Dietary intake in severe mental illness: systematic review and meta-analysis

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Abstract

Background. Severe mental illness (SMI) is thought to be associated with lower diet quality and adverse eating behaviours contributing towards the physical health disparities. A rigorous review of the studies looking at dietary intake in psychotic disorders and bipolar disorder is lacking.

Aim. To conduct a systematic, comprehensive evaluation of the published research on dietary intake in psychotic disorders and bipolar disorder.

Methods. Six electronic databases were searched for studies reporting on dietary intakes in psychotic disorders and bipolar disorder. Dietary assessment methods, and dietary intakes, were systematically reviewed. Where possible, data was pooled for meta-analysis and compared to healthy controls.

Results. Fifty-eight eligible studies were identified. People with SMI were found to have significantly higher dietary energy (MD = 1,332kJ, 95% C.I. +487 to +2,178kJ/day, p = 0.002, g = 0.463) and sodium (MD = 322mg, 95% C.I. 174 to 490mg, p<0.001, g=0.414) intake compared to controls. Qualitative synthesis suggested that higher energy and sodium intakes were associated with poorer diet quality and eating patterns.

Conclusion. These dietary components should be key targets for preventative intervention to improve weight and other physical health outcomes in people with SMI.

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Keywords: health behaviour, obesity, physical health, bipolar disorder, schizophrenia.

Introduction

People with severe mental illness (SMI) die approximately 15 years earlier than individuals in the general population [1], identified as a significant human rights issue and major source of inequity [2]. The vast majority of these earlier deaths are attributable to physical health conditions, primarily cardiovascular disease [3]. Understanding modifiable factors that may diminish or prevent the "scandal of premature mortality" is essential [2]. In the general population, there is robust evidence that excessive energy intake and poor diet quality is associated with adverse physical health including cardiovascular disease and premature mortality [4]. This evidence supports population-level state-sanctioned strategies that focus on nutrition as a cornerstone of health outcome determination.

For many people experiencing SMI, antipsychotic, anti-depressant and mood-stabilising medications may be essential components of treatment [5, 6]. Many of these medications are associated with substantial weight gain, obesity and associated cardiometabolic abnormalities [7-9]. It has been suggested that one of the key factors underlying these abnormalities are the effects of antipsychotic medication (APM) on dietary intake and eating behaviours [10]. People receiving APM report increased appetite, decreased satiety and increased cravings for sweet foods and beverages [11]. A range of lifestyle interventions have attempted to mitigate the obesogenic effects of these medications, however a clear understanding of the dietary intake in people experiencing psychotic illness is lacking. A key limitation in a previous systematic review of dietary patterns in schizophrenia [12], was lack of evaluation and critique of the quality of dietary intake assessment methods. Given the vast majority of dietary assessment methods are subjective, the strength of methodology in collecting, interpreting and analyzing dietary intakes is a crucial determinant for obtaining meaningful conclusions. Thus, a comprehensive systematic review and meta-analysis of the dietary intake of people with SMI, taking into account dietary assessment methodology, is

warranted to identify possible dietary treatment targets for interventions to improve the physical health of this vulnerable population.

Methods

Design

This study was pre-registered on the PROSPERO database (CRD42016048833) and conducted in accordance with the PRISMA [13] and MOOSE statements [14] (see Supplementary Files 1 and 2 for PRISMA and MOOSE checklists).

Search Strategy

An online search strategy was undertaken to identify studies published in the English language from 1975 to August 2017 through librarians within the University of Newcastle, Callaghan Campus. Cumulative Index to Nursing and Allied Health Literature (CINAHL), Cochrane, Embase, Medline, PsychINFO and Scopus databases were searched using common psychiatric and nutritional MeSH terms (feeding behavior OR eating OR food intake OR diet* OR nutrition* OR coffee OR caffeine OR beverages AND schizophrenia OR psychotic disorders OR bipolar disorder OR bipolar*; see Supplementary File 3 for comprehensive search list). Electronic searches were supplemented with manual crosschecking of the reference lists of relevant publications [12]. Cross-sectional and cohort studies in adults were included.

After the removal of duplicates, stage 2 involved the assessment of titles and abstracts of identified studies by two independent reviewers (ST and TB), with disagreements resolved by further discussion. A priori inclusion/exclusion criteria were applied to determine the eligibility of each publication for inclusion in the review, as per the following inclusion criteria;

Population: Adult populations (age ≥ 18 years or “adults” depending on the database

searched), Diagnostic and Statistical Manual of Mental Disorders (DSM) or International Statistical Classification of Disease and Related Health Problems (ICD) diagnosis of a severe mental illness (schizophrenia spectrum disorders, bipolar affective disorder, depression with psychosis, or other psychotic illness) or clinician diagnosed first-episode of psychosis. There were no limitations employed for rates of psychotropic medication prescription, as reporting of this was infrequently included.

Intervention: Types of studies included cross-sectional, cohort and longitudinal designs.

Control: There were no limits on comparison groups, although only studies with matched controls were eligible for meta-analysis.

Outcome: One or more nutritional outcomes, including energy, macronutrients, micronutrients, fat subgroups, fibre, diet quality, food groups and caffeine.

We excluded animal studies, studies of people with high-prevalence mental illness (depression and anxiety), or those with eating disorders (anorexia and bulimia nervosa), case studies, letters to the editor, intervention studies, and studies with eating behaviour outcomes that lacked specific dietary intake outcomes. Alcohol was excluded as an outcome as we did not include substance use in our search terms. Excluded articles are summarized in Figure 1.

Data extraction. Where necessary, corresponding authors of included studies were contacted for additional data for inclusion in meta-analysis. A follow-up email was sent three weeks later if corresponding authors did not reply to the initial request.

Data were extracted using standardised tables developed for this review and included study design, population demographics, and dietary intake assessment methods. In cases of uncertainty regarding quality assessment, or data extraction, a third independent reviewer was consulted, until consensus was reached.

Study quality. Study quality was assessed twice for each individual study using a standardised tool from the American Academy of Nutrition and Dietetics [15]. Two reviewers scored each study independently. The lead author resolved discrepancies between the different scorers. Scoring included ten quality criteria that were rated as being absent, present or unclear in each study. This included the assessment of population bias, study blinding, a description of the assessment tool, statistical methods and study funding. An overall quality rating was assigned, with each study being rated as: (i) negative (-) if 6 or more answers to the validity questions are 'No', (ii) Neutral (∅) if answers to validity criteria 2, 3, 6 and 7 do not indicate the study was strong, or (iii) positive (+) if most of the answers to validity criteria were 'Yes' (including criteria 2, 3, 6 and 7 plus one extra criteria). No studies were excluded based on quality ratings.

Data-analysis

Studies were eligible for meta-analysis if they; (i) utilised a recognised dietary assessment method (i.e. 24-hour recall) or cited a validation study for the tool utilised, (ii) had a matched control group who were assessed at the same time as the target group, and (iii) reported outcomes in a compatible metric/measure. Comparisons against national health surveys and other population data sources were not eligible for meta-analysis.

