risk factors included age, gender and country of birth (other vs Australian born); family history of diabetes (for blood relatives only); current medications identified for high blood pressure (Avapro,

Table 1 Baseline characteristics of participants in the SEEF subsample of the 45 and Up study cohort by T2D status at follow-up, including crude incidence and corresponding unadjusted ORs

	No T2D (n=49859)	Incident T2D (n=1067)	% with T2D	Unadjusted OR (95% CI)
Age (years)				
45–54	17387	241	1.37	1
55–64	16518	359	2.13	1.49 (1.26 to 1.76)
65 and over	17047	492	2.8	2.13 (1.80 to 2.52)
Gender				
Female	28181	521	1.81	1
Male	22771	571	2.45	1.27 (1.12 to 1.44)
Australian born				
Yes	39627	832	2.19	1
No	10885	244	2.05	1.12 (0.96 to 1.29)
Family history of diabetes (blood relatives only)				
No	40806	747	1.80	1
Yes	10146	345	3.29	1.83 (1.60 to 2.09)
Currently taking antihypertensive medications				
No	40765	729	1.76	1
Yes	10187	363	3.44	1.47 (1.28 to 1.68)
Current smoker				
No	48171	1013	2.05	1
Yes	2781	79	2.76	1.61 (1.25 to 2.03)
Insufficient physical activity				
No (≥150 min/week)	42669	861	1.97	1
Yes (<150 min/week)	8283	231	2.71	0.85 (0.74 to 1.00)
Usually eat vegetables or fruit serves daily				
No	19742	447	2.21	1
Yes	31210	645	2.02	0.98 (0.86 to 1.12)
Body mass index class (kg/m^2)				
Underweight (<18.50)	660	9	1.34	1.18 (0.56 to 2.18)
Healthy weight (18.50–24.99)	20896	229	1.11	1
Overweight (25.00–29.99)	20243	421	2.03	1.70 (1.45 to 2.01)
Obese (≥30.00)	9153	427	4.45	3.80 (3.22 to 4.50)
Psychological distress				
No (K10 score<19)	46411	951	3.01	1
Yes (K10 score≥19)	4541	141	2.01	1.48 (1.22 to 1.78)

SEEF, Social, Economic and Environmental Factors; T2D, type 2 diabetes

Karvea, Coversyl, Coversyl Plus, Micardis, Norvasc, Tritace); current regular smoker; insufficient daily serves of vegetables or fruit (none) and physical inactivity (less than 150 min in last week); and overweight and obesity based on BMI computed as weight in kilograms divided by height in metres squared. Standard international cut-off points were used to define underweight (BMI<18.50 kg/m^2), healthy weight (BMI 18.50–24.99 kg/m^2), overweight (BMI 25.00–29.99 kg/m^2) and obesity (BMI≥30.00 kg/m^2) categories.

Current symptoms of anxiety and depression were measured with the 10-item Kessler Psychological Distress Scale (K10), which was developed to monitor population prevalence and trends in non-specific psychological distress.[52] The K10 has been shown to accurately predict probable current anxiety and affective disorders according to the Composite International Diagnostic Interview, which corresponds to definitions and criteria of the Diagnostic and Statistical Manual of Mental Disorders

Table 2 Beta coefficients for risk factors from two logistic regression models, without (model 1) and with (model 2) the K10 binary variable

