**Prevalence of Underweight in People with Severe Mental Illness: Systematic Review and Meta-Analysis**

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**The number of words:**3,383 (excluding title page, abstract, references, tables)

**The number of tables:** 04

**The number of figures:**04

**Guarantor of the review:** Gerardo A Zavala

**Abstract**

**Introduction:** People with severe mental illness (SMI) have a higher prevalence of obesity as compared with the general population, however there is mixed evidence about the prevalence of underweight. Thus, the aim of this study is to determine the pooled prevalence of underweight in people with SMI and its association with socio-demographic factors; and to compare the prevalence of underweight between SMI and the general population.

**Methods:**  MEDLINE, PsycINFO, and EMBASE databases were searched to identify observational studies assessing the prevalence of underweight in adults with SMI (schizophrenia, major depressive disorder with psychotic features, and bipolar disorders). Screening, data extraction and risk of bias assessments were performed independently by two co-authors, with disagreements resolved by consensus. Random effect estimates for the pooled prevalence of underweight and the pooled odds of underweight in people with SMI compared with the general population were calculated. Subgroup analyses were conducted for type of SMI, setting, antipsychotic medication, region of the world, World Bank country income classification, data collection and sex.

**Result:** 40 estimates from 22 countries were included. The pooled prevalence of underweight in people with SMI was 3.8% (95% C.I. = 2.9-5.0). People with SMI were less likely to be underweight than the general population (OR 0.65; 95% C.I. = 0.4-1.0). The pooled prevalence of underweight in SMI in South Asia was 7.5% (95%C.I. = 5.8-14.1) followed by Europe and Central Asia at 5.2% (95%C.I. = 3.2-8.1) and North America at 1.8% (95%C.I. = 1.2-2.6).

**Conclusion:** People with SMI have lower odds of being underweight compared to the general population. People with schizophrenia had the highest prevalence of underweight compared to other types of SMI. Japan and South Asia have the highest prevalence of underweight in people with SMI.

**Keywords:** Severe mental illness; schizophrenia; bipolar disorder; underweight, systematic review

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# Introduction

Severe mental illness (SMI) includes schizophrenia, major depressive disorder with psychotic features and bipolar disorders (Evans et al., 2016). People with SMI have a high prevalence of physical health conditions and increased mortality [(Firth et al., 2019; World Health Organisation, 2018)](https://paperpile.com/c/vZxRdk/WaLXJ%2BDxxTr). Mortality rate is three times higher among people with SMI compared to the general population ([De Hert et al., 2009;](https://paperpile.com/c/vZxRdk/LTpkd) [Vancampfort et al., 2015](https://paperpile.com/c/vZxRdk/F2qft)[)](https://paperpile.com/c/vZxRdk/LTpkd). Both obesity and underweight have a negative impact on health and well-being as illustrated by the U-shaped association between body mass index (BMI) and mortality with both obesity and underweight being associated with increased mortality [(Berrington de Gonzalez et al., 2010)](https://paperpile.com/c/1C5sjz/b05ot). Underweight is associated with micronutrient deficiencies, impaired immune response, osteoporosis and asthma [(Popkin et al., 2020)](https://paperpile.com/c/1C5sjz/ZD4Fy), and recent studies [(Park et al., 2017)](https://paperpile.com/c/1C5sjz/55lWH) show that being underweight is a risk factor for cardiovascular disease. Conversely, those with severe physical illnesses such as cancer [(American Cancer Society, 2020)](https://paperpile.com/c/vZxRdk/YKlKl), diabetes, hyperthyroidism [(Kresimira, 2009)](https://paperpile.com/c/1C5sjz/3AvO6) and tuberculosis [(Hira et al., 1998)](https://paperpile.com/c/1C5sjz/IH0Bp) are more at risk of being underweight.

The prevalence and determinants of obesity in people with SMI have been studied [(Firth et al., 2019;](https://paperpile.com/c/1C5sjz/FFPbq%2BoiBAX)  [Holt et al., 2021](https://paperpile.com/c/1C5sjz/yx3qn); [Vancampfort et al., 2015](https://paperpile.com/c/1C5sjz/RECma); WHO, 2018). However, there is more limited evidence about the prevalence of underweight and its determinants. Genetics, metabolism, lack of food, poor appetite, and drug and tobacco use have all been proposed as possible mechanisms potentially linking underweight with SMI [(Sugawara et al., 2018)](https://paperpile.com/c/1C5sjz/yHIZu). A number of studies [(Inamura et al., 2012)](https://paperpile.com/c/1C5sjz/enqki) in people with schizophrenia in Japan have consistently found a high prevalence of underweight in this population. In contrast, a meta-analysis [(Sugawara et al., 2018)](https://paperpile.com/c/1C5sjz/yHIZu) of 17 studies of underweight in schizophrenia including other regions of the world reported mixed findings, with both higher and lower rates compared with the general population. Considering the lack of reviews on underweight including other types of SMI such as bipolar disorder and severe depression, rapid changes in health risk behaviours across the world, and the increasing number of studies evaluating the physical health of people with SMI, an up-to-date synthesis of the literature to estimate prevalence of underweight in SMI is needed. This could help clinicians and policymakers understand the trends of underweight and identify groups that might be at higher risk (i.e., region of the world, type of SMI, sex).