All meta-analyses were performed using Comprehensive Meta-Analysis 2.0 [16]. To account for expected heterogeneity between studies, a random-effects model was used throughout [17]. First, for studies that utilised validated, or recognised and acceptable, dietary assessment tools, comparative meta-analyses were performed to calculate a pooled mean difference (and 95% confidence intervals) between SMI and healthy control samples in daily total energy intake, the primary outcome of interest, measured in kilojoules per day (kJ).

As secondary outcomes, we also compared SMI and control groups on daily mean intake of each macronutrient and micronutrient, examined in a sufficient number of studies to justify meta-analysis (>2), using the standard units of measurements for these nutrients. If nonstandard means were used, we calculated means and standard deviations (SD) from the data of the studies where possible. Along with examining differences using standard nutrient measurement values, the overall difference between SMI and control groups for daily intake of each macro/micronutrient was computed as Hedge's G, with resultant effect sizes classified as small (<0.2), moderate (>0.2, <0.8) or large (>0.8). Statistical significance was set at $p<0.05$. For all analyses, the 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.

For the primary outcome, we also applied several tests to measure and adjust for publication bias: (i) Egger's regression test was used to quantify the risk of publication bias influencing findings, (ii) the 'Fail-Safe N' [18] was calculated to determine the number of unpublished null studies which would invalidate the findings, and (iii) Duval and Tweedie's trim-and-fill analysis was used to re-calculate the pooled difference after adjusting for any studies potentially reflecting publication bias.

Results

Identification and Selection of Studies.

Electronic database searches identified 5,538 unique titles after accounting for duplicates, as summarised in Figure 1. Five additional titles were sourced by screening a relevant references [12]. A review of titles and abstracts led to the exclusion of 5,394 titles. Full-texts were assessed for the remaining 149 titles, of which 91 were excluded for reasons detailed in figure 1. Fifty-eight studies were identified for critical appraisal and included in this review [19-76].

Insert figure 1 about here

The studies were conducted in 17 countries, with the majority conducted in the USA (N=14 studies, n=4,885 participants), UK (N=10, n=575), Spain (N=6, n=2,637) and Australia (N=6, n=1,899). The majority of studies were cross-sectional in design (N=48, n=33,915), whilst smaller numbers of cohort (N=6, n=924), and case control (N=2, n=275) studies were included, and one study each for longitudinal (n=352) and cross-cue reactivity (n=15).

Characteristics of Included Studies.

Participants. The 58 studies included a total of 35,481 people with SMI and 5,465 non-psychiatric controls. Diagnoses within the studies were: (i) limited to schizophrenia spectrum disorders (N= 27, 47%, n=26,230), (ii) mixed SMI diagnoses (N=20, 34%, n=8,301), (iii) limited to bipolar affective disorder (N=7, 12%, n=673), and (iv) limited to first-episode psychosis (N=4, 7%, n=277). The majority of studies described participants as outpatients or community-dwelling (N=40, n=6,944), followed by inpatients (N=8, n=886) and mixed settings (N=2, n=22,072). Eight studies did not

report participant setting. Nineteen studies (33%) used controls (n=5,465) and 20 studies (34%) used population data as a comparator group. Participants were receiving a range of psychotropic medications including antipsychotics, mood stabilisers, antidepressants and benzodiazepine medications. Medications were reported in a range of formats including (i) chlorpromazine equivalents, (ii) percent on psychotropic medications as a whole, (iii) percent prescribed APM or generation of APM and APM polypharmacy, (iv) percent prescribed mood stabiliser medication, and (iv) percent of prescription of individual medications. Seventeen studies (29%) did not describe medication prescription. See Supplementary File 4 for complete details.

Dietary intake assessment methods. Seventeen different types of dietary assessment methods were identified. Only twelve studies (21%) cited validation studies for the nutrition assessment method utilised. No study cited validation of the dietary assessment tool utilised, in a SMI population. One study reported piloting their FFQ in 15 people with SMI, however this data was unpublished. A further twenty-two studies (38%) utilised recognised acceptable dietary intake assessment measures such as 24-hour recall, however only 11 studies (50%) reported that dietitians or other trained interviewers completed dietary intake assessment and analysed it using nutrition data analysis software, and only four studies utilised multiple, non-consecutive recalls. Weighed food records, a more objective measure of dietary intake, was utilised for two of these studies. In these two studies, one study assessed seven-day dietary intake, and the other two-day dietary intake, both assessed by dietitian/nutritionist. One study utilised a three-day photographic food record assessed by a dietitian, also considered a more objective measure of dietary intake. For the remaining studies for which validity of the assessment tool was unclear, fourteen studies (24%) reported the assessment tool very broadly, such as ‘standardised questionnaire’ or ‘verbal questions’ and nine

studies (16%) report using FFQs without citing validity, or questions taken from National Health Surveys.

Dietary outcomes. A wide variety of dietary outcomes were assessed. The most common dietary outcome measures were energy intake (N=22), macronutrients (carbohydrate, protein, fat) (N=20), individual fatty acids or fat subgroups (N=20), fibre (N=16), food groups/categories (N=14), caffeine or coffee intake (N=12), overall dietary patterns (N=9), and micronutrients (N=9). One study also reported health (dietary) knowledge as a secondary outcome. Dietary outcomes were reported in a range of different metrics. For these reasons it was difficult to conduct direct comparisons.

Quality of studies. Thirty-nine studies (67%) received a neutral score, 13 studies (22%) received a negative score and six studies (11%) received a positive score. Key areas of weakness included; (i) lack of concurrent controls, and comparability of groups on important confounding factors, (ii) lack of use of independent assessors and blinding for data collectors (when concurrent comparator groups were used), (iii) measurements not being based on standard, valid and reliable methods and procedures (iv) measurements implemented at unclear level of precision, and (v) inconsistent measures used across groups. Individual study quality data are outlined in Supplementary File 5.

Quantitative Analysis

In two studies that only reported median averages [46, 50], medians were used as an imputed mean, and standard deviations were estimated from the pooled standard deviations across all other studies. For the one study that did not report SD for controls [54], SD was imputed from a study of similar sample size [42].

Energy. Seven studies (n=1,448) reported energy intakes for both people with SMI and controls [27, 32, 46, 47, 50, 51, 55]. Mean energy intake among individuals with SMI was 1,332kJ/day higher than among the control subjects (95% C.I. +487 to +2,178kJ/day, p = 0.002), with a moderate effect size for the difference between groups [N=7, g=0.463, (95% C.I. 0.159 to 0.767), p = 0.003]. Although there was heterogeneity across the study data (Q = 25.7, p < 0.001, I^2 = 76.7%), there was no evidence of publication bias (p = 0.328 for Egger's regression test), and the fail-safe N was 67 (estimating that 67 unpublished "null" studies would need to exist for the actual p value to exceed 0.05). A trim-and-fill analysis did not identify any outliers, and the random effects point estimate remained at g = 0.463. These findings were in line with the two studies which utilised weighed-food records that found, (i) energy intake was significantly higher in the schizophrenia group compared to general population [64], and (ii) energy intake increased with the commencement of olanzapine, in line with the weight gain observed [35].

