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Prevalence of underweight in patients with schizophrenia: A meta-analysis

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ABSTRACT

Aims: Although the relationship between body mass index and all-cause mortality is U-shaped, underweight has received comparatively less attention than obesity. There is only limited evidence to date regarding underweight among patients with schizophrenia. This is the first meta-analysis to address the prevalence of underweight in these patients.
Methods: We conducted database searches (PubMed, PsycINFO) to identify studies examining underweight in patients with schizophrenia. In total, 17 studies (18 groups) with 45,474 patients were included; data were extracted independently by two authors. A meta-analysis was performed to calculate the pooled prevalence of underweight in patients.
Results: The pooled prevalence of underweight was 6.2% (95% CI = 4.5–8.6) for the 18 groups, which included 45,474 patients with schizophrenia. The heterogeneity was $I^2 = 98.9\%$ (95% CI = 98.7–99.1%). Four studies with 4 groups, consisting of 30,014 individuals, focused on Japanese inpatients with schizophrenia. The pooled prevalence of underweight among inpatients in these 4 groups was 17.6% (95% CI = 15.5–20.0). Fourteen studies were conducted with non-Japanese inpatients and included 14 groups of 15,460 patients with schizophrenia. The pooled prevalence of underweight in non-Japanese inpatients was 4.6% (95% CI = 3.9–5.4). The proportion of underweight in the 18 groups significantly varied between Japanese inpatients and other patients.
Conclusions: The results indicated that Japanese inpatients with schizophrenia have a high proportion of underweight. Future research should focus on evaluating interventions that target underweight.

1. Introduction

Underweight has received comparatively less attention than obesity, and the evidence regarding underweight in patients with schizophrenia remains limited. In general populations, the relationship between body mass index (BMI) and all-cause mortality is U-shaped, with both obesity and underweight being associated with increased mortality (Berrington de Gonzalez et al., 2010; Nagai et al., 2010). Although several studies have stated that obesity could increase the health risks of patients with schizophrenia (Weiden et al., 2004; Chwastiak et al., 2009; Sugawara et al., 2013; Li et al., 2016; Heald et al., 2017), underweight should also receive considerable attention, especially in Asia, where the proportion of underweight in the population is relatively high (Moore et al., 2010).

The life expectancy of people with schizophrenia is approximately 20 years less than that of the general population, and this mortality gap has widened (Laursen, 2011; Nielsen et al., 2013; Walker et al., 2015). A recent study concerning patients with schizophrenia showed that the leading causes of excess deaths can be directly attributed to physical diseases, such as cardiovascular and respiratory diseases (Olfson et al., 2015). While obesity has been considered a major risk factor for metabolic syndrome (Zhang et al., 2011), cardiovascular disease (Marinou et al., 2010), and premature death (Adams et al., 2006; Pischon et al., 2008), several studies conducted in Asian populations have found that underweight is associated with mortality to the same extent as obesity due to the occurrence of ischemic heart disease (Chen et al., 2013).

Since Kitabayashi and colleagues first reported a high prevalence (16.1%) of underweight among Japanese inpatients with schizophrenia (Kitabayashi et al., 2006), other studies from Japan have supported this finding (Inamura et al., 2012; Suzuki et al., 2014). However, several studies conducted in other countries did not show similar results

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(Correll et al., 2008; Chu et al., 2011; Guo et al., 2013). The prevalence of underweight among patients with schizophrenia is still unknown. Although the causes of underweight among patients are not fully understood, several factors, including genetics, metabolism, drug use, over-exercise, lack of food (frequently due to poverty), and medical conditions, can affect weight status (Heymsfield and Wadden, 2017).

Given the aforementioned gap in the literature, we conducted a meta-analysis of underweight in people with schizophrenia. We aimed to (1) describe the pooled frequencies of underweight in patients with schizophrenia, and (2) clarify the variables that account for subgroup differences, and (3) compare the prevalence of underweight in patients with schizophrenia and the general population. To our knowledge, this is the first study to investigate the pooled prevalence of underweight in patients with schizophrenia. Knowledge of underweight in this population might help psychiatric clinicians identify patients at risk of mortality.

2. Method

2.1. Study selection

The systematic review was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards (a protocol used to evaluate systematic reviews) (Knobloch et al., 2011). Electronic databases, including PubMed and PsycINFO, were initially searched using six terms: the term 'underweight' or 'BMI' or 'body mass index' was paired with 'schizophrenia' or 'schizoaffective disorder' or 'schizophreniform disorder'. We included original studies: (1) observational studies (cross-sectional, prospective studies) and (2) baseline data of randomized controlled trials or prospective studies, regardless of clinical setting (inpatient, outpatient). We excluded the following: (1) case reports; (2) comments, editorials, letters; (3) studies not performed on human participants; (4) non-English publications; (5) studies including conditions likely to significantly affect the prevalence of underweight (e.g., retrospective studies of deceased patients, completers-only analysis of interventions, inclusion criteria limited to lower BMI, lack of BMI data, lack of classification as underweight); (6) studies that had <100 participants with schizophrenia (to avoid small-study effect) (Nüesch et al., 2010); and (7) studies including participants with other psychiatric diagnoses. Two researchers (NS and NYF) independently searched the literature. After all papers had been assessed, any discrepancies in the responses were identified and discussed to reach a consensus on the best option. Data were extracted from each article using a standardized form including the first author, publication year and other information.