We conducted a systematic literature review and meta-analysis to assess the prevalence of underweight in people with SMI. More specifically, our aims were 1) to determine the overall pooled prevalence of underweight and prevalence by type of SMI, setting, geographical region, country economy classification, year of data collection and sex; and 2) to assess the likelihood of underweight in people with SMI compared with matched controls from the general population.

# Materials and Methods

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA; [Moher et al., 2009)](https://paperpile.com/c/1C5sjz/6gCqo) and Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines [(Stroup et al., 2000)](https://paperpile.com/c/1C5sjz/BevmY). The protocol has been registered and published in the International prospective register of systematic reviews (PROSPERO) [CRD-42020200380](https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020200380) [(Afzal et al., 2020)](https://paperpile.com/c/1C5sjz/JQvRf). The protocol includes prevalence of overweight and obesity, the results for which are published in a separate manuscript [(Holt et al., 2021)](https://paperpile.com/c/1C5sjz/yx3qn).

# Search strategy

We conducted a systematic search of MEDLINE, PsycINFO, and EMBASE databases. Studies that were published from the date of inception up to July 2020 were included. Combining the following keywords, the search terms used were: 1) Population (“serious mental illness” OR “severe mental illness” OR “psychosis” OR “schizophrenia” OR “psychotic disorder\*” OR “psychosis” OR “psychotic” OR “schizo-affective” OR “schizoaffective” OR “manic” OR “bipolar disorder\*” OR “mania” OR “bipolar” OR “major depressive disorder” OR “depression” or “antipsychotic” ); 2) Outcome (“Body Mass Index” OR BMI OR “waist circumference” OR weight OR “percentage body fat” OR “waist to hip ratio” OR underweight OR undernourished\* OR thinness OR undernutrition \* OR malnutrition\* OR adiposity); 3) study design (cross-sectional\* OR “ cohort” OR epidemiology OR prevalence OR observant OR observational OR longitudinal OR survey OR case-control). In addition to that, we conducted citation searches for studies that were included and related systematic reviews to identify any significant additional studies.

# Study selection

For the systematic review and meta-analysis, studies were included according to the following criteria:

1. Studies included a diagnosis of SMI (bipolar affective disorder, schizophrenia and major depressive disorder with psychotic features) including adult populations (aged ≥18 years), using the definitions of standardised assessment tools such as the Diagnostic and Statistical Manual of Mental Disorders (DSM, [American Psychiatric Association, 2013)](https://paperpile.com/c/1C5sjz/quils), or the International Classification of Diseases (ICD; [WHO, 1993)](https://paperpile.com/c/1C5sjz/r2nWS);
2. Studies which estimated the prevalence of underweight using BMI, applying any established, standardised definition of underweight, i.e., the WHO criteria [(OECD/WHO, 2020; WHO Expert Consultation, 2004)](https://paperpile.com/c/vZxRdk/WqlBE%2BJVQZT) ;
3. Any observational studies (such as retrospective or prospective cohort studies, cross-sectional and case-control studies).

Studies with populations under 18 years of age, qualitative studies and those studies with a sample size below 30 were excluded. Initially our search strategy had no language restrictions, however at the full text screening stage due to resource restrictions we excluded papers if they were not in English.

# Outcomes

The primary outcome was prevalence of underweight among people with SMI.

Secondary outcomes were prevalence of underweight from matched controls from the general population (when available)

# Data Extraction (selection and coding)

Data selection and screening were completed using Covidence (Melbourne, Australia; [Covidence, 2016)](https://paperpile.com/c/1C5sjz/JmQHS). Two independent authors (HK, MA) completed the title and abstract and the full text screening; disagreements were resolved by consensus and consultation with a third and fourth independent author (GZ, BA). The full text was retrieved for articles that were considered eligible and those with insufficient information from the abstract.