Subgroup analysis found the mean difference in energy intake for the schizophrenia spectrum cohorts compared to controls was +1,695kJ/day (95% C.I. 380 to 3,010kJ/day), p = 0.012, and the mean difference between energy intake in BPD only cohorts compared to controls was +827kJ/day (95% C.I. 146 to 1,508kJ/day), p = 0.017. The between group difference in energy intake for BPD-only and schizophrenia spectrum-only cohorts was not statistically significant (Q = 1.32, p = 0.251). These are illustrated in Figure 2.

Insert Figure 2 about here

Additional Nutrients. Three studies (n=387) reported data able to be pooled for meta-analysis for sodium, vitamin B6, vitamin C and zinc [47, 50, 55]. Sodium intake was significantly higher in the SMI group [mean difference +332mg, 95% C.I. 174 to 490mg, Z = 4.121, p < 0.001, I^2 = 12%, g = 0.414]. There was no significant difference in pooled intakes of vitamin B6, vitamin C and zinc between people with SMI and controls (all p > 0.2). See Table 1 for meta-analysis results for energy and nutrient intakes.

Insert Table 1 about here

Qualitative Synthesis

Dietary patterns and diet quality scores were assessed in eight studies and two studies respectively. The SMI group was found to have less healthy dietary patterns in eight studies [36, 46-49, 58, 76] and females had lower diet quality in one study which assessed diet quality [20], and a mean diet score within the 'unhealthy' category for the other study assessing diet quality [63]. No included study found healthier dietary patterns for the SMI group when compared to control or population data. Four studies reported a relationship between dietary patterns and SMI; a higher 'western' and 'modern' dietary pattern was positively associated, and 'traditional' dietary pattern negatively associated with BPD [46], a 'cereal' dietary pattern (bread, rice, confectionary etc.) was positively associated with SCZ while a 'vegetable' dietary pattern was not [72], and higher energy intake, and lower protein intake, were positively associated with general symptom severity in early psychosis in one study [51], while life stress was positively associated with increased refined sugar intake in people experiencing psychosis but negatively associated with refined sugar intake in both high-risk for psychosis and healthy subjects, in the same study. A fourth study in Japan

found males who had infrequent intakes of vegetables, mayonnaise, potatoes, soy products, seaweed and fish products had more pronounced psychiatric symptoms, although this correlation was not found in women [76].

Fruit and vegetable intake was found to be lower in the SMI group compared to controls/population data in three studies [48, 52, 62] and less than country/region-specific recommendations in nine studies [26, 34, 39, 41, 43, 52-54, 63], and higher compared to the general population in one study [77]. Low intakes, or lower intakes than comparison groups, were found for fish [54, 63], and nuts and vegetable oils [20]. Large intakes, or higher intakes than comparison groups, were found for carbonated beverages [20], sweetened beverages [30], soft drinks [69], cakes and other sweets [69], white bread [43], hydrogenated oils [20] and fast-food/takeaway foods [43, 62]. In addition, one study found poor diet literacy [41] and one study found difficulties obtaining and/or cooking food [48] for people with SMI.

Results for macronutrients and micronutrients were mixed when compared to reference groups and recommended intakes, with no clear findings emerging. There were trends for studies to find lower mono- and poly-unsaturated fats [24, 28, 29, 55], and higher intakes of total and saturated fat [51, 54, 57, 64, 65, 72] and trans fats [55] in the SMI groups when compared to a comparator (control or population data). In addition, higher sugar intake was found in two studies [57, 72].

Results for fibre intakes were mixed when compared to controls or population data, although the SMI group consumed less than national/region recommendations in nine studies [24, 29, 42, 44, 47, 50, 54, 65, 68] and adequate in one study [55]. For caffeine intake, five studies found higher caffeine intakes, or high caffeine intakes (≥200mg/day)

to be more frequent, in the SMI group compared to reference group [19, 37, 44, 65, 66] and one study found no difference [22]. One study found people with psychosis to have a higher frequency of 'high' coffee consumption (≥5 cups/day) compared to other mental illnesses including depression and alcohol use disorder [75]. Seven studies found smokers in the SMI groups to have the highest caffeine intakes [19, 22, 23, 25, 37, 65, 66]. Differences in reporting of caffeine and caffeinated drinks as outcomes meant that data could not be pooled for meta-analysis.

Discussion

This is the first meta-analysis of dietary intake in people with either psychosis or bipolar disorder and showed significantly higher total energy and sodium intakes compared to controls. This study also found consistent reports of less healthy dietary patterns including low intakes of fruit and vegetables, and high intakes of take-away and other convenience foods, and sugar-sweetened beverages. A previous qualitative synthesis in schizophrenia and schizoaffective disorder [12] suggested poorer dietary patterns in this population. Poorer dietary patterns are not limited to schizophrenia and schizoaffective disorder and included all those with a SMI diagnosis, although energy intake appears to be highest for those with psychotic disorders. This was also the first study to systematically review dietary intake assessment methods and strength of reporting, fulfilling a need to improve scientific rigour in this area.

The strongest evidence was found for higher energy and sodium intakes in SMI populations, with statistically significant differences compared to control samples (+1,332kJ/day and +322mg/day higher in SMI respectively) when pooled intakes obtained from validated assessment tools were compared with matched controls. These findings are consistent with the two studies utilising weighed food records

(considered the most accurate method) which found; (i) a significant increase in caloric intake coinciding with weight gain [35], and (ii) SCZ group consumed more energy, sugar and fat compared to the general population [64]. Both meta-analyses revealed moderate effect sizes (g = 0.46 and g = 0.41 respectively), and are of considerable clinical relevance, particularly an increased energy intake of 1,332kJ per day, given that, i) the general population is already over-consuming energy [78] and salt [79], and ii) this is compounded with high levels of sedentary behaviour [80], and low cardiorespiratory fitness [81], which helps to explain the alarming rates of obesity, metabolic syndrome, diabetes, cardiovascular disease and premature mortality in people with SMI [3]. The weight change dynamics paradigm of Hall and co-workers' [82] predicts that every 100kJ intake excess will have an eventual body weight change of 1kg. Applied to the findings from this study, someone with SMI would weigh on average 13kg more than the general population (mean 8kg and 17kg in the BPD and SCZ groups respectively) from dietary factors alone.

Increased energy and sodium intakes are likely explained by increased hunger and preference for 'discretionary foods' such as sweetened beverages and convenience foods, which are high in sugar, salt and fat (and therefore energy) and low in beneficial nutrients such as fibre, vitamins and minerals. Reasons for increases in appetite remain to be clarified. A wide variety of neuroreceptor and neuroendocrine factors regulate eating behaviour and appetite in SMI [83]. Dopamine, serotonin, muscarinic and histamine receptors have all been implicated in antipsychotic-induced increases in hunger, with drugs with high affinity for $5HT_{2c}$ and muscarinic receptors associated with the greatest risk of weight gain [84, 85]. Compounded with the lower levels of physical activity among people with SMI [80], this helps to explain the stark difference in weight and BMI status between people with SMI and the general population [86].

