1	Title: Sex Differences in the Association of Psychological Status with Measures of Physical Activity
2	and Sedentary Behaviour in Adults with Type 2 Diabetes
3	
4	Short title: Psychological Status and Physical Activity in Type 2 Diabetes
5	
6	Authors: Indelicato Liliana ^{1*} ; Marco Dauriz ^{1*} ; Elisabetta Bacchi ^{1*} ; Silvia Donà ¹ ; Lorenza Santi ¹ ; Carlo
7	Negri ¹ ; Vittorio Cacciatori ¹ ; Enzo Bonora ¹ ; Arie Nouwen ² ; Paolo Moghetti ¹ .
8	* Equal contribution.
9	
10	Institutions:
11	¹ Division of Endocrinology, Diabetes and Metabolism, Department of Medicine, University and
12	Hospital Trust of Verona, Verona, Italy
13	² Department of Psychology, Middlesex University, London, UK
14	
15 16	Please address all the correspondence to:
17	Dr. Liliana Indelicato, Psy.D. Ph.D.
18	Division of Endocrinology, Diabetes and Metabolism
19	Department of Medicine
20	University of Verona and Hospital Trust of Verona
21	Piazzale Stefani, 1
22	37126 Verona - Italy

- 23Phone: +39 (045) 812-311024Fax: +39 (045) 802-7314
- 25 E-mail: <u>liliana.indelicato@univr.it</u>

27 ABSTRACT

Aim – To assess the association of psychological variables on leisure time physical activity and
 sedentary time in men and women with type 2 diabetes mellitus (T2D).

Methods – In this cross-sectional study, we evaluated 163 patients with T2D, consecutively recruited at the Diabetes Centre of the Verona General Hospital. Scores on depression and anxiety symptoms, psychosocial factors (including self-efficacy, perceived interference, perceived severity, social support, misguided support behaviour, spouse's positive behaviour), physical activity and time spent sitting were ascertained using questionnaires responses to the Beck Depression Inventory-II, Beck Anxiety Inventory, Multidimensional Diabetes Questionnaire, International Physical Activity Questionnaire.

37 Results – Physical activity was significantly associated with higher social support in women, and with 38 increased self-efficacy in men. Sedentary time was significantly associated with higher perceived 39 interference, anxiety and depressive symptoms, and with reduced diabetes self-efficacy in women, 40 while it was associated solely with anxiety in men. Depressive symptoms and self-efficacy in women 41 and anxiety symptoms in men were independent predictors of sedentary time when entered in a 42 multivariable regression model also including age, BMI, hemoglobin A1c, diabetes duration, 43 perceived interference and self-efficacy as covariates.

44 **Conclusions** – Lower self-efficacy and higher symptoms of depression were closely associated with 45 increased sedentary time in women, but not in men, with T2D. It is possible that individualized 46 behavioral interventions designed to reduce depressive symptoms and to improve diabetes self-47 efficacy would ultimately reduce sedentary behaviours, particularly in women with T2D.

48

49

Keywords (5): Diabetes; Depression; Anxiety; Physical Activity; Sedentary Behaviour

51 INTRODUCTION

52 Depression is diagnosed in about 15-20% of adults with type 2 diabetes (T2D), with women twice as 53 likely to be affected as men [1]. Depression interferes with diabetes self-management and metabolic 54 control [2-4] and may increase the risk of complications [5], cognitive decline [6] and mortality[7].

55 According to Mezuk et al. [8], diabetes and depression appear to share a bi-directional relationship, 56 with depression increasing the risk of incident diabetes and diabetes increasing the risk of 57 depression. However, according to recent meta-analyses [9, 10], the prevalence of depression 58 appears to be higher in individuals with known diabetes, than in those with impaired glucose 59 regulation or newly diagnosed diabetes, an observation also confirmed by a recent report from a 60 large cross-sectional study in Chinese individuals [11]. Moreover, a study from the English 61 Longitudinal Study of Aging (ELSA) database, found higher incident depressive symptoms in younger 62 older adults with diabetes than their non-diabetic counterparts (<65 years) but not in those 65 years 63 and older [12]. These studies suggest that the presence of T2D alone is not sufficient to increase the 64 prevalence or incidence of depression. Rather, they suggest that psychological factors are likely to 65 play a role in developing depression among people with diabetes but that it is the burden of living 66 with and having to care for diabetes especially in the presence of diabetes complications and the stresses of a working life that increases the risk of developing depression [13]. 67

Several studies have shown that increased physical activity levels are associated with lower symptoms of depression, stress and anxiety [14]. The evidence provided by the Diabetes Prevention Program and other landmark trials [15, 16] strongly support the benefits of physical activity to prevent T2D and relent its progression. Indeed, a general increase in daily physical activity is included among the first-line intervention of current structured programs for diabetes prevention and care [17, 18].

However, the achievement of recommended exercise goals is challenging, due to a number of limiting factors, such as individual motivation and accompanying comorbidities [19]. Therefore, despite the clear benefits of physical activity on metabolic control and mental health, many people

77 remain physically inactive [19, 20].

78

79 These observations have recently prompted research efforts to identify the psychological factors 80 associated with leisure physical activity in individuals with T2D [21]. A number of psychological 81 models have been developed to explore the reciprocal interaction of personal and environmental 82 factors as determinants of exercise behaviour change. For instance, the Social Learning Theory (SLT) 83 provides a theoretical framework to isolate the psychosocial variables specifically relevant to chronic 84 diseases, such as T2D, by emphasizing the reciprocal interactions occurring at the level of social 85 support, patients' idiosyncratic beliefs and social incentives related to self-care activities [22]. Self-86 efficacy, defined as a person's belief in his or her own ability to execute a specific behaviour [23], 87 candidates among the psychological variables as a major determinant of behaviour change. Indeed, 88 low self-efficacy percepts may underlie the difficulties experienced by T2D patients to start and 89 maintain a regular physical activity. In this context, the SLT provides a perspective that emphasizes 90 the role of self-efficacy in driving successful behaviour change [23].