Variables (exposure category)	Estimate (95% CI)
Model 1: without K10	
Age (55–65 years)	0.38 (0.20 to 0.54)
Age (65 years and over)	0.72 (0.55 to 0.88)
Gender (male)	0.23 (0.11 to 0.36)
BMI (underweight)	0.18 (-0.55 to 0.80)
BMI (overweight)	0.54 (0.37 to 0.70)
BMI (obese)	1.35 (1.18 to 1.51)
Smoking status (smoker)	0.51 (0.28 to 0.76)
Hypertensive medications (yes)	0.38 (0.25 to 0.52)
Diabetes history (yes)	0.61 (0.47 to 0.74)
Australian born (no)	0.12 (0.02 to 0.26)
Insufficient physical activity (yes)	0.16 (0.01 to 0.31)
Inadequate fruit or vegetables (yes)	−0.03 (0.14 to 0.10)
Model 2: with K10	
Age (55–65 years)	0.40 (0.21 to 0.55)
Age (65 years and over)	0.75 (0.57 to 0.91)
Gender (male)	0.24 (0.11 to 0.37)
BMI (underweight)	0.17 (0.57 to 0.78)
BMI (overweight)	0.53 (0.37 to 0.70)
BMI (obese)	1.33 (1.17 to 1.50)
Smoking status (smoker)	0.48 (0.25 to 0.73)
Hypertensive medications (yes)	0.38 (0.25 to 0.52)
Diabetes history (yes)	0.60 (0.46 to 0.73)
Australian born (no)	0.12 (0.03 to 0.26)
Insufficient physical activity (yes)	0.15 (0.001 to 0.30)
Inadequate fruit or vegetables (yes)	−0.01 (0.14 to 0.11)
Psychological distress (K10≥19) (yes)	0.39 (0.20 to 0.57)

BMI, body mass index

DSM-IV and the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10) Classification of Mental and Behavioural Disorders in several countries worldwide.[53–59] The K10 is used in all the national surveys in the WHO's World Mental Health Survey Initiative, which includes 27 countries representing all regions of the world.[60]

Participants were asked to rate how often, in the past 4 weeks, they felt negative emotions on 10 question items. The K10 has a five-value response option for each question—(1) all of the time, (2) most of the time, (3) some of the time, (4) a little of the time and (5) none of the time—that are scored in reverse. Thus, summed scores can range from 10 (indicating no distress) to 50 (indicating severe distress). The K10 was found to have good internal consistency (Cronbach's
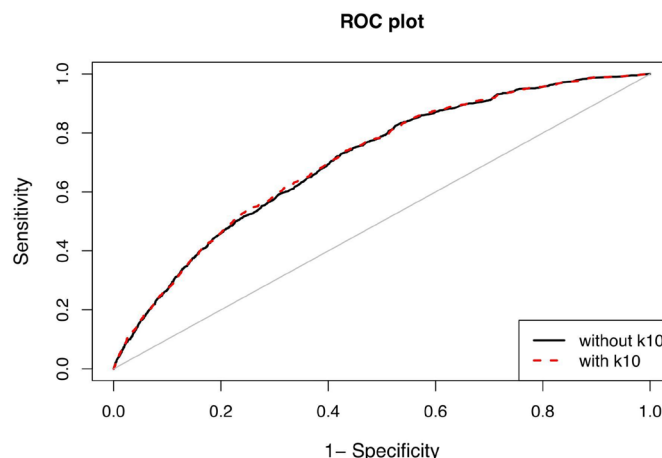

Figure 1 Receiver operating characteristics (ROC) curves based on 3-year type 2 diabetes risk predictions with and without the K10.

α coefficient of 0.85) based on the Australian 2004–2005 National Health Survey sample.[61]

Statistical analyses

First, we determined the optimal K10 cut-off in the logit used to predict diabetes at follow-up. We adopted the standard strategy of estimating different logit models using increasing values of K10 cut-offs, starting at 0. For each logit, and corresponding value of the cut-off, we compute a goodness-of-fit measure and then pick the optimal value of the K10 cut-off as the one that maximises this measure. We selected the Tjur's Coefficient of Discrimination (CoD)[47] as our goodness-of-fit measure and used the R package 'sjstats' to calculate it. While we considered alternatives such as the McFadden and Cox-Snell Pseudo R^2,[45 46] we selected the Tjur CoD because, in addition to being closely related to R^2 definitions for linear models,[47] it has a very intuitive definition: it is simply the difference between the average predicted probabilities for the two classes in the logit estimation. The optimal K10 cut-off was estimated to be 19, and therefore we created a binary