Intakes of the micronutrients vitamin B6, vitamin C and zinc were not significantly different from control in this study, although these analyses were limited to the few studies that included such data. Given a previous analysis found blood levels of micronutrients were significantly lower in SMI compared to healthy controls [87], more well-designed dietary intake studies should investigate micronutrients, particularly those with a close relationship to mental health, such as folate.

Strengths and limitations

The search strategy was limited to articles written in English and therefore articles written in another language were not reviewed. In addition, grey literature was not searched for this review. The study aimed to focus on naturalistic cohort data of real world patients dietary consumption such that the results would reflect clinical reality, hence the inclusion of cohort/cross sectional studies, and the exclusion of RCT data.

Attempts were made to disentangle the effects of antipsychotic and mood-stabilising medication, however due to insufficient reporting, limited conclusions could be made from this review. Given the differing effects on metabolic health of antipsychotics and mood-stabilising medications, more research is needed to explore the specific effects of individual medications on dietary intake and eating behaviours.

Qualitative synthesis found a large range of dietary assessment and analysis methods and outcomes were employed, a clear challenge for interpreting dietary intake. A large proportion (37%) either used an unvalidated tool or did not report whether the tool had undergone validation, which limits generalisability of any findings. Those studies which utilised validated assessment or recognised, acceptable methods were often not

specific to mental health populations; that is, it is unknown if the tools perform accurately or individuals with mental health diagnoses can accurately report on dietary intake. However, the two studies utilising weighed food records and one study utilising a photographic food diary, more objective measures of dietary intake, found results in line with the results obtained in the current review. The overall strength of reporting in many studies was also limited, with the majority considered to be neutral, i.e. neither strong nor weak (N=40).

The dietary intake methods utilised in studies included in this meta-analysis were based on self-report, so may reflect subjective bias. This review comprehensively and systematically reviewed all published studies, providing a best-guess insight into dietary intake in people with SMI. Misreporting is a common issue in the general population, with an average energy underreporting of approximately 20%, and higher in people who are obese (~30%). Given that people with SMI commonly experience additional barriers, including cognitive impairment, lack of motivation and poor memory, misreporting could be expected to be more common, and to have a larger impact, in this population, suggesting the findings on energy intake may be an underestimation. Comparisons against population data can be misleading as the population data can be captured years or even decades earlier, are generally unmatched to the target group and may have utilized a different nutrition assessment method to the target group. These provide potential explanations for conflicting results, which have been reported [47, 74].

Results from this review suggest that no dietary assessment method or tool has been thoroughly validated in SMI. There is a clear need for subjective measures of dietary assessment to be compared with objective measures, such as biomarkers, to assess

the accuracy of self-report measures in people with SMI. Biomarkers, such as carotenoids which are reflective of fruit and vegetable intake [88], or doubly-labelled water which is reflective of total energy intake [89], are validated specific measures of dietary intake in the general population. Whilst direct relationships between diet and objective biomarkers likely also exist in mental illness, consideration of certain factors is needed when interpreting results. For example, inflammation associated with mental illness may reduce the levels of these biomarkers. Given cognitive impairment, poor memory, motivation difficulties and potential recall bias, those assessing dietary intake need expertise or training in dietary assessment method selection and implementation, to ensure appropriate use of particular methods. Given short-term, 'snapshot' assessments of dietary intake were commonly used (such as the use of 24 hour recalls), long-term dietary intake in SMI may require further investigation. Meta-analyses in this review were also limited due to the range of metrics used to report outcomes, placing greater importance on complementary qualitative synthesis.

As the pooled prevalence of recovery in first-episode of psychosis (FEP) is 38% [90], and weight-gain and metabolic decline are most rapid in FEP in the earlier stages of psychotropic medication treatment [7], it was deemed imperative to review studies that included clinician-diagnosed FEP. The four identified studies in FEP found unfavourable dietary intakes [59, 60, 62, 74], in line with the results for established, enduring SMI. This is particularly important, since increased food intake and the majority of associated weight gain is believed to begin following initiation of antipsychotic treatment [11, 91]. Furthermore, FEP has been identified as a 'critical period' for targeting lifestyle behaviours in order to prevent obesity and metabolic dysfunction from arising later in life [92].

There was limited information obtained from the systematic review for the impact of diet on brain health and mental illness symptomatology however evidence in this area is growing. There appears to be a bidirectional relationship between diet quality and depression [93], with emerging RCT evidence finding improvements in diet quality correlate with improvements in depressive symptoms [94, 95]. Additionally, dietary intake appears to be a factor in brain health in humans, which may be of particular relevance given the neurodegeneration involved with SMI. High blood sugar and western diet, which is high in processed, non-nutritious foods, and low in commonly recommended foods of a healthy diet, are associated with smaller hippocampal volume [96, 97]. Further, a meta-analysis has also demonstrated the potential preventative action of diet on the development of a series of brain ailments including cognitive impairment (8 studies, RR=0.60, 95% CI 0.43-0.83) and depression (9 studies, RR=0.68, 95% CI 0.54-0.86) [98].

Future recommendations

Future recommendations include; (i) use of technology to assist people with mental illness to record/remember foods consumed, (ii) use of food models/images and a food checklist to assist people with remembering food and beverage items and to estimate portion sizes, (iii) utilising a trained interviewer or diet expert such as dietitian, (iv) utilising an online dietary assessment primer or published review [99] to choose the most appropriate assessment method, and (v) utilising relevant guidelines such as Strengthening the Reporting of Observational Studies in Epidemiology – nutritional epidemiology (STROBE-nut) [100] to enhance reporting of dietary intake studies.

Additionally, further research should be dedicated to the following areas; (i) comprehensive evaluation of dietary intake relative to psychotropic medications, (ii)

dietary intake in the early stages of illness as targets for preventative intervention, (iii) dietary intake pre-illness onset to observe if unhealthy dietary intake precedes illness onset i.e. at-risk mental state, and whether any dietary factors may indicate the onset of illness, (iv) the effect of dietary patterns on psychiatric symptoms, and characteristic of illness such as cognitive impairment, in people with SMI, and (v) evaluating the validity and reliability of dietary assessment methodologies in people with SMI to determine appropriate methods for future use, or facilitate the development of new methods. Validation should be completed using energy equations to determine accuracy, use of the method of trials to establish believability, and where possible use objective biomarkers to validate.

Overall, the findings of this study are clinically important, as poor dietary intake, particularly low intakes of fruit and vegetables, and high intakes of fast food and other convenience foods, and sweetened beverages, may lead to greater risk for future cardiometabolic illness. Dietary interventions should be a standard part of care for people with SMI, to help mitigate the physical health disparities in this population compared to the wider population.

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Contributions

ST conceived study idea. ST, PBW, KS, BS and TB developed PROSPERO proposal and search strategy. ST and TB screened potential titles and determined included studies with assistance from PBW. ST and TB led data extraction. BS and JF performed the meta-analysis and interpreted results with ST. ST and ET led study

quality checks. ST led manuscript preparation with input from all authors. All authors approved the final version of the manuscript.