91

Whereas some studies have investigated associations between psychological variables and leisure physical activity [24], the relationships of the former with sedentary behaviour have received much less attention, particularly among people suffering from chronic diseases such as T2D. Notably, sedentary behaviour is not the opposite of physical activity, rather it refers to behaviours that do not increase energy expenditure above resting levels [25]. Specifically, sedentary behaviour is defined as the time spent in non-exercising or reclining pursuits, including screen-time behaviours such as watching television or computer use [26].

99 Recent evidence revealed a direct association of daily sitting time and other sedentary habits with 100 all-cause mortality and cardiovascular diseases [27]. Other studies have shown that sedentary 101 behaviour *per se* adversely affects individual health, independent of the amount of physical activity 102 in the general population [28] and in individuals with T2D [29, 30]. These evidences suggest that

103 sedentary behaviour recognizes specific biological pathways distinct from those elicited by physical 104 activity [31]. Of note, the psychosocial mechanisms leading to sedentary behaviour differ from those 105 leading to physical activity, thus supporting the rationale for testing the hypothesis that sedentary 106 behaviours may recognize specific psychological determinants also in patients with T2D. Moreover. 107 Hamer et al. [32] have observed that sedentary behaviour is actually associated with depression and 108 that this relationship remains significant after controlling for physical activity, thus providing 109 compelling evidence that physical activity and sedentary behaviour have distinct and independent 110 associations with depressive symptoms. The direct relationship existing between depressive 111 symptoms and sedentary behaviour has been highlighted by a recent review [33], thus corroborating 112 previous findings by Vallance et al. [34] that depressive symptoms are twice as high in adults 113 spending more time in sedentary behaviours.

In the light of this evidence, novel approaches to reduce sedentary behaviours are urgently needed, as well as updated public health recommendations increasing awareness of the risk associated with these behaviours. This is particularly relevant for individuals with T2D, as they are exposed to an increased demand of self-care and, simultaneously, they typically display an increased vulnerability to psychological distress [2, 35, 36], which, in turn, is associated with poorer clinical outcomes and a higher occurrence of un-healthy behaviours.

120

The research efforts hitherto conducted to unravel the motivational determinants of physical activity engagement in adults have shown that behavioral and cognitive factors (particularly selfefficacy) are crucial for the initiation and long-term maintenance of physical activity. However, it is currently unknown whether the same factors also act on sedentary behaviour. Furthermore, there are no studies that have examined the association between physical activity measures (including time spent sitting and leisure physical activity), psychological distress (depression and anxiety) and psychological factors (e.g. self-efficacy) in individuals with T2D.

128 Hence, the present study aimed at investigating the associations of anxiety, depression and other

psychosocial variables with leisure physical activity and sedentary behaviour in individuals with T2D.
Since the relationship of the psychological variables with the individual sedentary behaviour or the
attitude at exerting physical activity may vary by sex in the general population [37] and in patients
with T2D [38], a secondary objective of the study was to examine these relationships in men and
women, separately. We therefore examined associations first in the entire cohort, then for men and
women separately.

- 135
- 136

137 METHODS

138 Participants

139 In this cross-sectional study, we report baseline data of 163 individuals with T2D, recruited among 140 the outpatients included in the larger research project "glycemic COntrol, Psychological distrEss and 141 Self-efficacy in Type 2 diabetes" (COPEST), conducted at the Diabetes Centre of Verona City Hospital. 142 As specified elsewhere[2], the COPEST study tested the effect of a self-efficacy oriented 143 psychological intervention on glycaemic control in T2D patients with baseline suboptimal glucose 144 control. The study protocol was approved by the Ethics Committee of the Hospital Trust of Verona. 145 All participants gave written informed consent upon recruitment. Further details on the study design 146 and enrollment criteria are provided as online Supplementary Material.

147

148 Assessment of depressive and anxiety symptoms

149 Depressive symptoms were assessed by the validated Italian version of the Beck Depression 150 Inventory-II (BDI-II) [39]. The BDI-II is a 21-item questionnaire assessing the intensity of depressive 151 symptoms as defined by the Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition 152 (DSM-IV). Internal consistency (Cronbach's alpha) was $\alpha = 0.80$.

153 Anxiety symptoms were assessed by the validated Italian version of the Beck Anxiety Inventory (BAI)

154 [40]. The BAI consist of 21-items developed to assess the severity of anxiety symptoms ($\alpha = 0.89$).

155

156 Assessment of diabetes psychological adjustments

157 Diabetes-related cognitive and social factors were assessed by the validated Italian version of the 158 Multidimensional Diabetes Questionnaire (MDQ), which includes three sections [41]. The first 159 section is designed to assess the general perception of diabetes and related social support. 160 Cronbach's alphas for the subscales ranged from 0.81 to 0.92. The second section measures social 161 incentives in relation to self-care activities. Cronbach's alpha for positive and misguided 162 reinforcement behaviours was 0.88 and 0.83, respectively. The third section measures self-efficacy 163 and outcome expectancies ($\alpha = 0.84$ and 0.90, respectively). In particular, the self-efficacy measure 164 stands on a 7-item scale assessing the patients' confidence in their ability to perform behaviours specific 165 to diabetes self-care activities including diet, exercise, medication, self blood glucose monitoring and 166 general diabetes management. Sample items include "How confident are you/your ability to: (1) follow 167 your diet, (2) test your blood sugar at the recommended frequency, (3) to exercise regularly?".