Table 3 Risk table for reclassified persons with the addition of K10 score

Reclassification*	Events	Non-events	n	% Risk (95% CI)
Low->Low	231	26 085	26 316	0.88 (0.77 to 1.00)
High->Low	39	1399	1438	2.71 (1.94 to 3.69)
Low->High	12	698	710	1.69 (0.88 to 2.93)
High->High	794	22 330	23 124	3.43 (3.2 to 3.68)
Total	1076	50 512	51 588	2.09 (1.96 to 2.21)
NRI events=(12−39)/1076=−2.51%				
NRI non-events=(1399−698)/50 512=1.39%				
NRI=[(12−39)/1076]+[(1399−698)/50 512]=−1.12%				
ΔNB=(−27−0.0168723043676495×−701)/51 588=−0.0003				

*Based on a cut-off maximising sensitivity and specificity to define high versus low risk of incident type 2 diabetes.
NB, net benefit; NRI, net reclassification improvement.

Table 4 Risk table for reclassified persons with the addition of K10 score

Reclassification*	Events	Non-events	n	% Risk (95% CI)
Low->Low	966	49345	50311	1.92 (1.80 to 2.04)
High->Low	10	129	139	7.19 (3.50 to 12.83)
Low->High	27	199	226	11.95 (8.02 to 16.9)
High->High	73	839	912	8.00 (6.33 to 9.96)
Total	1076	50512	51588	2.09 (1.96 to 2.21)
NRI events=(27−10)/1076=1.58%				
NRI non-events=(129−199)/50 512=−0.14%				
NRI=[(27−10)/1076]+[(129−199)/50 512]=1.44%				
ΔNB=(17−0.0742212045061077×70)/51 588=0.0002				

*Based on a cut-off corresponding to the top 10th percentile to define high versus low risk of incident type 2 diabetes.
NB, net benefit; NRI, net reclassification improvement.

Table 5 Risk table for reclassified persons with the addition of hypertensive medications

Reclassification*	Events	Non-events	n	% Risk (95% CI)
Low->Low	292	28830	29122	1.00 (0.89 to 1.12)
High->Low	56	2413	2469	2.27 (1.72 to 2.94)
Low->High	23	1125	1148	2.00 (1.27 to 2.99)
High->High	705	18144	18849	3.74 (3.47 to 4.02)
Total	1076	50512	51588	2.09 (1.96 to 2.21)
NRI events=(23−56)/1076=−3.06%				
NRI non-events=(2413−1125)/50 512=2.55%				
NRI=[(23−56)/1076]+[(2413−1125)/50 512]=−0.52%				
ΔNB=(−33−0.0193115966766661×−1288)/51 588=−0.0001				

*Based on a cut-off maximising sensitivity and specificity to define high versus low risk of incident type 2 diabetes.
NB, net benefit; NRI, net reclassification improvement.

variable which is 0 for K10 score less than or equal to 19 and 1 otherwise. For simplicity, we refer to this binary predictor as the K10 variable in the rest of analysis.

Then, we assessed performance measures for the incremental value of K10 using the area under the receiver operating characteristics (AROC) and associated 95% CIs, net reclassification improvement (NRI) and net benefit (NB) decision analytics.[39] We used sensitivity analysis techniques to assess the robustness of the decision analytics, and to test if the incremental predictive value of the K10 was dependent on size of the coefficient. We repeated the base model (model 1) replacing hypertensive medications with the K10, and assessed the incremental predictive value of hypertensive medications. We chose the hypertensive medications variable, which is commonly featured among T2D risk assessment tools, because it yielded a similar coefficient as the K10 (0.38 vs 0.39) in model 2.

RESULTS

Table 1 shows baseline characteristics of participants in the SEEF subsample of the 45 and Up study cohort by T2D status at follow-up, including crude incidence and corresponding age-adjusted ORs. A cut-off point of ≥19 for the K10 was optimal for predicting T2D risk (sensitivity 77%, specificity 53% and Positive Predictive Value (PPV) 3%) with an OR of 1.70 (95% CI 1.41 to 2.03, P<0.001). The unadjusted relative incidence of T2D was highest for: older age; male gender; Australian born; family history of diabetes; currently taking antihypertensive medications; current smoker; insufficient physical activity; do not usually eat vegetables or fruit every day; underweight, overweight and obese; and psychological distress risk groups. The incidence rate of T2D was 2.1% (1076/51 588) over an average follow-up of 3.4 (SD=0.95) years (annual incidence rate was 0.61%).