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References

1. Walker ER, McGee RE, Druss BG. Mortality in mental disorders and global disease burden implications: a systematic review and meta-analysis. *JAMA Psychiatry* 2015; **72**: 334-41.
2. Thornicroft G. Physical health disparities and mental illness: the scandal of premature mortality. *Br J Psychiatry* 2011; **199**: 441-2.
3. Correll CU, Solmi M, Veronese N, Bortolato B, Rosson S, Santonastaso P, et al. Prevalence, incidence and mortality from cardiovascular disease in patients with pooled and specific severe mental illness: a large-scale meta-analysis of 3,211,768 patients and 113,383,368 controls. *World Psychiatry* 2017; **16**: 163-80.
4. Gakidou E, Afshin A, Abajobir AA, Abate KH, Abbafati C, Abbas KM, et al. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990-2016. *Lancet* 2017; **390**: 1345-422.
5. Lieberman JA, Stroup TS, McEvoy JP, Swartz MS, Rosenheck RA, Perkins DO, et al. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. *N Engl j Med* 2005; 353: 1209-23.
6. Galletly CA, Castle D, Dark F, Humberstone V, Jablensky A, Killacky E, et al. Australian and New Zealand clinical practice guidelines for the treatment of bipolar disorder. *Aust N Z J Psychiatry* 2016; **50**: 1-117.
7. Álvarez-Jiménez M, González-Blanch C, Crespo-Facorro B, Hetrick S, Rodriguez-Sánchez JM, Pérez-Iglasias R, et al. Antipsychotic-induced weight gain in chronic and first-episode psychotic disorders. *CNS Drugs* 2008; **22**: 547-62.

8. Correll CU, Manu P, Olshanskiy V, Napolitano B, Kane JM, Malhotra AK. Cardiometabolic risk of second-generation antipsychotic medications during first-time use in children and adolescents. *JAMA* 2009; **302**: 1765-73.

9. Vancampfort D, Stubbs B, Mitchell AJ, De Hert M, Wampers M, Ward PB, et al. Risk of metabolic syndrome and its components in people with schizophrenia and related psychotic disorders, bipolar disorder and major depressive disorder: a systematic review and meta-analysis. *World Psychiatry* 2015; **14**: 339-47.

10. Elman I, Borsook D, Lukas SE. Food intake and reward mechanisms in patients with schizophrenia: implications for metabolic disturbances and treatment with second-generation antipsychotic agents. *Neuropsychopharmacology* 2006; **31**: 2091-120.

11. Blouin M, Tremblay A, Jalbert ME, Venables H, Bouchard RH, Roy MA, et al. Adiposity and eating behaviors in patients under second generation antipsychotics. *Obesity* 2008; **16**: 1780-7.

12. Dipasquale S, Pariante CM, Dazzan P, Aguglia E, McGuire P, Mondelli V. The dietary pattern of patients with schizophrenia: a systematic review. *J Psychiatr Res* 2013; **47**: 197-207.

13. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. *JAMA* 2000; **283**: 2008-12.

14. Moher D, Liberati A, Tetzlaff J, Altman TG, Altman D, Antes G, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Ann Intern Med* 2009; **151**: 264-9.

15. Academy of Nutrition and Dietetics. *Evidence Analysis Manual: Steps in the Academy Evidence Analysis Process*. Chicago: Evidence Analysis Library, 2016.

16. Borenstein M, Hedges LV, Higgins JPT, Rothstein HR. *Comprehensive meta-analysis* version 2. Englewood, NJ: Biostat, 2005, 104.

17. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials* 1986; **7**: 177-88.

18. Orwin RG. A fail-safe N for effect size in meta-analysis. *J Educ Stat* 1983; **8**: 157-9.

19. Adolfo AB, AhnAllen CG, Tidey JW. Effects of smoking cues on caffeine urges in heavy smokers and caffeine consumers with and without schizophrenia. *Schizophr Res* 2009; **107**: 192-7.

20. Amani R. Is dietary pattern of schizophrenia patients different from healthy subjects? *BMC Psychiatry* 2007; **7**: 15.

21. Archie SM, Goldberg JO, Akhtar-Danesh N, Landeen J, McColl L, McNiven J. Psychotic disorders, eating habits, and physical activity: who is ready for lifestyle changes? *Psychiatr Serv* 2007; **58**: 233-9.

22. Arrojo-Romero M, Armas Barbazán C, López-Moriñigo JD, Ramos-Rios R, Gurpegui M, Martinez-Ortega JM, et al. Caffeine consumption in a long-term psychiatric hospital: Tobacco smoking may explain in large part the apparent association between schizophrenia and caffeine use. *Schizophr Res* 2015; **164**: 234-41.

23. Baethge C, Tondo L, Lepri B, Baldessarini RJ. Coffee and cigarette use: association with suicidal acts in 352 Sardinian bipolar disorder patients. *Bipolar Disord* 2009; **11**: 494-503.

24. Bly MJ, Taylor SF, Dalack G, Pop-Busui R, Burghardt KJ, Evans SJ, et al. Metabolic syndrome in bipolar disorder and schizophrenia: dietary and lifestyle factors compared to the general population. *Bipolar Disord* 2014; **16**: 277-88.

25. Bobes J, Arango C, Garcia-Garcia M, Rejas J. Healthy lifestyle habits and 10-year cardiovascular risk in schizophrenia spectrum disorders: An analysis of the impact of smoking tobacco in the CLAMORS schizophrenia cohort. *Schizophr Res* 2010; **119**: 101-9.

26. Brown S, Birtwistle J, Roe L, Thompson C. The unhealthy lifestyle of people with schizophrenia. *Psychol Med* 1999; **29**: 697-701.

27. Chang YW, Assari S, Prossin AR, Stertz L, McInnis MG, Evans SG. Bipolar disorder moderates associations between linoleic acid and markers of inflammation. *J Psychiatr Res* 2017; **85**: 29-36.

28. Clayton EH, Hanstock TL, Hirneth SJ, Kable CJ, Garg ML, Hazell PL. Long-chain omega-3 polyunsaturated fatty acids in the blood of children and adolescents with juvenile bipolar disorder. *Lipids* 2008; **43**: 1031-8.

29. Ellingrod VL, Taylor SF, Brook RD, Evans SJ, Zölliner SK, Grove TB, et al. Dietary, lifestyle and pharmacogenetic factors associated with arteriole endothelial-dependent vasodilatation in schizophrenia patients treated with atypical antipsychotics (AAPs). *Schizophr Res* 2011; **130**: 20-6.

30. Elmslie JL, Mann JI, Silverstone JT, Williams SM, Romans SE. Determinants of overweight and obesity in patients with bipolar disorder. *J Clin Psychiatry* 2001; **62**: 486-91.

31. Evans SJ, Assari S, Harrington GJ, Chang YW, Burant CF, McInnis MG. Plasma linoleic acid partially mediates the association of bipolar disorder on self-reported mental health scales. *J Psychiatr Res* 2015; **68**: 61-7.

32. Evans SJ, Ringrose RN, Harrington GJ, Mancuso P, Burant CF, McInnis MG. Dietary intake and plasma metabolomic analysis of polyunsaturated fatty acids in bipolar subjects reveal dysregulation of linoleic acid metabolism. *J Psychiatr Res* 2014; **57**: 58-64.