168

169 Physical activity and sedentary behaviour measurements

170 Assessment of leisure physical activity and time spent sitting were assessed using the Italian 171 shortened version of the International Physical Activity Questionnaire (IPAQ) [42]. This version 172 provides information on time spent walking or on sedentary pursuits or being engaged in vigorous-173 to-moderate intensity over the last 7 days. The IPAQ questionnaire estimates the total weekly 174 physical activity by weighting the reported minutes-per-week within each activity category by an 175 energy expenditure estimate (dubbed as MET, metabolic equivalent, according to Jetté et al. [43]) 176 assigned to each category of activity (3.3 METs for moderate walking, 4.0 METs for moderate 177 physical activity and 8.0 METs for vigorous physical activity). The weighted MET-min per week 178 (MET·min·wk⁻¹) were calculated as duration·frequency·MET intensity, which were summed across 179 activity domains to produce a weighted estimate of total physical activity from all reported activities 180 per week. In terms of sedentary behaviour, sitting questions were developed as separate indicators

and not as part of physical activity score. Participants were instructed to consider the time spent sitting (hours and minutes per day) at work, at home, while doing course work and during leisure time. Both the leisure physical activity and sedentary behaviour measures assessed by IPAQ are supported by validated data [44, 45].

185

186 Statistical analysis

187 Data are presented as mean and standard deviation (SD) or median and interguartile range [IQR], 188 unless otherwise indicated. Standard normal distribution of the variables was assessed by the 189 Kolmogorov-Smirnov test. Variables deviating from the Gaussian distribution (leisure physical 190 activity, anxiety, depressive symptoms, perceived interference) were naturally log-transformed to 191 improve normality before analysis. Data analysis was conducted firstly in the overall cohort and 192 thereafter separately for men and women. The comparisons of clinical, socio-psychological and 193 physical activity parameters between women and men were conducted by Student's t-test. Simple 194 correlations (expressed as Pearson's r) were calculated to explore the relationship of sedentary 195 behaviour and physical activity with depressive and anxiety symptoms, diabetes-specific self-efficacy 196 and other psychological variables. Partial correlations controlling for age, BMI, diabetes duration and 197 HbA1c were also calculated. We then explored whether symptoms of depression and anxiety, self-198 efficacy and perceived interference were independent predictors, alone or in combination, of 199 sedentary behaviour and physical activity by entering these variables in linear regression models 200 with age, BMI, diabetes duration, HbA1c and sex (coded as female=1; male=0) as covariates. The 201 latter was then excluded in the analyses by sex subgroups. All covariates were selected for inclusion 202 in the partial correlations and regression models if significant in univariate analysis or according to 203 their biological plausibility. All statistics were carried out with IBM SPSS 22.0® software. Statistical 204 significance was declared at two-tailed *P*-value <0.05 for all comparisons.

205

207 **RESULTS**

208**Table 1** summarizes the clinical, socio-demographic and psychological characteristics of the study209cohort (N = 163). The study participants included marginally more men (59.5%); age (mean ±SD) was210 62.7 ± 7.6 years, while diabetes duration and HbA1c were 11.1 ± 8.6 years and 7.6 ± 1.3 %, respectively.211The majority of patients was on oral hypoglycemic agents (OHA, 70.3%), while a smaller number of212them were prescribed a combination therapy (OHA + insulin, 18.8%) or insulin alone (10.9%). No213sex-differences were found for any of the clinical study variables, with the only exception of BMI,214which was significantly higher in men than in women (32.0±4.3 vs. 30.6±3.6 Kg/m², p<0.05).</td>

215 Compared to men, women reported higher levels of anxiety but lower social support, spouse's 216 misguided support behaviour and spouse's positive reinforcing behaviour. However, these 217 differences reached statistically significance only after adjustment for BMI. Both men and women 218 reported similar physical activity rates, but men spent more time in sedentary behaviours than 219 women.

220

221 We considered physical activity and sedentary time as health behaviour variables and we calculated 222 their simple correlations (reported as Pearson's r) with the psychological variables. As shown in 223 Table 2, higher degrees of physical activity showed a significant relationship with increasing self-224 efficacy, while no significant figure was apparent in relation to other psychological variables. In 225 contrast, sedentary behaviour exhibited an inverse association with self-efficacy and it was related 226 to more severe symptoms of anxiety and depression and with an increased occurrence of misguided 227 support behaviours. Hence, in contrast to what observed for physical activity, sedentary behaviour 228 appeared to be significantly related to negative emotions.

When the same analyses were conducted separately in men and women, we observed that physical activity was associated with social support in women and with diabetes self-efficacy in men. For women, sedentary behaviour showed a negative and significant association with diabetes selfefficacy and a positive association with symptoms of depression and anxiety and with perceived

interference. In contrast, sedentary time in men was only associated with anxiety symptoms. Thus,
 in contrast to what observed in men, sedentary behaviour in women appeared to be linked with
 negative emotions and with the impact of diabetes in their lives.

236

237 In order to further investigate the association of these psychological variables with sedentary 238 behaviour in light of accompanying confounding variables, we calculated partial correlations by 239 controlling for age, BMI, diabetes duration and HbA1c in the whole sample and separately for men 240 and women. As reported in Table S1, the relationship of sedentary behaviour with depressive 241 symptoms and self-efficacy in women held statistical significance and effect direction. The same 242 applied to the association of sedentary behaviour with anxiety symptoms in men. However, anxiety 243 symptoms and perceived interference in women did not retain statistical significance for the 244 association with sedentary behaviour after adjustment for confounders.

