

# SYSTEMATIC REVIEW OR META-ANALYSIS

# The bidirectional longitudinal association between depressive symptoms and HbA<sub>1c</sub>: A systematic review and meta-analysis

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# Abstract

**Aim:** To investigate whether there is a bidirectional longitudinal association of depression with  $HbA_{1c}$ .

**Methods:** We conducted a systematic literature search in PubMed, PsycINFO, CINAHL and EMBASE for observational, longitudinal studies published from

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**Results:** We retrieved 1642 studies; 26 studies were included in the systematic review and eleven in the meta-analysis. Most studies (16/26) focused on type 2 diabetes. Study quality was rated as good (n = 19), fair (n = 2) and poor (n = 5). Of the meta-analysed studies, six investigated the longitudinal association between self-reported depressive symptoms and  $HbA_{1c}$  and five the reverse longitudinal association, with a combined sample size of n = 48,793 and a mean follow-up of 2 years. Higher levels of baseline depressive symptoms were associated with subsequent higher levels of  $HbA_{1c}$  (partial r = 0.07; [95% CI 0.03, 0.12];  $I^238\%$ ). Higher baseline  $HbA_{1c}$  values were also associated with 18% increased risk of (probable) depression  $(OR = 1.18; [95\% CI 1.12,1.25]; I^20.0\%)$ .

**Conclusions:** Our findings support a bidirectional longitudinal association between depressive symptoms and  $HbA_{1c}$ . However, the observed effect sizes were small and future research in large-scale longitudinal studies is needed to confirm this association. Future studies should investigate the role of type of diabetes and depression, diabetes distress and diabetes self-management behaviours. Our results may have clinical implications, as depressive symptoms and  $HbA_{1c}$  levels could be targeted concurrently in the prevention and treatment of diabetes and depression.

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### KEYWORDS

 $depression, diabetes \ mellitus, glycated \ haemoglobin \ A, longitudinal \ studies, \ meta-analysis, \ systematic \ review$ 

# 1 | INTRODUCTION

Depression and diabetes mellitus are among the leading causes of disability worldwide. The most recent estimates, available for 2017, suggest worldwide 264 million people living with depression and 476 million with diabetes; these figures are expected to rise. The co-occurrence of type 2 diabetes and depression is frequently reported, and their association is suggested to be bidirectional.<sup>2-7</sup> Metaanalyses report a 15% increased risk of depression in individuals with diabetes.<sup>2</sup> For incident diabetes in individuals with depression, risk estimates in meta-analyses vary from% 38 to 60%. <sup>2,8</sup> Individuals with comorbid depression and diabetes have shown a greatly reduced health-related quality of life, compared to individuals with only depression or only diabetes.9 Moreover, depression in the presence of diabetes has been linked to an increased risk of incident diabetes complications such as retinopathy, neuropathy, and nephropathy, 10 as well as cardiac events, 11 cardiovascular mortality<sup>11,12</sup> and all-cause mortality.<sup>12</sup>

# **Novelty Statement**

- The association between depression and diabetes has been suggested to be bidirectional.
   A possible mechanism linking depression and diabetes are suboptimal HbA<sub>1c</sub> levels. Prior studies regarding the association between depression and HbA<sub>1c</sub> levels showed mixed results and have not been systematically summarised.
- The present meta-analysis suggests a bidirectional longitudinal association between depressive symptoms and HbA<sub>1c</sub>. Due to the low number of eligible studies, further research in large-scale longitudinal studies is needed to confirm this association.
- Depressive symptoms and HbA<sub>1c</sub> levels may be targeted concurrently by prevention and treatment efforts.