33. Fawzi MH, Fawzi MM, Said NS, Fawzi MM, Fouad AA, Abdel-Moety H. Effect of Ramadan fasting on anthropometric, metabolic, inflammatory and psychopathology status of Egyptian male patients with schizophrenia. *Psychiatry Res* 2015; **225**: 501-8.

34. Fusar-Poli P, De Marco L, Cavallin F, Bertorello A, Nicolasi M, Politi P. Lifestyles and cardiovascular risk in individuals with functional psychoses. *Perspect Psychiatr Care* 2009; **45**: 87-99.

35. Gothelf D, Falk B, Singer P, Kairi M, Philliip M, Zigel L, et al. Weight gain associated with increased food intake and low habitual activity levels in male adolescent schizophrenic inpatients treated with olanzapine. *Am J Psychiatry* 2002; **159**: 1055-7.

36. Gupta A, Craig TK. Diet, smoking and cardiovascular risk in schizophrenia in high and low care supported housing. *Epidemiol Psichiatr Soc* 2009; **18**: 200-7.

37. Gurpegui M, Aguilar MC, Martinez-Ortega JM, Diaz FJ, de Leon J. Caffeine intake in outpatients with schizophrenia. *Schizophr Bull* 2004; **30**: 935-45.

38. Gurpegui M, Aguilar MC, Martinez-Ortega JM, Jurado D, Diaz FJ, Quintana HM, et al. Fewer but heavier caffeine consumers in schizophrenia: a case-control study. *Schizophr Res* 2006; **86**: 276-83.

39. Hahn LA, Galletly CA, Foley DL, Mackinnon A, Watts GF, Castle DJ, et al. Inadequate fruit and vegetable intake in people with psychosis. *Aust N Z J Psychiatry* 2014; **48**: 1025-35.

40. Hamera E, Schneider JK, Deviney S. Alcohol, cannabis, nicotine, and caffeine use and symptom distress in schizophrenia. *J Nerv Ment Dis* 1995; **183**: 559-65.

41. Hardy S, Gray R. The secret food diary of a person diagnosed with schizophrenia. *J Psychiatr Ment Health Nurs* 2012; **19**: 603-9.

42. Haruyuki ITO, Kumagai T, Kimura M, Kolke S, Shimizu T. Dietary Intake in Body Mass Index Differences in Community-Based Japanese Patients with Schizophrenia. *Iranian J Public Health* 2015; **44**: 639-645.

43. Heald A, Pendlebury J, Anderson S, Narayan V, Guy M, Gibson M, et al. Lifestyle factors and the metabolic syndrome in Schizophrenia: A cross-sectional study. *Ann Gen Psychiatry* 2017; **16**: 12.

44. Henderson DC, Borba CP, Daley TB, Boxill R, Nguyen DD, Culhane MA, et al. Dietary intake profile of patients with schizophrenia. *Ann Clin Psychiatry* 2006; **18**: 99-105.

45. Henderson DC, Cagliero E, Copeland PM, Borba CP, Evins E, Hayden D, et al. Glucose metabolism in patients with schizophrenia treated with atypical antipsychotic agents: A frequently sampled intravenous glucose tolerance test and minimal model analysis. *Arch Gen Psychiatry* 2005; **62**: 19-28.

46. Jacka FN, Pasco JA, Mykletun A, Williams LJ, Nicholson GC, Kotowicz MA, et al. Diet quality in bipolar disorder in a population-based sample of women. *J Affect Disord* 2011; **129**: 332-7.

47. Jahrami HA, Faris MAE, Saif ZQ, Hammad LH. Assessing dietary and lifestyle risk factors and their associations with disease comorbidities among patients with schizophrenia: A case-control study from Bahrain. *Asian J Psychiatr* 2017; **28**: 115-23.

48. Kilbourne AM, Rofey DL, McCarthy JF, Post EP, Welsh D, Blow FC. Nutrition and exercise behavior among patients with bipolar disorder. *Bipolar Disord* 2007; **9**: 443-52.

49. Kilian R, Becker T, Krüger L, Schmid S, Frasch K. Health behavior in psychiatric in-patients compared with a German general population sample. *Acta Psychiatr Scand* 2006; **114**: 242-8.

50. Konarzewska B, Stefańska E, Wendolowicz A, Cwalina U, Golonko A, Malus A, et al. Visceral obesity in normal-weight patients suffering from chronic schizophrenia. *BMC Psychiatry* 2014; **14**: 35.

51. Manzanares N, Monseny R, Ortega L, Montalvo I, Franch J, Gutliérrez-Zotes A, et al. Unhealthy lifestyle in early psychoses: the role of life stress and the hypothalamic-pituitary-adrenal axis. *Psychoneuroendocrinology* 2014; **39**: 1-10.

52. McCreadie RG, Scottish Schizophrenia Lifestyle Group. Diet, smoking and cardiovascular risk in people with schizophrenia: descriptive study. *Br J Psychiatry* 2003; **183**: 534-9.

53. Mucheru D, Hanlon MC, Campbell LE, McEvoy M, MacDonald-Wicks L. Social Dysfunction and Diet Outcomes in People with Psychosis. *Nutrients* 2017; **9**: 80.

54. Nenke MA, Hahn LA, Thompson CH, Liu D, Galletly CA. Psychosis and cardiovascular disease: is diet the missing link? *Schizophr Res* 2015; **161**: 465-70.

55. Nunes D, Eskinazi B, Cambolm Rockett F, Delgado VB, Schwelgert Perry ID. Nutritional status, food intake and cardiovascular disease risk in individuals with schizophrenia in southern Brazil: a case-control study. *Rev Psiquiatr Salud Ment* 2014; **7**: 72-9.

56. Osborn DP, Nazareth I, King MB. Physical activity, dietary habits and Coronary Heart Disease risk factor knowledge amongst people with severe mental illness. *Soc Psychiatry Psychiatr Epidemiol* 2007; **42**: 787-93.

57. Ratliff JC, Palmese LB, Reutenauer EL, Liskov E, Grilo CM, Tek C. The effect of dietary and physical activity pattern on metabolic profile in individuals with schizophrenia: a cross-sectional study. *Compr Psychiatry* 2012; **53**: 1028-33.

58. Roick C, FritzWieacker A, Matschinger H, Heider D, Schindler J, Riedel-Heller S, et al. Health habits of patients with schizophrenia. *Soc Psychiatry Psychiatr Epidemiol* 2007; **42**: 268-76.

59. Ryan MC, Flanagan S, Kinsella U, Keeling F, Thakore JH. The effects of atypical antipsychotics on visceral fat distribution in first episode, drug-naive patients with schizophrenia. *Life Sci* 2004; **74**: 1999-2008.

60. Ryan MCM, Collins P, Thakore JH. Impaired fasting glucose tolerance in first-episode, drug-naive patients with schizophrenia. *Am J Psychiatry* 2003; **160**: 284-9.

61. Saarni S, Saarni SI, Fogelholm M et al. Body composition in psychotic disorders: a general population survey. *Psychol Med* 2009; **39**: 801-10.