245

246 We then explored, in the whole sample, whether symptoms of depression and anxiety, self-efficacy 247 and perceived interference were independent predictors, alone or in combination, of sedentary 248 behaviour by entering these variables in a linear regression model with age, BMI, diabetes duration, 249 HbA1c and sex as covariates (Table 3). Results showed that lower self-efficacy and increased anxiety 250 symptoms were independent predictors of sedentary behaviour. Among the other variables 251 included in the analysis, a clear contribution of sex to the variance of sedentary behaviour prompted 252 a stratified analysis separately for men and women. Depressive symptoms ($\beta_{std} = 0.30, p = 0.023$) and 253 diabetes-specific self-efficacy (β_{std} = -0.27, p = 0.041) were independent predictors of sedentary 254 behaviour in women only (adjusted model- R^2 = 0.21). Conversely, only anxiety symptoms were found 255 to be independent predictors of sedentary time, when the same model was applied to men (β_{std} = 256 0.24, p = 0.023), despite a negligible overall explained variance (adjusted model- $R^2 = 0.05$).

257

258 The association of physical activity with social support in women and with self-efficacy in men was

investigated by applying distinct linear regression models also including age, BMI, diabetes duration and HbA1c as covariates. Social support was found to be the unique predictor of physical activity in women ($\beta_{std} = 0.27$, p = 0.027), with an overall explained variance of 6.1%. The model did not retain self-efficacy, but only BMI ($\beta_{std} = -0.33$, p = 0.001), as a predictor of physical activity in men (adjusted model- $R^2 = 0.10$).

264 265

266 **DISCUSSION**

In this study we have examined the relationship of sedentary behaviour and physical activity with
 symptoms of depression and anxiety and with diabetes-specific psychosocial variables in adults with
 T2D admitted to the outpatient clinic of a major diabetes referral centre.

270 The observation that sedentary behaviour and physical activity show distinct associations with the 271 psychosocial variables herein evaluated stands as a key finding of our study. While physical activity 272 showed a significant relationship with increasing diabetes self-efficacy only, the opposite was 273 observed in relation to sedentary behaviour, which also appeared to be significantly related with a 274 more articulated combination of psychosocial variables, namely more severe symptoms of anxiety 275 and depression and an increased occurrence of misguided support behaviours. More specifically, we 276 observed that women, in contrast to men, were less sedentary and were characterized by a closer 277 relationship of sedentary behaviour with negative emotions and with the impact of diabetes in their 278 lives.

To date, research has mainly focused on the determinants of physical activity, whereas sedentary behaviour has received much less attention. Our study evaluated both of these aspects and provided supporting evidence that, similarly to recent observations in the general population [33], sedentary behaviour and physical activity recognize differential psychosocial variables as underlying factors also in individuals with T2D.

284 Some studies have previously reported that sedentary behaviour is associated with depression

285 independently of extant physical activity levels [32]. On the other hand, a recent study by Breland et 286 al. [46] showed that daily sitting time, but not physical activity, increases the risk of depressive 287 symptoms. Accordingly, in our study, we found no evidence of association between physical activity 288 and symptoms of depression and anxiety. One possible explanation for the lack of association is 289 that, on average, the individuals included in our study did not engage in high intensity exercise and 290 they were not formally enrolled in a structured physical activity program. Therefore, although 291 physical activity and depression are closely linked [47],), it could be reasonably assumed that low 292 levels of unstructured physical activity may have no major effect on mental health.

Alernatively, the lack of association between physical activity and symptoms of depression and anxiety results might be inherent to the instrument employed to evaluate physical activity. Indeed, the IPAQ score does not allow to clearly discriminate among different classes of physical activity or to clarify whether physical activity is conducted alone or in concert with significant others. For example, Teychenne *et al.* [48] observed that only leisure-time physical activity was associated with a lower risk of depression.

299

300 Our results also confirm previous findings [38, 49], in that we observed differential patterns 301 between men and women regarding the associations of psychological variables with sedentary 302 behaviour and physical activity. Indeed, diabetes-specific self-efficacy and depressive symptoms in 303 women and anxiety symptoms in men resulted as independent predictors of sedentary time, while 304 social support retained statistically significant association with physical activity in women only. 305 These data may provide rationale for further intervention studies targeting negative mood (anxiety 306 in men; depression in women) and diabetes self-efficacy in women in order to reduce sedentary 307 behaviours and, ultimately, to improve the individual cardiovascular risk profile.

308 In contrast with previous studies in T2D individuals [37, 38], we have observed that men and women 309 reported comparable physical activity levels. The potential causes of disparities in physical activity 310 levels between men and women are likely to be multiple. However, most studies (including the

present one) investigating this issue have not assessed all sex-specific activities, in particular, activities of lower intensity or more relevant to women's lives. In this regard, Hallal *et al.* [50] showed that, when specific domains of activity practice are considered, no sex differences are observed.

315 Conversely, as compared to men, women showed significantly lower propensity to spend time in 316 sedentary pursuits, an observation that may be amenable to a number of possible explanations. 317 First, it is well known that men and women hold distinct social roles in society. Women are more 318 likely to assume greater domestic responsibilities than men, thus reducing the time spent sitting at 319 home. Second, there is evidence that sex differences in the daily time spent in sedentary activities 320 are more accentuate among people ≥ 60 years of age. Martin *et al.* [51] have demonstrated that 321 older men replace higher-intensity activity with sedentary behaviour compared to women, which 322 maintained relatively constant levels of light intensity activities in each age group.

