

An epidemiological approach to depression

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Summary

This thesis was prepared at The Maastricht Study, CAPHRI Care and Public Health Research Institute, and CARIM School for Cardiovascular Disease at Maastricht University, in collaboration with University Vita-Salute San Raffaele, Milan (Italy).

As described in chapter 1, depression is one of the most prevalent mental disorders with a high burden of disease. It causes severe symptoms that negatively affect how individuals feel, think, and handle daily activities, such as performing PA, eating, interact with others or working. Despite research efforts, the aetiology of depression, as well as treatment are still far from being known. Population-based studies are ideal to investigate/identify risk and/or protective factors associated with depression.

In the current thesis we focused on social network characteristics and the lifestyle factors 24-hour pattern of physical activity (PA) and sedentary behaviour, cardiorespiratory fitness (CRF) and diet in relation to depression. For all studies conducted in this thesis, with the exception of the umbrella review, data from The Maastricht Study were used, a population-based observational prospective cohort study, which enrolled individuals aged between 40 and 75 years and living in the southern part of the Netherlands. In all chapters, except chapter 5, we assessed prevalent depressive symptoms using a validated Dutch version of the 9-item Patient Health Questionnaire (PHQ-9) at baseline and annually during follow-up. Moreover, a prevalent and lifetime episode of major depressive disorder (MDD) was assessed by the Mini-International Neuropsychiatric Interview.

In **chapter 2** we analysed the association between social network characteristics and prevalent and incident depressive symptoms and social network characteristics were assessed at baseline through a name generator method from which a broad range of functional and structural social network characteristics were assessed. Our results showed that less emotional support was consistently associated with both prevalent MDD, as well as prevalent and incident depressive symptoms. In addition, the proportion of family members, whom may be crucial in the delivery of emotional support, was significantly associated with both prevalent and incident depressive symptoms. In light of this, our results indicate that educating family members about their important role in depression, as well as the importance of being supportive, could be a useful strategy in reducing the burden of depression.

In **chapter 3** we assessed the association between prevalent and incident depressive symptoms with daily patterns of sedentary behaviour and different levels of PA. PA and sedentary time were measured using the activPAL3TM physical activity monitor, and all the movements activities were estimated hourly. Our results show that having prevalent depressive symptoms was significantly associated with more sedentary time, especially during afternoon and early evening hours, less LiPA during the whole day, and less moderate-to-vigorous physical activity (MVPA) during the morning, early afternoon and during the evening, without differences between week or weekend days. Similar patterns, but attenuated, were also found for incident depressive symptoms. Hence, no specific time slots seemed to be associated with both prevalent or incident depressive symptoms. For this reason, our findings may indicate that less sedentary time and more intense PA can be important targets for the prevention of depression irrespective of the timing of the day.

In **chapter 4** we evaluated the association between cardiorespiratory fitness (CRF) and incident depressive symptoms. As an objective measure of CRF, estimated maximum power output adjusted for body mass (W_{max} kg⁻¹) was used. W_{max} was estimated from a graded submaximal exercise protocol performed on a cycle ergometer system. Our findings show that in adult Caucasian population, a higher CRF was associated with a reduced risk of incident depressive symptoms. Compared to individuals with a low CRF, those with a moderate-to-high CRF had 50% lower risk of developing clinically relevant depressive symptoms. Same results were obtained also after additional adjustment for moderate-to-vigorous PA. Since moderate to vigorous physical activity (MVPA) is one of the factors affecting CRF but its effect on CRF is variable among individuals, future studies should help to understand which factors could improve CRF especially in those MVPA-non-responders.

In **chapter 5** we conducted an umbrella review assessing the strength and quality of the available evidence on the associations of different dietary patterns on depression. In February 2022 we searched on PubMed/MEDLINE, Scopus, Web of Science, EMBASE, PsycINFO and Cochrane Database, collecting 1,799 articles. After the selection process, a total of 19 articles were included, assessing a wide range of diets, including healthy dietary patterns (n= 8), Mediterranean diet (MedDiet) (n= 6), Dietary Inflammatory Index (DII) (n= 5); Western diet (n= 4), Dietary Approaches to Stop Hypertension (DASH) (n= 2), vegetarian diets (n=4), and other dietary interventions (n=2) (the sum does not come to 19 since some studies assessed more than one diet). The methodological quality of the included meta-analyses was generally low or critically low. The strength of evidence was generally weak; however, convincing or suggestive evidence was only found for an association of MedDiet, DII and depression. Higher adherence to the MedDiet and lower DII score was significantly associated with lower risk of depression.

In **chapter 6** we verified the association between three different healthy dietary patterns, defined *a priori*, and depression. Diet was assessed at baseline using a validated, self-administered food frequency questionnaire (FFQ). Based on this FFQ, the Dutch Healthy Diet Score (DHD), the adherence to MedDiet, and the DASH score were assessed. In the fully adjusted model, we found only a significant association between the DHD and incident depressive symptoms. We did not find any association between the three dietary pattern scores and prevalent depressive symptoms or MDD. Our study confirms the important role of healthy diet in preventing depression.

Finally in **chapter 7** the main observations of this thesis are discussed and are also put in perspective of the current scientific literature. Moreover, limitations and strengths of the current work are also discussed. In particular, selection and information bias are commented, as well as overadjustment and confounding. To conclude, in the current thesis we assessed the association between several lifestyle factors and social network characteristics; however, future studies should help in understanding the dose-response effect of these determinants and depression (if any), or even if a combined effect of two or more of them can reduce the risk of depression.