62. Samele C, Patel M, Boydell J, Leese M, Wessely S, Murray R. Physical illness and lifestyle risk factors in people with their first presentation of psychosis. *Soc Psychiatry Psychiatr Epidemiol* 2007; **42**: 117-24.

63. Simonelli-Muñoz AJ, Fortea MI, Salorio P, Gallego-Gomez JI, Sánchez-Bautista S, Balanza S. Dietary habits of patients with schizophrenia: A self-reported questionnaire survey. *Int J Ment Health Nurs* 2012; **21**: 220-8.

64. Stokes C, Peet M. Dietary sugar and polyunsaturated fatty acid consumption as predictors of severity of schizophrenia symptoms. *Nutr Neurosci* 2004; **7**: 247-9.

65. Strassnig M, Singh Brar J, Ganguli R. Nutritional assessment of patients with schizophrenia: a preliminary study. *Schizophr Bull* 2003; **29**: 393-7.

66. Strassnig M, Singh Brar J, Ganguli R. Increased caffeine and nicotine consumption in community-dwelling patients with schizophrenia. *Schizophr Res* 2006; **86**: 269-75.

67. Strassnig M, Singh Brar J, Ganguli R. Dietary fatty acid and antioxidant intake in community-dwelling patients suffering from schizophrenia. *Schizophr Res* 2005; **76**: 343-51.

68. Sugawara N, Yasui-Furukori N, Sato Y, Saito M, Furukori H, Nakagami T, et al. Dietary patterns are associated with obesity in Japanese patients with schizophrenia. *BMC Psychiatry* 2014; **14**: 184.

69. Sugawara N, Yasui-Furukori N, Yamazaki M, Shimoda K, Mori T, Sugai T, et al. Attitudes toward metabolic adverse events among patients with schizophrenia in Japan. *Neuropsychiatr Dis Treat* 2016; **12**: 427-36.

70. Suvisaari JM, Saarni SI, Perälä J, Suvisaari JV, Härkänen T, Lönnqvist J, et al. Metabolic syndrome among persons with schizophrenia and other psychotic disorders in a general population survey. *J Clin Psychiatry* 2007; **68**: 1045-55.

71. Treuer T, Hoffman VP, Chen AK, Irimia V, Ocampo M, Wang G, et al. Factors associated with weight gain during olanzapine treatment in patients with schizophrenia or bipolar disorder: results from a six-month prospective, multinational, observational study. *World J Biol Psychiatry* 2009; **10**: 729-40.

72. Tsuruga K, Sugawara N, Sato Y, Saito M, Furukori H, Nakagami T, et al. Dietary patterns and schizophrenia: A comparison with healthy controls. *Neuropsychiatr Dis Treat* 2015; **11**: 1115-20.

73. Wallace B, Tennant C. Nutrition and obesity in the chronic mentally ill. *Aust N Z J Psychiatry* 1998; **32**: 82-5.

74. Williamson K, Kilner K, Clibbens N. A comparison of the nutrient intake of a community-dwelling first-episode psychosis cohort, aged 19-64 years, with data from the UK population. *J Nutr Sci* 2015; **4**: e28.

75. Winstead DK. Coffee consumption among psychiatric inpatients. *Am J Psychiatry*, 1976; **133**: 1447-50.

76. Noguchi R, Hiraoka M, Watanabe Y, Kagawa Y. Relationship between dietary patterns and depressive symptoms: difference by gender, and unipolar and bipolar depression. *J Nutr Sci Vitaminol*, 2013; **59**: 115-22.

77. Archie SM, Goldberg JO, Akhtar-Danesh N, Landeen J, McColl L, McNiven J. Psychotic disorders, eating habits, and physical activity: who is ready for lifestyle changes? *Psychiatr Serv* 2007; **58**: 233-9.

78. Duffey KJ, Popkin BM. Energy density, portion size, and eating occasions: contributions to increased energy intake in the United States, 1977–2006. *PLoS Med* 2011; **8**: e1001050.

79. Appel LJ, Frohlich ED, Hall JE, Pearson TA, Sacco RL, Seals DR, et al. The importance of population-wide sodium reduction as a means to prevent cardiovascular disease and stroke: a call to action from the American Heart Association. *Circulation* 2011; **123**: 1138-43.

80. Vancampfort D, Firth J, Schuch FB, Rosenbaum S, Mugisha J, Hallgren M, et al. Sedentary behavior and physical activity levels in people with schizophrenia, bipolar disorder and major depressive disorder: a global systematic review and meta-analysis. *World Psychiatry* 2017; **16**: 308-15.

81. Vancampfort D, Rosenbaum S, Schuch FB et al. Cardiorespiratory fitness in severe mental illness: a systematic review and meta-analysis. *Sports Med* 2017; **47**: 343-52.

82. Hall KD, Heymsfield SB, Kemnitz JW, Klein S, Schoeller DA, Speakman JR. Energy balance and its components: implications for body weight regulation. *Am J Clin Nutr* 2012; **95**: 989-94.

83. Werneke U, Taylor D, Sanders TAB. Behavioral interventions for antipsychotic induced appetite changes. *Curr Psychiatry Rep* 2013; **15**: 347.

84. Lett TA, Wallace TJ, Chowdhury NI, Tiwari AK, Kennedy JL, Müller DJ. Pharmacogenetics of antipsychotic-induced weight gain: review and clinical implications. *Mol Psychiatry* 2012; **17**: 242-66.

85. Reynolds GP, Kirk SL. Metabolic side effects of antipsychotic drug treatment–pharmacological mechanisms. *Pharmacol Ther* 2010; **125**: 169-79.

86. Mitchell AJ, Vancampfort D, Sweers K, van Winkel R, Yu K, De Hert M. Prevalence of metabolic syndrome and metabolic abnormalities in schizophrenia and related disorders—a systematic review and meta-analysis. *Schizophr Bull* 2011; **39**: 306-18.

87. Firth J, Carney R, Stubbs B, Teasdale SB, Vancampfort D, Ward PB, et al. Nutritional deficiencies and clinical correlates in first-episode psychosis: a systematic review and meta-analysis. *Schizophr Bull* [epub ahead of print Nov 2017].

88. Burrows TL, Williams R, Rollo M, Wood L, Garg ML, Jensen M, et al. Plasma carotenoid levels as biomarkers of dietary carotenoid consumption: A systematic review of the validation studies. *J Nutr Intermediary Metabolism*, 2015; **2**: 15-64.

89. Hill RJ, Davies PSW. The validity of self-reported energy intake as determined using the doubly labelled water technique. *Br J Nutr*, 2001; **85**: 415-30.

90. Lally J, Ajnakina O, Stubbs B, Cullinane M, Murphy KC, Gaughran F et al. Remission and recovery from first-episode psychosis in adults: systematic review and meta-analysis of long-term outcome studies. *Br J Psychiatry*, 2017; **211**: 350-8.

91. Fountaine RJ, Taylor AE, Mancuso JP, Greenway FL, Byerley LO, Smith SR, et al. Increased food intake and energy expenditure following administration of olanzapine to healthy men. *Obesity* 2010; **18**: 1646-51.