323

324 As for the novelty of our study, we believe that it fills important gaps in the existing literature, as to 325 date no study has specifically and thoroughly explored the association of psychological factors with 326 physical activity and sedentary behaviours in men and women with T2D. Indeed, our findings extend 327 previous observations and suggest that the relationship of psychological variables with health 328 outcomes depends on sex-related factors, although the underlying mechanisms yet remain to be 329 completely understood. Taken together, our results and the evidence from other studies suggest 330 that the identification of predictors of healthy behaviours by sex is warranted to develop 331 intervention programs suitable for the different needs of women and men with T2D.

Nonetheless, we should acknowledge some limitations. First, the generalizability of the study findings is limited, as it was conducted in a single Diabetes Centre and the study participants were relatively homogeneous in terms of age, health and educational status. Second, physical activity and sedentary behaviour were evaluated by self-assessment measures, which imply inherent inaccuracies in the reported estimates. Third, the relatively limited sample size and the gender

imbalance towards male participants may have lead to imperfect estimates of the association findings. Finally, the cross-sectional study design precludes any inference of causation: although sedentary behaviour may induce negative emotions, the causal arrow could indeed point the other way, i.e. negative emotions may be responsible for un-healthy behaviour. Therefore, the interpretation of our data should be made with caution and prospective longitudinal and experimental studies are advocated to confirm and expand our results.

- 343
- 344

345 **CONCLUSIONS**

346 In conclusion, we have shown that, at variance to what observed for physical activity, sedentary 347 behaviour is closely linked to a more articulated pattern of psychological variables, largely 348 influenced by sex-related differences in the individual psychological characteristics. Diabetes is a 349 chronic progressive condition that calls for a profound change in the perception of the individual's 350 health status and demands a pro-active involvement in several self-care activities. While it is 351 possible that interventions to increase physical activity and decrease sedentary time could in turn 352 improve emotional health, our results may indicate depressive symptoms and self-efficacy in women 353 and anxiety symptoms in men as potential targets for tailored interventions that may ultimately 354 benefit the individual health status by reducing the time spent sitting. Further studies are needed to 355 verify whether this approach would ultimately soften the negative effects of sedentary behaviours 356 on glycemic control and other relevant cardiovascular risk factors.

357

358 Acknowledgements

This study was supported by Fondazione Diabete Ricerca (Fo.Di.Ri, Rome, Italy). The funder had no role in the study design, data collection, data analysis, manuscript preparation and/or publication decision. The support of the administrative and clinical personnel of the Verona Diabetes Center (University and General Hospital of Verona, Verona, Italy) is gratefully acknowledged.

363

364 Author Contributions

- 365 L.I., M.D. and El.B., and researched and analyzed data and wrote the manuscript. L.S. analyzed data.
- 366 C.N. and V.C. provided care for study patients. A.N., E.B. and PM edited the manuscript and provided
- 367 substantial contribution to the overall discussion. L.I., M.D. and El.B are the guarantors of this work
- 368 and, as such, had full access to all the data in the study and take responsibility for the integrity and
- the accuracy of the data analysis.
- 370
- 371 Conflict of interest
- 372 <u>None to disclose.</u>

- 374 REFERENCES
- 3751.Anderson RJ, Freedland KE, Clouse RE, Lustman PJ: The prevalence of comorbid depression376in adults with diabetes: a meta-analysis. Diabetes Care 2001, 24(6):1069-1078.

Indelicato L, Dauriz M, Santi L, Bonora F, Negri C, Cacciatori V, Targher G, Trento M, Bonora
 E: Psychological distress, self-efficacy and glycemic control in type 2 diabetes. *Nutr Metab Cardiovasc Dis* 2017, 27(4):300-306.

- 380
 3. Rubin RR, Peyrot M: Psychological issues and treatments for people with diabetes. *J Clin* 381 *Psychol* 2001, 57(4):457-478.
- 3824.Ehrmann D, Schmitt A, Reimer A, Haak T, Kulzer B, Hermanns N: The affective and somatic383side of depression: subtypes of depressive symptoms show diametrically opposed associations384with glycemic control in people with type 1 diabetes. Acta Diabetol 2017, 54(8):749-756.
- Lin EH, Rutter CM, Katon W, Heckbert SR, Ciechanowski P, Oliver MM, Ludman EJ, Young BA,
 Williams LH, McCulloch DK *et al*: Depression and advanced complications of diabetes: a prospective
 cohort study. *Diabetes Care* 2010, 33(2):264-269.
- Demakakos P, Muniz-Terrera G, Nouwen A: Type 2 diabetes, depressive symptoms and
 trajectories of cognitive decline in a national sample of community-dwellers: A prospective cohort
 study. *PLoS One* 2017, 12(4):e0175827.
- 391 7. van Dooren FE, Nefs G, Schram MT, Verhey FR, Denollet J, Pouwer F: Depression and risk of
 392 mortality in people with diabetes mellitus: a systematic review and meta-analysis. *PLoS One* 2013,
 393 8(3):e57058.
- 3948.Mezuk B, Eaton WW, Albrecht S, Golden SH: Depression and type 2 diabetes over the395lifespan: a meta-analysis. Diabetes Care 2008, 31(12):2383-2390.
- 3969. Tong A, Wang X, Li F, Xu F, Li Q, Zhang F: Risk of depressive symptoms associated with397impaired glucose metabolism, newly diagnosed diabetes, and previously diagnosed diabetes: a398meta-analysis of prospective cohort studies. Acta Diabetol 2016, 53(4):589-598.
- Nouwen A, Nefs G, Caramlau I, Connock M, Winkley K, Lloyd CE, Peyrot M, Pouwer F,
 European Depression in Diabetes Research C: Prevalence of depression in individuals with impaired
 glucose metabolism or undiagnosed diabetes: a systematic review and meta-analysis of the
 European Depression in Diabetes (EDID) Research Consortium. *Diabetes Care* 2011, 34(3):752-762.
- 403 11. Sun JC, Xu M, Lu JL, Bi YF, Mu YM, Zhao JJ, Liu C, Chen LL, Shi LX, Li Q *et al*: Associations of
 404 depression with impaired glucose regulation, newly diagnosed diabetes and previously diagnosed
 405 diabetes in Chinese adults. *Diabet Med* 2015, 32(7):935-943.
- 406 12. Demakakos P, Zaninotto P, Nouwen A: Is the association between depressive symptoms
 407 and glucose metabolism bidirectional? Evidence from the English Longitudinal Study of Ageing.
 408 Psychosom Med 2014, 76(7):555-561.
- 409 13. Kuniss N, Rechtacek T, Kloos C, Muller UA, Roth J, Burghardt K, Kramer G: Diabetes-related
 410 burden and distress in people with diabetes mellitus at primary care level in Germany. *Acta* 411 *Diabetol* 2017, 54(5):471-478.
- 412 14. Babyak M, Blumenthal JA, Herman S, Khatri P, Doraiswamy M, Moore K, Craighead WE,

