CrossMark

Are people with schizophrenia adherent to diabetes medication? A comparative meta-analysis

Paul Gorczynski[a,*], Joseph Firth[b], Brendon Stubbs[c,d], Simon Rosenbaum[e], Davy Vancampfort[f,g]

[a] University of Portsmouth, Department of Sport and Exercise Science, Portsmouth, UK PO1 2UP
[b] Institute of Brain, Behaviour and Mental Health, University of Manchester, Manchester, UK M13 9PL
[c] Physiotherapy Department, South London and Maudsley NHS Foundation Trust, London, UK SE5 8AZ
[d] Health Service and Population Research Department, Institute of Psychiatry, Psychology and Neuroscience, King's College London, De Crespigny Park, London, UK WC2R 2LS
[e] Department of Exercise Physiology, School of Medical Sciences, University of New South Wales, Sydney 2052 Australia
[f] KU Leuven – University of Leuven, Department of Rehabilitation Sciences, 3000 Leuven, Belgium
[g] KU Leuven – University of Leuven, University Psychiatric Center KU Leuven, 3000 Leuven-Kortenberg, Belgium

ARTICLE INFO

ABSTRACT

Individuals living with schizophrenia are 2–3 times more likely to experience type 2 diabetes mellitus. Diabetes medication adherence is essential to reduce morbidity and mortality in this population. We conducted a meta-analysis of diabetes medication adherence among people with schizophrenia, and compared this to those without schizophrenia. A systematic search strategy was used to identify all articles reporting adherence to diabetes medications among patients with schizophrenia. In total, 10 unique studies reporting data from 33,910 people with schizophrenia were included. Random effects meta-analysis showed people with schizophrenia adhered to medication on 77.3% of days prescribed (n=32080, 95%CI=73.6–81%, I^2=99.2%,), and adhered on 4.6% more days per year than those without schizophrenia (p < 0.01, 95%CI=2.4–6.7%, I^2=92.5%, schizophrenia n=19367, controls=170,853). Furthermore, 56% of individuals with schizophrenia (n=33680) were considered "adherent" (i.e. > 80% adherence over 12–24 month) to diabetes medication, which was significantly more than those without schizophrenia (OR=1.34, 95%CI: 1.18–1.52, p < 0.01). Factors which were positively associated with diabetes medication adherence were age, number of outpatient visits, along with multiple medication administration variables. Future prospective research should examine diabetes monitoring, medication prescription, and subsequent adherence in fully representative samples. Novel interventions for maximizing compliance to diabetes medication in this vulnerable population should also be explored.

1. Introduction

Individuals living with schizophrenia are highly susceptible to type 2 diabetes mellitus (T2DM) (de Hert et al., 2009). Current estimates show that individuals with schizophrenia are 2–3 times more likely to acquire T2DM than the general population (Stubbs et al., 2015). It is believed that approximately 10 to 15% of individuals with schizophrenia have T2DM (Vancampfort et al., 2016). A number of factors contribute to a higher T2DM prevalence in this population, including family history, cardio-metabolic side effects of antipsychotic medication, and lifestyle factors such as physical inactivity and poor diet quality (Stubbs et al., 2015).

Higher T2DM prevalence carries a number of health consequences for individuals with schizophrenia. Both T2DM and excess weight are independent risk factors for developing cardiovascular disease and place individuals with schizophrenia at greater risk of early mortality (Ribe et al., 2014). Previous research has demonstrated that as a result of cardiovascular disease, individuals with schizophrenia have a shortened life expectancy of approximately 10 to 20 years (Ribe et al., 2014).

A number of strategies have been recommended for helping individuals with schizophrenia to manage T2DM, and to maintain and promote cardio-metabolic health. These strategies have primarily focused on lifestyle changes, such as increasing physical activity and maintaining a low-calorie and low fat diet (Annamalai and Tek, 2015). Additional strategies have included regular blood glucose monitoring and encouraging adherence to diabetes medication. Medication adherence can be defined as voluntary involvement of taking medication in

pursuit of a therapeutic result (Delamater, 2006). Adequate diabetes medication adherence can help individuals to maintain glycemic control and reduce the likelihood of microvascular complications that result from of diabetes, including blindness, renal failure, and amputations (Cade, 2008). In the general population, adherence is determined by multiple factors including: patient-related (younger age, female gender, smoking, impulsivity ethnic minority groups), condition-related (the presence of depression or other chronic diseases, shorter duration of diabetes, fewer diabetes complications), socioeconomic (lack of financial resources/increased medication costs, lower education level, lack of family support), health system-related (increased distance to nearest pharmacy, lower continuity of care) and therapy-related (concurrent medication use, adverse effects, poor previous experience with medication) (World Health Organization, 2003). In comparison to the general population, individuals with schizophrenia are less likely to receive diabetes education, and less likely to have glycated hemoglobin (HbA1C) and serum lipid levels regularly monitored (Cimo et al., 2012; Dickerson et al., 2005; Goldberg et al., 2007). To our knowledge, only one previous narrative systematic review has examined diabetes medication adherence in people with schizophrenia, and results were limited to only six studies (Gorczynski et al., 2014). The purpose of this study was to provide an update on diabetes medication adherence in individuals with schizophrenia, and apply meta-analytic techniques to obtain an aggregated understanding of diabetes medication adherence rates in people with schizophrenia compared to those without. A secondary purpose of this meta-analysis was to determine factors associated with medication adherence in people with schizophrenia.