One author (BA, RA, MA, SR, or HK) extracted and reviewed data for each included study by using a pre-designed data extraction form. The details included: title, authors, study design, year of data collection, sample size, geographical region according to World Bank region classification [(Fantom, Neil James & Serajuddin, 2016)](https://paperpile.com/c/1C5sjz/zV1Bh), study settings (community-based, inpatient and outpatient), country income classification (High-income countries (HIC) or low and middle-income countries (LMIC)) according to World Bank [(Fantom, Neil James & Serajuddin, 2016)](https://paperpile.com/c/1C5sjz/zV1Bh), the prevalence of underweight by gender as compared to the general population, BMI criteria of classification and prevalence of underweight, use of antipsychotic medications (open SMI population versus antipsychotic-naive cohort) and diagnosis criteria of SMI.

We also extracted the prevalence of underweight by sex and for matched controls from the general population from the available studies. For papers that reported data of the same study, we selected the paper with the most recent date of publication and with the largest sample size (if the sample size was the same). Papers that reported data independently for different countries or SMI conditions, data was separated and the underweight estimates were considered as independent studies.

# Risk of bias

Two independent authors (GZ, SR) evaluated the quality of included studies following the criteria of Joanna Briggs Institute *Critical Appraisal Checklist* [(Munn et al., 2020)](https://paperpile.com/c/1C5sjz/3N0O5)**.** The Cochrane Risk of Bias tool [(Higgins et al., 2019)](https://paperpile.com/c/1C5sjz/IHl1u) was used to carry out the overall risk of bias assessment. Studies were considered as: “low risk of bias” if all domains of the tool were scored as “yes” or only one domain was marked as “unclear”; “medium risk of bias” if two or three domains were marked as “unclear”; and “high risk of bias” if there were four or more domains marked as “unclear” or at least one of them was marked as “no” [(Lundh & Gøtzsche, 2008)](https://paperpile.com/c/1C5sjz/5Xa2y).

# Data analysis

*Descriptive analysis*

Characteristics of eligible papers were summarised, providing information on the number and frequency of studies according to the World Bank income classification, the World Bank geographical region, type of SMI (schizophrenia, bipolar disorder, or a combination of SMI operationalised as “any”), the diagnostic tool to define the SMI, the study design, year of data collection, BMI classification, gender and overall risk of bias. Using standard procedures [(Spineli et al., 2015)](https://paperpile.com/c/1C5sjz/B3a94), we imputed the year of data collection, whenever this information was not available.

*Meta-analysis*

To account for the high heterogeneity that was expected between the studies, we used random effect models. The first analysis determined the pooled prevalence of underweight. The second analysis was used to determine the odds of people with SMI of being underweight compared with matched controls from the general population. The third analysis was used to determine the odds of women with SMI being underweight compared with men with SMI. For the second and third analyses, we used those studies with data available on underweight for matched control from the general population independently.

*Sensitivity analyses*

To assess the reliability of the results, multiple sensitivity analyses were performed. First, “high risk of bias” studies were removed from the analysis. The studies which had different cut-off points for underweight from WHO classification were then removed for the second analysis. And lastly, for the overall high-income analysis, we removed those studies where data were incomplete.

The pooled prevalence of underweight was mapped by country in a world map. A weighted mean was calculated for countries with more than one study by using data from all the available studies. The R world-map library in R V4.1.1 (Vienna, Austria; [R Core Team, 2020)](https://paperpile.com/c/1C5sjz/V5jvt) was used to generate maps.

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# Results

As shown in Figure 1, after excluding 720 duplicate records, we screened 12,653 papers, of which 725 were screened for full text. We separated the estimates of underweight for each country/region for; one paper (Park et al., 2020) that provided estimates from five South Asian countries; one paper (Post et al., 2014) that reported estimates from Europe and USA; and one paper (Zavala et al., 2020) which provided estimates from Bangladesh and Pakistan. This meant from a total of 34 records, we extracted 40 independent estimates of underweight (Table 1).

[Insert **Figure 1**: *PRISMA Chart*]