- Baldewicz TT, Krishnan KR: Exercise treatment for major depression: maintenance of therapeutic
 benefit at 10 months. *Psychosom Med* 2000, 62(5):633-638.
- 415 15. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, Nathan DM,
 416 Diabetes Prevention Program Research G: Reduction in the incidence of type 2 diabetes with
 417 lifestyle intervention or metformin. *N Engl J Med* 2002, 346(6):393-403.
- Tuomilehto J, Lindstrom J, Eriksson JG, Valle TT, Hamalainen H, Ilanne-Parikka P, KeinanenKiukaanniemi S, Laakso M, Louheranta A, Rastas M *et al*: Prevention of type 2 diabetes mellitus by
 changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med* 2001,
 344(18):1343-1350.
- 422 17. American Diabetes A: 5. Prevention or Delay of Type 2 Diabetes: Standards of Medical Care
 423 in Diabetes-2018. *Diabetes Care* 2018, 41(Suppl 1):S51-S54.
- 424 18. Force IDFCGT: Global Guideline for Type 2 Diabetes: recommendations for standard,
 425 comprehensive, and minimal care. *Diabet Med* 2006, 23(6):579-593.
- 426 19. Kirk AF, Barnett J, Mutrie N: Physical activity consultation for people with Type 2 diabetes:
 427 evidence and guidelines. *Diabet Med* 2007, 24(8):809-816.
- Balducci S, D'Errico V, Haxhi J, Sacchetti M, Orlando G, Cardelli P, Vitale M, Bollanti L, Conti F,
 Zanuso S *et al*: Effect of a Behavioral Intervention Strategy for Adoption and Maintenance of a
 Physically Active Lifestyle: The Italian Diabetes and Exercise Study 2 (IDES_2): A Randomized
 Controlled Trial. *Diabetes Care* 2017, 40(11):1444-1452.
- Bauman AE, Sallis JF, Dzewaltowski DA, Owen N: Toward a better understanding of the
 influences on physical activity: the role of determinants, correlates, causal variables, mediators,
 moderators, and confounders. Am J Prev Med 2002, 23(2 Suppl):5-14.
- Talbot F, Nouwen A, Gingras J, Gosselin M, Audet J: The assessment of diabetes-related
 cognitive and social factors: the Multidimensional Diabetes Questionnaire. *J Behav Med* 1997,
 20(3):291-312.
- 438 23. Bandura A: Social Foundations of thought and action: A social Cognitive Theory: Prentice
 439 Hall, Englewood Cliffs, NJ, US; 1986.
- 44024.Dunn AL, Trivedi MH, O'Neal HA: Physical activity dose-response effects on outcomes of441depression and anxiety. Med Sci Sports Exerc 2001, 33(6 Suppl):S587-597; discussion 609-510.
- 44225.Pate RR, O'Neill JR, Lobelo F: The evolving definition of "sedentary". Exerc Sport Sci Rev4432008, 36(4):173-178.
- 44426.Sedentary Behaviour Research N: Letter to the editor: standardized use of the terms445"sedentary" and "sedentary behaviours". Appl Physiol Nutr Metab 2012, 37(3):540-542.
- Fitzgerald JD, Johnson L, Hire DG, Ambrosius WT, Anton SD, Dodson JA, Marsh AP,
 McDermott MM, Nocera JR, Tudor-Locke C *et al*: Association of objectively measured physical
 activity with cardiovascular risk in mobility-limited older adults. *J Am Heart Assoc* 2015, 4(2).
- Tremblay MS, Colley RC, Saunders TJ, Healy GN, Owen N: Physiological and health
 implications of a sedentary lifestyle. *Appl Physiol Nutr Metab* 2010, **35**(6):725-740.

451 29. Cooper AJ, Brage S, Ekelund U, Wareham NJ, Griffin SJ, Simmons RK: Association between
452 objectively assessed sedentary time and physical activity with metabolic risk factors among
453 people with recently diagnosed type 2 diabetes. *Diabetologia* 2014, 57(1):73-82.

454 30. Cooper AR, Sebire S, Montgomery AA, Peters TJ, Sharp DJ, Jackson N, Fitzsimons K, Dayan
455 CM, Andrews RC: Sedentary time, breaks in sedentary time and metabolic variables in people with
456 newly diagnosed type 2 diabetes. *Diabetologia* 2012, 55(3):589-599.