2.2. Data extraction

All authors independently extracted data on the number of total patients and those with underweight. We also extracted data regarding the demographic and clinical characteristics of the participants in the studies. The characteristics of the studies included in this meta-analysis are shown in Table 1.

2.3. Statistical analysis

First, we assessed the pooled prevalence of underweight in patients with schizophrenia who were treated at hospitals. We calculated the pooled prevalence and its 95% confidence interval (CI) with a fixed-effects and a random-effects model (DerSimonian and Laird, 1986). Additionally, we performed subgroup analysis by clinical setting [(Japanese vs non-Japanese patients) or (Japanese inpatients vs other patients)]. Second, we conducted meta-regression analyses including the binary subgroup indexes above as the exploratory variables to investigate the differences by clinical setting. Third, we calculated the relative risk to investigate the differences in the prevalence of underweight between patients with schizophrenia and members of the general population. We used the I^2 statistic and its 95% CI to estimate heterogeneity. The I^2 statistic was considered high when it was 75% or more (Higgins et al., 2003). The significance level was set at $p < 0.05$. The meta-analysis and related statistical analyses were performed with meta package version 4.8-2 in R version 3.3.0 (Schwarzer, 2017; Venables et al., 2016).

3. Results

3.1. Search results and included participants

After excluding duplicates and non-relevant hits, our search yielded 17 publications (18 groups) that met the inclusion criteria (Fig. 1). All included studies adopted a cross-sectional design. The final sample comprised 45,474 patients with schizophrenia but no matched controls. The sample sizes of groups ranged from 100 to 15,171 patients, with a median sample size of 303. At the group level, the mean age of patients with schizophrenia ranged from 23.6 to 60.0 years, and 55.7% (25,336/45,474) were male. More details of the included studies and participants are presented in Table 1.

3.2. Prevalence of underweight and subgroup analyses

The pooled prevalence of underweight based on the random-effects model was 6.2% (95% CI = 4.5–8.6) for the 18 groups, which included 45,474 patients with schizophrenia (Supplementary Fig. S1). The heterogeneity was $I^2 = 98.9\%$ (95% CI = 98.7–99.1%).

Under the same model, the 5 groups, including 35,455 Japanese patients, showed a pooled prevalence of underweight of 13.0% (95% CI = 8.8–18.7) (Fig. 2). The heterogeneity was $I^2 = 99.4\%$. Thirteen studies (13 groups), which were conducted in non-Japanese patients, included 10,019 patients with schizophrenia. The pooled prevalence of underweight in non-Japanese patients with schizophrenia was 4.6% (95% CI = 3.7–5.7) for the 13 groups. The heterogeneity was $I^2 = 65.3\%$. The prevalence of underweight in the 18 groups significantly varied (Q value = 20.65, $p < 0.001$) between Japanese and non-Japanese patients.

We identified 4 groups focusing on Japanese inpatients with schizophrenia that included 30,014 individuals. In the random-effects model, the pooled prevalence of underweight in Japanese inpatients with schizophrenia in the 4 groups was 17.6% (95% CI = 15.5–20.0) (Fig. 3). The heterogeneity was $I^2 = 93.2\%$. Fourteen studies (14 groups) conducted in non-Japanese inpatients included 15,460 patients with schizophrenia. Under the same model, the pooled prevalence of underweight in non-Japanese patients with schizophrenia was 4.6% (95% CI = 3.9–5.4) for the 14 groups. The heterogeneity was $I^2 = 63.0\%$. The pooled prevalence of underweight was significantly higher among Japanese inpatients than in other patients (Q value = 154.54, $p < 0.001$).

The meta-regression analysis revealed that setting had a significant effect on the prevalence of underweight in Japanese patients (regression coefficient: 1.16, 95% CI: 0.64, 1.69, $p < 0.001$) and in Japanese inpatients (regression coefficient: 1.48, 95% CI: 1.26, 1.71, $p < 0.001$).

Among studies that included healthy controls (Supplementary Table 1), pooling data from 35,555 people with schizophrenia and 36,374 controls yielded a significant RR of 2.13 (95% CI = 1.65–2.76). Of these studies, an analysis restricted to studies conducted in Japan showed a significant RR of 2.18 (95% CI = 1.66–2.86). Furthermore, an analysis restricted to studies of Japanese inpatients showed a significant RR of 2.33 (95% CI = 2.08–2.60) (Fig. 4).

4. Discussion

To the authors' knowledge, this is the first meta-analysis concerning the prevalence of underweight in people with schizophrenia. Approximately one in 16 individuals with schizophrenia was underweight,

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