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| **Table 1.** Characteristics of the studies included in the meta-analysis |
| **Author** | **Sample size** | **SMI** | **Setting** | **Country** | **WB region** | **WB income classification** | **Study design** | **Comparison with the general population** | **Comparison Males and Females** | **Overall risk of bias** |
| [Annamalai *et al.*, 2017](https://paperpile.com/c/x5aI6V/pSa7) | 326 | Schizophrenia | Outpatient | US | North America | HIC | Cohort | Yes | No | Medium |
| [Bernstein *et al.*, 2015](https://paperpile.com/c/x5aI6V/vvgE) | 62 | Bipolar disorders | Outpatient | US | North America | HIC | Cross-sectional | No | No | High |
| [Calkin *et al.*, 2009](https://paperpile.com/c/x5aI6V/br4u) | 276 | Bipolar disorders | Inpatient | Canada | North America | HIC | Cross-sectional | No | No | Medium |
| [Correll *et al.*, 2008](https://paperpile.com/c/x5aI6V/UqrD) | 185 | Any | Inpatient | US | North America | HIC | Cross-sectional | No | No | High |
| [Davidson *et al.*, 2001](https://paperpile.com/c/x5aI6V/zrYK) | 234 | Any | Outpatient | Australia | East Asia & Pacific | HIC | Cross-sectional | Yes | Yes | High |
|  [de Caluwé *et al.*, 2019](https://paperpile.com/c/x5aI6V/sjGO) | 350 | Any | Out and Inpatient | Curaçao | Latin America & Caribbean | HIC | Cross-sectional | No | No | Low |
|  [Dickerson *et al.*, 2006](https://paperpile.com/c/x5aI6V/J2iJ) | 169 | Any | Outpatient | US | North America | HIC | Cross-sectional | Yes | Yes | Low |
| [Fagiolini *et al.*, 2005](https://paperpile.com/c/x5aI6V/g9SZ) | 171 | Bipolar disorders | Outpatient | US | North America | HIC | Cross-sectional | No | No | Low |
| [Feiler *et al.*, 2012](https://paperpile.com/c/x5aI6V/qJN7) | 106 | Any | Inpatient | Australia | East Asia & Pacific | HIC | Cross-sectional | Yes | Yes | Low |
| [Fiedorowicz *et al.*, 2008](https://paperpile.com/c/x5aI6V/Gwdb) | 217 | Bipolar disorders | Inpatient | US | North America | HIC | Cross-sectional | Yes | Yes | High |
| [Galletly *et al.*, 2012](https://paperpile.com/c/x5aI6V/Cwm5) | 1286 | Any | Community | Australia | East Asia & Pacific | HIC | Cross-sectional | No | Yes | Low |
| [Huang *et al.*, 2009](https://paperpile.com/c/x5aI6V/WvBw) | 650 | Schizophrenia | Inpatient | Taiwan | East Asia & Pacific | LMIC | Cross-sectional | No | Yes | Low |
| [Inamura *et al.*, 2012](https://paperpile.com/c/x5aI6V/TZB7) | 15171 | Schizophrenia | Inpatient | Japan | East Asia & Pacific | HIC | Cross-sectional | No | Yes | Low |
| [Kitabayashi *et al.*, 2006](https://paperpile.com/c/x5aI6V/OOoG) | 273 | Schizophrenia | Inpatient | Japan | East Asia & Pacific | HIC | Cross-sectional | Yes | Yes | Low |
| [Lee *et al.*, 2012](https://paperpile.com/c/x5aI6V/JzUg) | 100 | Schizophrenia | Out and Inpatient | Singapore | East Asia & Pacific | HIC | Cross-sectional | Yes | No | Low |
| [Leitão-Azevedo *et al.*, 2006](https://paperpile.com/c/x5aI6V/GDHv) | 121 | Schizophrenia | Outpatient | Brazil | Latin America & Caribbean | HIC | Cross-sectional | No | No | Low |
| [Limosin *et al.*, 2008](https://paperpile.com/c/x5aI6V/9UDu) | 5962 | Schizophrenia | Out and Inpatient | France | Europe & Central Asia | HIC | Cross-sectional | No | Yes | Low |
| [Łopuszańska *et al.*, 2016](https://paperpile.com/c/x5aI6V/Bcmo) | 91 | Any | Inpatient | Poland | Europe & Central Asia | HIC | Cross-sectional | No | Yes | Low |
| [Mackin *et al.*, 2007](https://paperpile.com/c/x5aI6V/wddN) | 106 | Any | Outpatient | England | Europe & Central Asia | HIC | Cross-sectional | No | Yes | Low |
| [Maina *et al.*, 2008](https://paperpile.com/c/x5aI6V/16xh) | 76 | Bipolar disorders | Out and Inpatient | Italy | Europe & Central Asia | HIC | Cross-sectional | No | No | High |
| [Marthoenis *et al.*, 2014](https://paperpile.com/c/x5aI6V/TlMZ) | 86 | Schizophrenia | Inpatient | Indonesia | East Asia & Pacific | LMIC | Cross-sectional | No | No | Medium |
| [McElroy *et al.*, 2011](https://paperpile.com/c/x5aI6V/NRLK) | 875 | Bipolar disorders | Community | UK | Europe & Central Asia | HIC | Cross-sectional | No | No | Low |
| [McLaren *et al.*, 2008](https://paperpile.com/c/x5aI6V/Qeb4) | 5137 | Any | Out and Inpatient | Canada | North America | HIC | Cross-sectional | No | No | Medium |
| [Minsky *et al.*, 2013](https://paperpile.com/c/x5aI6V/dB80) | 586 | Any | Out and Inpatient | US | North America | HIC | Cross-sectional | No | No | High |
| [Nishiyama *et al.*, 2007](https://paperpile.com/c/x5aI6V/qg1G) | 208 | Schizophrenia | Inpatient | Japan | East Asia & Pacific | HIC | Cross-sectional | Yes | Yes | Medium |
| [Park *et al.*,2020](https://paperpile.com/c/x5aI6V/My6C) | 420 | Schizophrenia | Out and Inpatient | India | South Asia | LMIC | Cross-sectional | No | No | Low |
| [Park *et al.*,2020](https://paperpile.com/c/x5aI6V/My6C) | 463 | Schizophrenia | Out and Inpatient | Indonesia | East Asia & Pacific | LMIC | Cross-sectional | No | No | Low |
| [Park *et al.*, 2020](https://paperpile.com/c/x5aI6V/My6C) | 145 | Schizophrenia | Out and Inpatient | Japan | East Asia & Pacific | HIC | Cross-sectional | No | No | Low |
|  [Park *et al.*, 2020](https://paperpile.com/c/x5aI6V/MjH3) | 230 | Schizophrenia | Out and Inpatient | Malaysia | East Asia & Pacific | LMIC | Cross-sectional | No | No | Low |
|  [Park *et al.*, 2020](https://paperpile.com/c/x5aI6V/My6C) | 184 | Schizophrenia | Out and Inpatient | Taiwan | East Asia & Pacific | LMIC | Cross-sectional | No | No | Low |
| [Post *et al.*, 2014](https://paperpile.com/c/x5aI6V/nIOq) | 165 | Bipolar disorders | Outpatient | Europe | Europe & Central Asia | HIC | Prospective Longitudinal | No | No | Medium |
| [Post *et al.*, 2014](https://paperpile.com/c/x5aI6V/nIOq) | 676 | Bipolar disorders | Outpatient | US | North America | HIC | Prospective Longitudinal | No | No | Medium |
| [Smith *et al.*, 2020](https://paperpile.com/c/x5aI6V/X28y) | 46 | Any | Outpatient | UK | Europe & Central Asia | HIC | Cross-sectional | No | Yes | Low |
| [Sugai *et al.*, 2015](https://paperpile.com/c/x5aI6V/xSgt) | 19678 | Schizophrenia | Out and Inpatient | Japan | East Asia & Pacific | HIC | Cross-sectional | No | No | Low |
| [Sušilová *et al.*, 2017](https://paperpile.com/c/x5aI6V/u0Eo) | 462 | Schizophrenia | Inpatient | Czech Republic | Europe & Central Asia | HIC | Prospective Longitudinal | No | Yes | High |
| [Tzeng et al., 2020](https://paperpile.com/c/x5aI6V/EYts) | 260 | Any | Inpatient | Taiwan | East Asia & Pacific | LMIC | Cross-sectional | No | No | Medium |
| [Vedal *et al.*, 2019](https://paperpile.com/c/x5aI6V/nRrQ) | 750 | Any | Outpatient | Norway | Europe & Central Asia | HIC | Cross-sectional | No | Yes | Low |
| [Zavala *et al.*, 2020](https://paperpile.com/c/x5aI6V/4Osj) | 1500 | Any | Out and Inpatient | Bangladesh | South Asia | LMIC | Cross-sectional | No | No | Low |
| [Zavala *et al.*, 2020](https://paperpile.com/c/x5aI6V/4Osj) | 858 | Any | Out and Inpatient | Pakistan | South Asia | LMIC | Cross-sectional | No | No | Low |
| [Zhao *et al.*, 2018](https://paperpile.com/c/x5aI6V/4cyV) | 466 | Schizophrenia | Inpatient | China | East Asia & Pacific | LMIC | Cohort | Yes | No | Low |
| SMI: Severe mental illness; WB: World Bank; HIC: high Income Country; LMIC; Low and middle-income country; US: United States; UK: United Kingdom |