2. Methods

This systematic review adhered to the PRISMA statement to ensure transparency and comprehensive reporting of methodology and results (Moher et al., 2009). The protocol for this systematic review adhered directly to the methodology of a previously-published review (Gorczynski et al., 2014), only using an updated search to identify more recent studies. The statistical analyses were also pre-determined in advance of conducting the review to aggregate all eligible data on adherence to anti-diabetic medications in naturalistic settings among people with schizophrenia.

2.1. Search strategy and selection criteria

All studies included in an earlier systematic review of anti-diabetes medication adherence in schizophrenia (Gorczynski et al., 2014) were automatically eligible for this meta-analysis. We also performed an updated electronic database search of Cochrane Central Register of Controlled Trials, AMED (Allied and Complementary Medicine), Embase, MEDLINE, PsycINFO, PsycARTICLES and Ovid MEDLINE using the following keyword search terms: "compliance" or "adherence" AND "hypoglycemic agents" or "insulin" or "metformin" or "diabetes" AND "psychosis" or "antipsychotic" or "schiz*". This search was conducted from 01/01/2013 – 08/02/2016 in order to update the results of the earlier systematic review which used an identical search protocol. The reference lists of retrieved articles were searched and a basic search of Google Scholar was conducted using the same key words in an effort to identify additional relevant publications.

Only peer-reviewed, English-language, original research articles were included in this review. We aimed to include all studies which reported adherence to diabetes medications among patients with schizophrenia in naturalistic settings as a dependent variable. Our review focused on T2DM. Intervention studies reporting adherence rates over the course of a randomized trial were not eligible for inclusion, since medication adherence in clinical trials differs significantly from real-life observations.

Studies were excluded from this review if they failed to report adherence data for diabetes medication in schizophrenia or schizophrenia-like disorders. Studies with mixed samples of psychiatric disorders were eligible if > 80% of the sample had a diagnosis of schizophrenia/schizoaffective disorder. Data from studies in which < 80% of the sample had a confirmed diagnosis of schizophrenia / schizophrenia-like disorders were only included if adherence specifically among the patients with schizophrenia / schizophrenia-like disorders could be accurately determined and extracted. Where this was not reported, the corresponding author of the article was contacted to obtain this information. Studies which did not disclose specific diagnoses of the sample were eligible for inclusion provided that the entire sample was receiving antipsychotic medications.

2.2. Data extraction and analysis

Two reviewers (JF and PG) screened the articles independently to assess eligibility. Any discrepancies were resolved through discussion between authors until agreement was reached. A systematic tool was developed to extract the following information from each study:

(1) Study characteristics: sample size, demographics, location and setting, study design, type of medications examined, and measurement methods used.
(2) Adherence to diabetes medications: (i) mean daily adherence i.e. number of days-per-year on which medication was taken as prescribed, and (ii) the number of patients who were 'adherent', defined as achieving > 80% adherence to medication regimes (Kreyenbuhl et al., 2010). Identical data was also extracted from non-schizophrenia control samples. Additionally, any factors found to be associated with diabetes medication adherence in patients with schizophrenia were extracted and systematically reviewed.

2.3. Statistical analyses

Statistical analysis was conducted in OpenMetaAnalyst (Wallace et al., 2009). Random-effects models were applied to all meta-analyses in order to account for the variance between studies (DerSimonian and Laird, 1986).

The primary outcome was the overall daily adherence to diabetes medication regimes in people with schizophrenia, as assessed by quantitative measures. Data from all studies reporting the number of days-per-year on which medication was taken as prescribed were pooled (Wallace et al., 2009), to determine overall adherence. Following this, pooled estimates of daily adherence rates in schizophrenia and non-schizophrenia samples were compared to estimate the difference in adherence between the two groups.

As a secondary outcome, we examined the proportion of schizophrenia patients who were 'adherent' to diabetes medications (i.e. > 80% on objective measures (Kreyenbuhl et al., 2010). Therefore, the proportions of adherent patients were pooled across all studies reporting this variable, in order to calculate a weighted estimate with 95% confidence intervals. Additionally, the numbers of adherent people with schizophrenia was compared to samples without schizophrenia using odds-ratio meta-analysis.

Variance between studies was assessed using Cochran's Q and reported as I^2, which quantifies the degree of variance resulting from between-study heterogeneity, rather than by chance. The degree of potential publication bias was examined through visual inspection of funnel-plots of the association between proportion estimate and SE standard errors and Egger's test for small-study bias. Eligible studies reporting data not able to be pooled for meta-analysis were included in the systematic review of study findings.

To assess determinants of diabetes medication adherence, a framework established by Gorczynski et al. (2014) was used for this analysis. Independent variables that were shown to be significantly associated