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The relationship between gluten free diet adherence and depressive symptoms in adults with coeliac disease: A systematic review with meta-analysis

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ABSTRACT

Purpose: Depressive symptoms are common in patients with coeliac disease (CD) and may represent a barrier to gluten free diet (GFD) adherence. The aims of this meta-analysis were: (1) to synthesise the evidence on the relationship between depression or depressive symptoms and degree of adherence to a GFD in patients with CD who are already attempting a GFD (i.e., post-diagnosis and onset of GFD), and (2) to summarise the direction of causation of any observed relationship.
Methods: A random effects meta-analysis of 8 cross-sectional studies (N = 1644) was conducted. Included studies measured self-reported depressive symptoms and GFD adherence using either a dietitian interview or validated self-report questionnaire that considered unintentional gluten consumption.
Results: There was a moderate association between poorer GFD adherence and greater depressive symptoms ($r = 0.398$, 95% CI = 0.321–0.469), with marked heterogeneity in the effects ($I^2 = 66.8\%$). A sensitivity analysis excluding studies with a moderate/high (k = 1) or unclear risk of bias (k = 1) did not change the results.
Conclusion: The low number of studies meeting inclusion criteria limits the strength of the conclusions. Available evidence suggests there is an association between poorer GFD adherence and self-reported depressive symptoms; however, studies using longitudinal and prospective designs, and reliable measures, particularly for adherence, are needed to confirm this association. The direction of causation between depression and adherence remains unclear.

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1. Introduction

Coeliac disease (CD) is a chronic autoimmune condition involving intolerance to dietary gluten, for which clinical management involves lifelong strict adherence to a gluten free diet (GFD; Green & Cellier, 2007). Undiagnosed or poorly managed, CD is associated with gastrointestinal and malabsorption symptoms and increased risk of long-term health complications, including intestinal cancers, osteoporosis, and infertility (Green & Cellier, 2007; Green & Jabri, 2003). Depression is also often cited as a symptom of undiagnosed CD (Jackson, Eaton, Cascella, Fasano, & Kelly, 2012), and clinically diagnosed depression and/or depressive symptoms (typically collapsed in reviews) appear to occur with greater frequency and/or severity in CD than healthy samples (Smith & Gerdes, 2012; Zingone et al., 2015).

Meta-analyses conducted in other chronic illnesses (e.g., diabetes) have found significant associations between depression and non-adherence to medication and other treatment components (e.g., diet and physical activity recommendations; DiMatteo, Lepper, & Croghan, 2000; Gonzalez et al., 2008; Grenard et al., 2011), with depressed patients being 1.76-to-3 times less likely to adhere to medical treatment recommendations than non-depressed patients (DiMatteo et al., 2000; Grenard et al., 2011). Further, reduced treatment adherence is one mechanism via which the link between depression and many preventable chronic illnesses may be explained (Katon, 2011). That is, depression may act as a barrier to good self-care (e.g., resulting in poor diet and physical inactivity – or in the case of CD, poor management of the GFD) via deficits in energy and memory, which leads to the development of risk factors such as obesity, which prompt or exacerbate the symptoms of chronic illness (e.g., diabetes), and, in turn, become further barriers to good adherence (Katon, 2011).

The literature on a comparable relationship between depression and GFD adherence in CD patients has yet to be synthesised, with existing reviews on the incidence of depression in CD (Smith & Gerdes, 2012; Zingone et al., 2015) being methodologically unable to answer the more specific question regarding GFD adherence. Firstly, evidence for the depression-adherence association comes primarily from studies assessing differences in depression between newly-diagnosed patients and those already being managed on a GFD, without assessment of the adequacy of dietary adherence in the established gluten free patients. Secondly, amongst studies that have specifically measured GFD adherence, conclusions have been drawn without due consideration of the impact of unreliable measurement of GFD adherence. Finally, the absence of a healthy control group (inclusion criteria for both previous reviews) meant that many studies relevant to answering this more specific question were excluded.

Debate exists on the optimal way to measure GFD adherence (Leffler et al., 2007; Ludvigsson et al., 2014; Vahedi et al., 2003), resulting in large variation in definitions and measurement across studies (Hall, Rubin, & Charnock, 2009). Intentional gluten consumption in patients with CD appears rare, with unintentional non-adherence (e.g., due to cross contamination or errors in label reading) representing the most common reason for lapsing from the GFD (Hall, Rubin, & Charnock, 2013; Sainsbury, Mullan, & Sharpe, 2013a). Commonly used adherence measures, such as single-item self-report questions (e.g., 'how strictly do you adhere to your GFD?' with Likert or visual analogue response scales from 'not at all' to 'very strictly') and serological analyses, are unreliable at detecting incomplete adherence, particularly with increased time on a GFD (Leffler et al., 2007). These methods also do not correlate well with dietitian-rated assessments (Fera, Cascio, Angelini, Martini, & Guidetti, 2003; Leffler et al., 2007; Vahedi et al., 2003), the method currently deemed the 'gold standard' (Leffler et al., 2007; Ludvigsson et al., 2014). The dietitian assessment involves completion of a 3-day food record (prior to the session), a food ingredient quiz, and a dynamic clinical interview in which an experienced dietitian evaluates the food record with the patient to identify any gluten consumption or sources of cross-contamination that may compromise adherence. Regarding simple self-report measures, the discrepancy with dietitian assessments probably results from their failure to consider unintentional gluten consumption, which, by definition, occurs outside of conscious awareness, as well as inaccuracies in patient understanding and knowledge of the GFD (Leffler et al., 2007; Silvester, Weiten, Graff, Walker, & Duerksen, 2016). Serological results adequately indicate gluten-related damage at diagnosis; however, once on a GFD, produce frequent false negative results in known partially adherent individuals (Leffler et al., 2007; Vahedi et al., 2003).

To fill the gap in the availability of valid and reliable tools for assessing GFD adherence and provide a feasible measure within the research context, several questionnaires that do account for unintentional gluten exposure have been designed. These include the Coeliac Dietary Adherence Test (CDAT; Leffler et al., 2009), which was developed in consultation with an expert panel, and has demonstrated psychometric properties. The CDAT has acceptable sensitivity and specificity when compared against a dietitian assessment, and is superior to serological analysis in predicting dietitian-rated adherence categories (Leffler et al., 2009). The Biagi GFD score (Biagi et al., 2009) and the Morisky Medication Adherence Scale (Morisky, Ang, Krousel-Wood, & Ward, 2008; Morisky, Green, & Levine, 1986), adapted to GFD adherence (Casellas et al., 2008) have also been proposed and undergone some psychometric evaluation, although neither have been validated against the gold standard. While measures that consider unintentional gluten exposure are an advancement over single-items that rely on accurate patient recall, truly reliable assessment of GFD adherence is difficult and remains a challenge in both research and clinical practice.

Current guidelines on the management of CD (Ludvigsson et al., 2014; NICE, 2015) and other chronic physical health problems