Table 1 shows the characteristics of the studies included in the meta-analysis. The sample size of the studies ranged from 46 to 19,678 with a mean of 1478 participants. More than 60% of the studies were classified as having “low” risk of bias, 20% as “medium risk” and 17.5% as “high risk”. (Table 1). The age of participants ranged from 24 to 61 years, with mean age of 43.6 years. More studies were conducted in high-income countries (HICs) as compared to low- and middle-income countries (LMICs). More than 50% of the studies used DSM-5 [(American Psychiatric Association, 2013)](https://paperpile.com/c/1C5sjz/quils) or ICD-10 [(WHO, 1993)](https://paperpile.com/c/1C5sjz/r2nWS), while majority used the WHO international classification of BMI [(OECD/WHO 2020)](https://paperpile.com/c/vZxRdk/WqlBE) to define underweight (<18.5 kg/m2), with the other 10% [(Anuurad et al., 2003; Chobanian et al., 2003; Takimoto et al., 2004)](https://paperpile.com/c/1C5sjz/whMAK%2By2j4R%2BkCam0) using ethnicity adjusted classifications, which usually have a lower cut off value. As shown in Table 2, the pooled prevalence of underweight was 3.8% (95% C.I. = 2.9-5.0; n=59,127), with an heterogeneity of 98.2%, and T2 =c0.7159, p<0.01. The pooled prevalence in LMICs was higher than HICs. A substantial difference was identified among SMI diagnoses; such that the pooled prevalence of underweight in people with schizophrenia was highest people with bipolar disorder, and a pooled prevalence for people with any disorder at was lower. We also found that number of inpatients was higher than outpatients (Figure 2).