- 457 31. Owen N, Healy GN, Matthews CE, Dunstan DW: Too much sitting: the population health
 458 science of sedentary behavior. *Exerc Sport Sci Rev* 2010, **38**(3):105-113.
- 459 32. Hamer M, Stamatakis E, Mishra GD: Television- and screen-based activity and mental well460 being in adults. *Am J Prev Med* 2010, **38**(4):375-380.
- 461 33. Teychenne M, Ball K, Salmon J: Sedentary behavior and depression among adults: a review.
 462 Int J Behav Med 2010, 17(4):246-254.
- 463 34. Vallance JK, Winkler EA, Gardiner PA, Healy GN, Lynch BM, Owen N: Associations of
 464 objectively-assessed physical activity and sedentary time with depression: NHANES (2005-2006).
 465 Prev Med 2011, 53(4-5):284-288.
- 466 35. Kato A, Fujimaki Y, Fujimori S, Isogawa A, Onishi Y, Suzuki R, Yamauchi T, Ueki K, Kadowaki T,
 467 Hashimoto H: Association between self-stigma and self-care behaviors in patients with type 2
 468 diabetes: a cross-sectional study. *BMJ Open Diabetes Res Care* 2016, 4(1):e000156.
- 36. Snoek FJ, Bremmer MA, Hermanns N: Constructs of depression and distress in diabetes:
 time for an appraisal. *Lancet Diabetes Endocrinol* 2015, 3(6):450-460.
- 471 37. Pinto BM, Marcus BH, Clark MM: Promoting physical activity in women: the new
 472 challenges. *Am J Prev Med* 1996, **12**(5):395-400.
- 473 38. Barrett JE, Plotnikoff RC, Courneya KS, Raine KD: Physical activity and type 2 diabetes:
 474 exploring the role of gender and income. *Diabetes Educ* 2007, 33(1):128-143.
- 475 39. Ghisi M FG, Montano A, Sanavio E, Sica C: BDI-II, Beck Depression Inventory-II. Manuale:
 476 Giunti O.S.; 2006.
- 477 40. Sica C CD, Ghisi M, Sanavio E: **BAI, Beck Anxiety Inventory. Manuale**: Giunti O.S.; 2006.
- 478 41. Lazzari D, Pisanti R, Marici CG, Fatati G: Il Multidimensional Diabetes Questionnaire (MDQ):
 479 analisi fattoriale confermativa e proprietà psicometriche della traduzione italiana. . *Psicoterapia*480 *Cognitiva e Comportamentale (Italian)* 2009, **15**(2):171-188.
- 481 42. Bauman A, Ma G, Cuevas F, Omar Z, Waqanivalu T, Phongsavan P, Keke K, Bhushan A, Equity,
 482 Non-communicable Disease Risk Factors Project Collaborative G: Cross-national comparisons of
 483 socioeconomic differences in the prevalence of leisure-time and occupational physical activity,
 484 and active commuting in six Asia-Pacific countries. *J Epidemiol Community Health* 2011, 65(1):35485 43.
- 48643.Jetté M, Sidney K, Blumchen G: Metabolic equivalents (METS) in exercise testing, exercise487prescription, and evaluation of functional capacity. Clin Cardiol 1990, 13(8):555-565.
- 488 44. Craig CL, Marshall AL, Sjostrom M, Bauman AE, Booth ML, Ainsworth BE, Pratt M, Ekelund U,

- 489 Yngve A, Sallis JF *et al*: International physical activity questionnaire: 12-country reliability and
 490 validity. *Med Sci Sports Exerc* 2003, 35(8):1381-1395.
- 49145.Rosenberg DE, Bull FC, Marshall AL, Sallis JF, Bauman AE: Assessment of sedentary behavior492with the International Physical Activity Questionnaire. J Phys Act Health 2008, 5 Suppl 1:S30-44.
- 493
 46. Breland JY, Fox AM, Horowitz CR: Screen time, physical activity and depression risk in
 494 minority women. *Ment Health Phys Act* 2013, 6(1):10-15.
- 49547.Salmon P: Effects of physical exercise on anxiety, depression, and sensitivity to stress: a496unifying theory. Clin Psychol Rev 2001, 21(1):33-61.
- 497 48. Teychenne M, Ball K, Salmon J: Physical activity, sedentary behavior and depression among
 498 disadvantaged women. *Health Educ Res* 2010, 25(4):632-644.
- 499 49. Cherrington A, Wallston KA, Rothman RL: Exploring the relationship between diabetes self500 efficacy, depressive symptoms, and glycemic control among men and women with type 2
 501 diabetes. J Behav Med 2010, 33(1):81-89.
- 50250.Hallal PC, Victora CG, Wells JC, Lima RC: Physical inactivity: prevalence and associated503variables in Brazilian adults. Med Sci Sports Exerc 2003, 35(11):1894-1900.
- 50451.Martin KR, Koster A, Murphy RA, Van Domelen DR, Hung MY, Brychta RJ, Chen KY, Harris TB:505Changes in daily activity patterns with age in U.S. men and women: National Health and Nutrition506Examination Survey 2003-04 and 2005-06. J Am Geriatr Soc 2014, 62(7):1263-1271.