Table 2 shows the beta coefficients for risk factors from two logistic regression models, without (model 1) and

with (model 2) the K10 binary variable. Model 1 shows that all of the variables except for country of birth and diet from the AUSDRISK[44] were significant predictors of incident T2D. Model 2 shows that the addition of K10, which was an independent predictor of incident T2D, resulted in no or very small changes in the beta coefficients for the remaining risk factors. Both models resulted in good performance for predicting incident T2D (AROC for model 1 and model 2 was 0.705 (0.69 to 0.72) and 0.708 (0.69 to 0.72), respectively). There was evidence of slight improvement to model 1 after fitting K10 (net change in AROC was 0.003, P=0.04; figure 1).

Table 3 shows the results for reclassified persons with the addition of K10 based on a risk threshold to define low and high risk of incident T2D at which both sensitivity and specificity were maximised on the AROC (sensitivity 77%, specificity 53% and positive predictive value 3%). A small net −0.0251 decrease in high-risk classifications for those with events (NRI events) and a small net increase in low-risk classifications for those without events (NRI non-events) resulted in a negative NRI of −1.12%. The net number of true positive classifications decreased by 0.03% on a scale of 0%–2.1% incidence rate. This implies that 3333 additional K10 screening assessments result in one less T2D case without increasing high-risk classifications for those without incident T2D.

Sensitivity analyses

Table 4 shows the results for reclassified persons with the addition of K10 based on a top 10th percentile threshold to define high versus low risk of incident T2D. This means that an individual is classified at high risk if the risk predicted by the logit model is higher than 90%. A small net increase (1.58%) in high-risk classifications for those with events and a small net decrease (−0.14%) in low-risk classifications for those without events resulted in a positive NRI of 1.44%. The net number of true positive classifications increased by 0.02% on a scale of 0%–2.1% incidence rate. This implies that 5000 additional K10

screening assessments would identify one more T2D case without increasing high-risk classifications for those without incident T2D. We simulated increases in the size of the K10 coefficient and studied the effect on the NB. Changes in the coefficient of the order of 10% were associated with changes in NB of the order of less than 0.1%.

Table 5 shows the results for reclassified persons with the addition of hypertensive medications to a base model that includes the K10. A small net decrease (−3.06%) in high-risk classifications for those with events and a small net increase (2.55%) in low-risk classifications for those without events resulted in a small negative NRI of −0.52%. The net number of true positive classifications decreased by −0.01% on a scale of 0%–2.1% incidence rate. This implies that 10 000 additional screening for hypertensive medications would identify one less T2D case without increasing high-risk classifications for those without incident T2D.

DISCUSSION

In this study, we considered various statistical analyses, summary measures and graphs to assess the incremental predictive value of screening for anxiety and depression beyond current T2D risk models. First, we determined that a K10 score of ≥19 was optimal for predicting approximate 3-year risk of developing T2D independent of age and gender. Second, we showed that variables from T2D risk models or tools applicable for use in routine clinical practice, including the AUSDRISK,[44–50] resulted in good performance for predicting incident T2D in the 45 and Up Study cohort. Third, we showed that symptoms of anxiety and depression, assessed using an optimal K10 score of ≥19, were associated with an increased risk of developing T2D independent of risk factors from current T2D risk models, consistent with previous research.[37 62–64] Unlike previous research, however, we showed for the first time that adding the K10 variable resulted in no incremental value beyond current T2D risk models and, in fact, resulted in a very small increase in the fraction of false positive classifications. Sensitivity analysis showed a very small positive incremental value when using a much higher decision threshold for the K10 (>90th percentile). This implies that additional screening for anxiety and depression using the K10 to current T2D risk assessment tools is unlikely to confer benefit, both to health professionals and consumers, and may lead to overtreatment for clinical prevention. However, the poor incremental predictive value of the K10 was partially explained by the baseline model as well as the small effect size that was similar compared with other risk factors. This highlights several limitations of the current approaches (AROC, NRI, NB decision analytics) for investigating incremental predictive value of novel risk factors in standard risk models.