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| **Table 2:** *Summary of the studies and the pooled prevalence of underweight according to World Bank classification, World Bank region, type of severe mental illness, setting, antipsychotic medication, and year of data collection* |
| **Variable** | **Number of studies** | **Percentage of studies (%)** | **Underweight (95% C.I.)** |
| Overall Pooled Prevalence  | 40 | 100% | 3.78% (2.85-4.99) |
| World Bank classification |   |   |  |
|  Higher Income Countries  | 30 | 75% | 3.40% (2.38-4.83) |
|  Low and Lower Middle Income Countries | 10 | 25% | 5.25% (3.73-7.34) |
| World Bank region |   |   |  |
|  East Asia and Pacific | 16 | 40% | 4.96% (3.20-7.62) |
|  North America | 10 | 25% | 1.78% (1.24-2.55) |
|  Europe and Central Asia | 9 | 22.5% | 5.15% (3.24-8.11) |
|  South Asia | 3 | 7.5% | 7.50% (5.76-9.71) |
| Latin America and Caribbean | 2 | 5% | 2.55% (1.45-4.43) |
| Year of data collection |   |   |  |
|  2000 – 2005 | 10 | 25% | 2.22% (1.16-4.21) |
|  2006 – 2010 | 9 | 22.5% | 3.28% (2.02-5.26) |
|  2011 – 2015 | 11 | 27.5% | 3.28% (1.75-6.04) |
|  2016 – 2021 | 10 | 25% | 5.07% (3.46-7.39) |
| Type of SMI |   |   |  |
|  Any SMI1 | 15 | 37.5% | 3.33% (2.24-4.91) |
|  Schizophrenia | 17 | 42.5% | 5.35% (3.46-8.17) |
|  Bipolar disorder | 8 | 20% | 2.36% (1.61-3.45) |
| Setting |   |   |  |
|  Inpatient | 13 | 32.5% | 4.26% (2.34-7.64) |
|  Outpatient | 11 | 27.5% | 2.59% (1.50-4.43) |
|  Inpatient and outpatient | 14 | 35% | 4.6% (3.23-6.49) |
|  Community | 2 | 5% | 2.37% (1.23-4.53) |
| Antipsychotic medication |   |   |  |
|  Prescribed2 | 36 | 90% | 3.70% (2.80-4.88) |
|  Not prescribed | 2 | 5% | 2.88% (0.98-8.17) |
|  Not reported | 2 | 5% | 7.09% (0.99-4.92) |
| SMI diagnostic tool |   |   |  |
|  DSM | 21 | 52.5% | - |
|  ICD | 9 | 22.5% | - |
|  DSM and ICD | 2 | 5% | - |
|  Not specified | 8 | 20% | - |
| Study design |   |   |  |
|  Cross-sectional | 35 | 87.5% | - |
| Cohort | 2 | 5% | - |
| Prospective Longitudinal | 3 | 7.5% | - |
| Body mass index classification |   |   |  |
| World Health Organization | 36 | 90% | - |
|  Taiwan Standards | 1 | 2.5% | - |
|  Japanese Society for the Study of Obesity | 2 | 5% | - |
|  Indonesian Standards | 1 | 2.5% | - |
| Overall risk of bias |  |
|  Low | 25 | 62.5% | - |
|  Medium | 8 | 20% | - |
|  High | 7 | 17.5% | - |
| SMI: Severe mental illness, DSM: Diagnostic and Statistical Manual for Mental Disorders, ICD: International Classification of Diseases. 1The “any'' category includes studies where the estimates of underweight were not separated between the type SMI, we did not find studies looking at major depression with psychotic features independently and only found one study looking at first episode of psychosis which was included in the “schizophrenia” category; 2 Studies including participants with prescribed antipsychotic medication or open population (mix of participants taking and not taking antipsychotic medication). |