Variables	All	Females	Males	P *	\pmb{P}_{adj}
Ν	163	66	97	-	-
Age (years)	62.7±7.6	63.5±6.5	62.1±8.1	0.24	-
Diabetes duration (years)	11.1±8.6	10.7±9.9	11.2±7.6	0.71	-
BMI (Kg·m ⁻²)	31.5±4.1	30.6±3.6	32.0±4.3	0.02	-
HbA1c _{DCCT} (%)	7.6±1.3	7.6±1.1	7.5±1.3	0.52	
HbA1c _{IFCC} (mmol/mol)	59.1±14.5	59.9±12.9	58.5±14.8	0.52	-
Diabetes medication (%)					
OHA	63.4	70.8	69.8		
Insulin	11.2	9.2	12.5	0.79	-
OHA+insulin	18.6	17.7	20.0		
Education (%)					
Primary school	27.7	35.9	22.1		
Junior high school	31.4	31.3	31.6	0.11	
Senior high school	33.3	29.7	35.8	0.11	-
University	7.5	3.1	10.5		
Work status (%)					
Employed	28.4	22.7	32.3		
Unemployed	3.1	3.0	3.1	0.40	
Retired	68.5	74.2	64.6		-
Marital status (%)					
Single	8.0	4.5	10.3		
Widower	11.7	21.2	5.2	-0.001	
Divorced/separated	4.9	10.7	1.0	<0.001	-
Married	75.5	63.6	83.5		
Leisure Physical Activity (MET·min·wk ⁻¹)	245 [0-525]	332.5 [70-630]	210.0 [0-476]	0.02	0.23
Sedentary Behaviour (hours/day)	6.0 [5-9]	6.0 [4.5-8]	7.0 [5-10]	0.01	0.03
Depression (BDI-II score)	5.0 [1-10]	4.0 [1-10]	5.0 [1-9]	0.22	0.39
Anxiety (BAI-score)	4.0 [1-8]	5.0 [1.8-13.5]	3.0 [1-7]	0.002	0.007
Psychosocial variables (MDQ score)					
Self-efficacy	58.7 [44.2-71.4]	56.4 [43.5-70.4]	60.0 [44.2-72.8]	0.46	0.18
Perceived interference	1.1 [0.2-2.1]	1.1 [0.2-2.4]	1.1 [0.3-2.0]	0.17	0.28
Perceived severity	4.0 [3.0-5.3]	4.3 [2.9-5.6]	3.6 [3.0-5.0]	0.26	0.22
Social support	4.0 [2.5-5.2]	3.5 [2.1-4.6]	4.0 [3.0-5.2]	0.04	0.02
Misguided support behaviour	1.6 [0.2-3.2]	0.5 [0.0-2.5]	2.2 [0.7-3.6]	0.05	0.008
Spouse's positive behaviour	2.7 [1.4-4.2]	2.1 [0.5-3.4]	3.2 [1.7-4.3]	0.05	0.005

Table 1 – Descriptive characteristics of the study population

<u>Abbreviations</u>: BMI, Body Mass Index; OHA, oral hypoglycemic agents; HbA1c_{DCCT}, Diabetes Control and Complication Trial-Aligned Hemoglobin A1c; HbA1c_{IFCC}, International Federation of Clinical Chemistry-Aligned Hemoglobin A1c; BDI-II, Beck Depression Inventory II; BAI, Beck Anxiety Inventory; MDQ, Multidimensional Diabetes Questionnaire. Data expressed as mean ±SD, median [IQR] or percentage; * Pearson's *P* value for sex-comparison. *P*_{adj}, BMI-adjusted Pearson's *P* value. Statistically significant figures are provided in boldface type.

	All	All		Females		
	Physical Activity	Sedentary Behaviour	Physical Activity	Sedentary <mark>Behaviour</mark>	Physical Activity	Sedentary Behaviour
Depressive symptoms (BDI-II score)	0.02	0.22**	-0.15	0.49**	0.12	0.10
Anxiety symptoms (BAI score)	-0.05	0.20*	-0.11	0.30*	-0.05	0.27*
Self-efficacy (MDQ score)	0.21**	-0.25**	0.20	-0.44**	0.23*	-0.13
Perceived Interference (MDQ score)	-0.08	0.16	-0.11	0.25*	-0.04	0.11
Perceived severity (MDQ score)	-0.06	0.10	-0.03	0.13	-0.05	0.09
Social support (MDQ score)	0.11	-0.03	0.27*	-0.19	0.05	-0.01
Misguided support behaviour (MDQ score)	-0.03	0.23**	0.14	0.19	-0.07	0.14
Spouse's positive behaviour (MDQ score) -0.04	0.14	0.11	0.20	-0.11	0.01

*Significance at two-tailed P <0.05; **P <0.001. Statically significant figures are reported in boldface type

	All	All		Females		
	ß _{std}	Р	ß _{std}	Ρ	ß _{std}	Р
Depressive symptoms	0.06	0.61	0.30	0.02	-0.15	0.31
Anxiety symptoms	0.18	0.03	-0.13	0.44	0.24	0.02
Self-efficacy	-0.20	0.01	-0.27	0.04	-0.09	0.39
Perceived interference	0.05	0.57	0.06	0.66	0.01	0.91
Age	-0.001	0.99	0.01	0.96	0.04	0.74
BMI	0.09	0.25	0.18	0.14	0.04	0.68
Diabetes duration	-0.007	0.93	0.15	0.19	-0.09	0.41
HbA1c	0.006	0.94	0.12	0.32	0.002	0.41
Sex	-0.22	0.006	-		-	
Adjusted model-R ²	<i>R</i> ² =10.6%		<i>R</i> ² =21.29	%	<i>R</i> ² =4.6%	

Table 3 - Association of sedentary behaviour with symptoms of depression and anxiety, diabetes self-efficacy and perceived interference by liner regression analyses in the overall cohort and separately for men and women.