Screening for both anxiety and depression using a broad non-specific psychological distress published evidence on the risk of developing T2D associated with anxiety

remains inconsistent.[65–67] Furthermore, one of these cohort studies from USA showed that the increased risk of incident diabetes associated with both clinically relevant symptoms of anxiety and depression was observed in women but not men. Thus, future research should determine the incremental predictive value of specific anxiety and depression screening tools for T2D risk assessment, and in men and women separately, if indeed a gender interaction is found.

The poor incremental predictive value of the K10 in this context has health policy implications, especially in the Australian healthcare setting for population-based screening strategies for preventing T2D. For example, the AUSDRISK tool is used in general population screening to determine eligibility for a general practitioner Health Assessment provided as part of a T2D risk evaluation for people aged 40–49 years covered by Medicare (Australia's federally funded universal healthcare scheme). In practice, patients with a 'high' (12 or more) score are eligible for the Health Assessment, and subsequent referral to allied health services to provide lifestyle programmes. The addition of the K10 to this current publicly funded T2D risk-screening programme would be unjustified, especially since the application rate of the AUSDRISK tool in general practice has reportedly been very low (approximately 14%).[68] Furthermore, the predictive value of T2D risk-screening tools for primary prevention is questionable. For instance, the AUDRISK tool has been used in diabetes prevention trials in Australia (including the Greater Green Triangle Diabetes Prevention Project,[69] Melbourne Diabetes Prevention Study,[70] Sydney Diabetes Prevention Program[71] and Victorian *Life!* Program[72]) targeting high-risk individuals identified using the AUSDRISK,[44] none of which have demonstrated effectiveness for reducing the incidence of T2D. This highlights the importance of risk stratification beyond those identified using the AUSDRISK score of 12 or more[44] for primary prevention of T2D.

Despite the poor incremental predictive value of the K10, it remained a predictor of developing T2D after correction for all of the other predictors. This suggests that screening for anxiety and depression would identify a large group of individuals otherwise not apparent with current T2D risk assessment tools, which might be clinically important for treatment decision making for the management of psychological comorbidity. Previous systematic reviews of RCTs have shown that exercise (an integral component of lifestyle intervention) is effective for improving both depression score (standardised mean difference was −0.82 (95% CI −1.12 to −0.51)) and HbA1c level (weighted mean difference was −0.67% (95% CI −0.84 to −0.49)),[73 74] and the size of these effects are substantially larger than what we found for collaborative care for depression.[75] Overall, this evidence suggests that lifestyle intervention integrated within the collaborative care model would be most effective for preventing T2D in people with comorbid anxiety and depression.

Strengths of this study include the recruitment of a large (over 250 000 participants) population-based sample at baseline,[41] and the high (over 60%) response rate achieved in the subsample at follow-up.[76] Study weaknesses include the low incidence of T2D observed in the cohort, reliance on self-report measures, low (less than 18%) response rate achieved at baseline,[41] residual confounding and misclassification of variables potentially resulting in bias. Further evidence from prospective cohort studies is needed to confirm the generalisability of these findings and the applicability of specific screening tools for anxiety and depression in specific healthcare settings.

In conclusion, anxiety and depressing screening with the K10 adds no meaningful incremental value beyond current T2D risk models applicable for use in routine clinical practice. Additional screening for anxiety and depression using the K10 is unlikely to confer benefit, both to health professionals and consumers and may lead to overtreatment for clinical prevention. However, since the lack of incremental predictive value of the K10 was partially explained by the baseline model as well as the small effect size, our main finding should be interpreted with caution. The clinical importance of anxiety and depression screening for preventing T2D in primary healthcare requires further consideration and research.

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