[Insert **Figure 2.** *Forest plot representing the pooled prevalence of underweight in people with severe mental illness according to severe mental illness, geographical region, World Bank classification,* *antipsychotic medication use and year of data collection.*]

As shown in Figure 3, there were considerable country differences in pooled prevalence of underweight, with the highest prevalence in Japan (16.4%), and Czech Republic (14.1%), and the lowest prevalence in Australia (1.7%) and the US (1.5%).

[Insert **Figure 3.** *Geographical variation in the prevalence of underweight in people with severe mental illness*]

From the included studies, nine compared the prevalence of underweight in people with SMI (n=2066) and the general population (n=42055). The pooled odds of people with SMI of being underweight were 0.65 (95% C.I. = 0.44-0.95. p=0.02) lower as compared with the general population (I2 =55%, t2=0.16). Figure 4 shows the odds of people with SMI being underweight compared with the general population, according to type of SMI, World Bank country classification, World Bank region and year of data collection. The odds of people with SMI of being underweight compared to the general population were lower in HIC than in LMICs. North America was the region with the highest odds ratio followed by East Asia and Pacific. However, in all regions the odds of underweight were lower in SMI than in the general population.

There were differences according to the specific SMI, people with bipolar disorder had higher odds of having underweight compared with the general population, while people with schizophrenia had lower odds of having underweight. We found 5 studies where the prevalence of underweight was provided for females and males, females with SMI had higher odds of having underweight as compared to men with SMI (n=37405, I2 =83%, t2=6.67).

[Insert **Figure 4.** Odds of people with severe mental illness of being underweight compared with the general population]

# Discussion

This is the first systematic review to investigate the prevalence of underweight in people with SMI according to type of SMI, setting and region of the world. We found a relatively higher prevalence of underweight in Japan and the region of South Asia, Europe and Central Asia and a lower prevalence in the region of North America. The pooled prevalence of underweight was higher in people with bipolar disorder than in schizophrenia, and women with SMI had higher odds of being underweight than men with SMI.

The pooled prevalence of underweight in people with schizophrenia found in the current meta-analysis is lower (5.4%) than the pooled prevalence found by Sugawara et al. (2018) which reported a pooled prevalence of 6.2%. This marginal difference in people with schizophrenia might be due to the proportion of studies from Japan (country with the highest prevalence of underweight) included in both reviews (24% vs 5%). The higher prevalence of underweight found in people with schizophrenia (compared with people with bipolar disorder) might be due to social withdrawal, isolation, self-neglect and the higher prevalence of negative symptoms seen in this population [(Ng et al. 2021)](https://paperpile.com/c/plkes6/PxtU). Lack of motivation and negative symptoms can contribute to insufficient dietary intake and therefore undernutrition [(Sugai et al., 2015)](https://paperpile.com/c/1C5sjz/I7D3h). It should be acknowledged that the lower odds of having underweight found in people with bipolar disorder (as compared with the general population) was based on the single estimate from one study investigating people with bipolar disorder, which reduces the reliability and representativeness of this figure. Women with SMI were more likely to be underweight, which is in line with global trends seen in the general population [(](https://paperpile.com/c/vZxRdk/dVjKN)Global Nutrition Report, 2020) showing higher prevalence of underweight in women than men.

The lower odds of people with SMI of having underweight compared with the general population was expected considering the high rates of obesity reported in this population due to the metabolic side effects of antipsychotic medication, prevalence of health risk behaviours and socioeconomic disadvantages related to higher unemployment rates [(](https://paperpile.com/c/vZxRdk/Df1cm)[Adams, 2020](https://paperpile.com/c/vZxRdk/gNGt0); [Holt & Peveler, 2009)](https://paperpile.com/c/vZxRdk/Df1cm). Antipsychotic medication adversely impacts metabolism through direct and indirect effects on lipids and insulin sensitivity, therefore contributing to the increasing rates of weight gain and metabolic syndrome seen in this population [(Libowitz & Nurmi, 2021)](https://paperpile.com/c/1C5sjz/rYZdI). In line with this finding, a recent meta-analysis [(Holt et al., 2021)](https://paperpile.com/c/1C5sjz/yx3qn) including 24 studies found that people with SMI are 3.04 times more likely of being obese than people in the general population. Despite the low prevalence of underweight and the lower odds of people with SMI of having underweight, other forms of malnutrition should not be discounted. A few studies [(Grønli et al., 2013; Nunes et al., 2014)](https://paperpile.com/c/1C5sjz/iIseb%2BlMUr3) have demonstrated that people with SMI have a poor diet with excess of calories, sugar and saturated fat with low nutritional quality and are more likely to have a micronutrient deficiency than the general population. More research is required to investigate the double burden of malnutrition (i.e., obesity and micronutrient deficiencies) in this population, to better understand undernutrition in this population and help inform future health strategies.

The higher prevalence of underweight in inpatients (compared with outpatients) was also reported by Sugai et al. (2015) where Japanese inpatients were more likely to be underweight than their counterparts in the community. Long term hospitalisation often leads to reduced physical activity therefore lowering bone density, which has been reported to be related to underweight [(Carter & Hinton, 2014](https://paperpile.com/c/vZxRdk/jXXpZ); [Pines, 2012)](https://paperpile.com/c/vZxRdk/Ube7n). Another reason may be because inpatients are more likely to have a refractory degree of mental illness that can manifest with cognitive impairment and psychotic symptoms, leading to an element of diagnostic overshadowing, where health professionals may mistakenly attribute symptoms of a physical illness to their underlying psychiatric illness ([Molloy et al., 2020)](https://paperpile.com/c/1C5sjz/eM82O). This may lead to clinicians overlooking or undertreating physical health problems that could be contributing to being underweight [(Sugai et al., 2015)](https://paperpile.com/c/1C5sjz/I7D3h). It is therefore important that signs of undernutrition are acknowledged and adequately assessed in this at-risk population.

The pooled prevalence of underweight of people with SMI living in LMICs was higher than those living in HICs. Being underweight is associated with increased susceptibility to infection and reduced work capacity leading to lower income and increased mortality. [(Fekadu et al., 2015](https://paperpile.com/c/vZxRdk/aXBmR); [Flegal et al., 2005)](https://paperpile.com/c/vZxRdk/Twi1z). The differences between HICs and LMICs might be explained by the same sociodemographic factors seen in the general population such as higher unemployment rates, and limited access to social programmes as well as other factors specific to the SMI population such as depression and negative symptoms which are associated with higher unemployment rates and lower food intake.

# Strengths and limitations

Due to the variety of geographical regions, intake of antipsychotic drugs and types of SMI, there was considerable heterogeneity between the studies which cannot be mitigated by sample stratification. We did not adjust for unmeasured variables such as dietary intake of the population. Also, there were limited studies conducted in LMICs compared to HICs, which reduces the confidence in the LMIC estimate. Two studies were also excluded due to not being in English. Another potential limitation is that most of the included studies are cross-sectional, so it is difficult to establish the temporal relationship between underweight and SMI. Despite these limitations, this is the first study conducted to examine the prevalence of underweight in people with SMI from a global perspective, estimating the prevalence and trend of underweight from every region of the world and according to the type of SMI and setting.

# Conclusion

We found that people with any SMI are less likely to be underweight compared to the general population. People with schizophrenia had the highest prevalence of underweight compared to other types of SMI, this was still lower than the general population. The pooled prevalence of underweight in Japan and South Asia was significantly higher than any other world region.

There is scope for further research into the prevalence of underweight in people with SMI in LMIC, which is under-represented in the current data and may provide contextual information to produce targeted interventions.

# Data availability

The data are publicly available at: [**https://pure.york.ac.uk/portal/files/74735049/Underweight\_and\_obesity\_people\_wit\_SMI\_Dataset**](https://pure.york.ac.uk/portal/files/74735049/Underweight_and_obesity_people_wit_SMI_Dataset_11_11_21.xlsx)

# Conflict of interests

*The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest*.

# Author contributions

GZ, MA and RH designed the study, GZ and MA drafted the manuscript, BA, HK, FA, MB and RA have made substantial contributions to the conception of the manuscript and interpretation of data, BA, FA, HK, SR, and RA made substantial contributions to acquisition of data and BA, FA, GZ and RA conducted the analysis, NS, FA, MB, KA, MA, RH and GZ critically revised the manuscript. All authors read and approved the final manuscript.

# Funding

This research was funded by the National Institute for Health Research (NIHR) (Grant: GHRG 17/63/130:) using UK aid from the UK Government to support global health research. The views expressed in this publication are those of the author(s) and not necessarily those of the NIHR or the UK Department of Health and Social Care.

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