92. Teasdale SB, Ward PB, Rosenbaum S, Samaras K, Stubbs B. Solving a weighty problem: systematic review and meta-analysis of nutrition interventions in severe mental illness. *Br J Psychiatry*, 2017; **210**: 110-8.

93. Quirk SE, Williams LJ, O'Neil A, Pasco JA, Jacka FN, Housden S, et al. The association between diet quality, dietary patterns and depression in adults: a systematic review. *BMC Psychiatry* 2013; **13**: 175.

94. Jacka FN, O'Neil A, Opie R, Itsiopoulos C, Cotton S, Mohebbi M, et al. A randomised controlled trial of dietary improvement for adults with major depression (the 'SMILES'trial). *BMC Med* 2017; **15**: 23.

95. Opie RS, O'Neil A, Jacka FN, Pizzinga J, Itsiopoulos C. A modified Mediterranean dietary intervention for adults with major depression: Dietary protocol and feasibility data from the SMILES trial. *Nutr Neurosci* [epub ahead of print Apr 2017].

96. Cherbuin N, Sachdev P, Anstey KJ. Higher normal fasting plasma glucose is associated with hippocampal atrophy The PATH Study. *Neurology*, 2012; **79**: 1019-26.

97. Jacka FN, Cherbuin N, Anstey KJ, Sachdev P, Butterworth P. Western diet is associated with a smaller hippocampus: a longitudinal investigation. *BMC Med*, 2015; **13**: 215.

98. Psaltopoulou T, Sergentanis TN, Panagiotakos DB, Sergentanis IN, Kosti R, Scarmeas N. Mediterranean diet, stroke, cognitive impairment, and depression: a meta-analysis. *Ann Neurol*, 2013; **74**: 580-91.

99. Shim JS, Oh K, Kim HC. Dietary assessment methods in epidemiologic studies. *Epidemiol Health*, 2014; **36**: e2014009.

100. Lachat C, Hawwash D, Ockè MC, Berg C, Forsum E, Hörnell A, et al. Strengthening the Reporting of Observational Studies in Epidemiology–

nutritional epidemiology (STROBE-nut): An extension of the STROBE statement. *Nutr Bull* 2016; **41**: 240-51.

Table 1. Meta-analysis of dietary energy and nutrient intakes.

Comparison	Number studies	Hedges-G	Lower limit	Upper limit	Z-value	P-value	I^2	Mean difference	Lower Limit	Upper limit	Z-value	P-value	I^2
Energy (kJ)	7	0.463	0.159	0.767	2.986	0.003	77	1332	487	2178	3.089	0.002	76
Sodium (mg)	3	0.414	0.181	0.646	3.488	<0.001	12	322	174	490	4.121	<0.001	0
Vitamin B6	3	0.484	-0.532	1.499	0.933	0.351	95	0.4	-0.4	1.2	0.999	0.318	96
Vitamin C (mg)	3	0.132	-0.530	0.794	0.391	0.696	88	8.7	-47.0	64.4	0.305	0.760	86
Zinc (mg)	3	0.369	-0.233	0.971	1.202	0.229	85	1.6	-1.4	4.5	1.038	0.299	85

Figure 1. PRISMA Flowchart

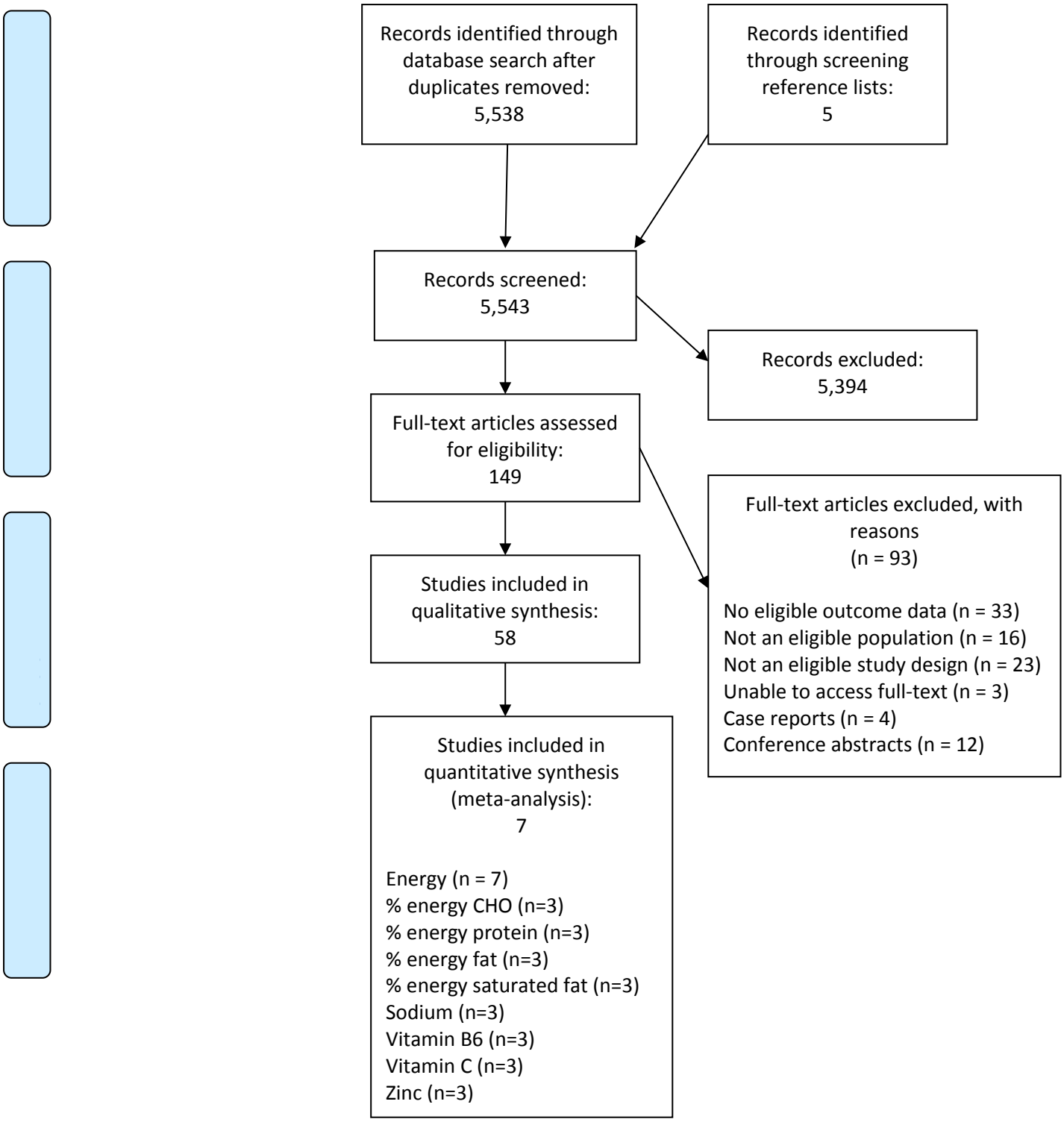
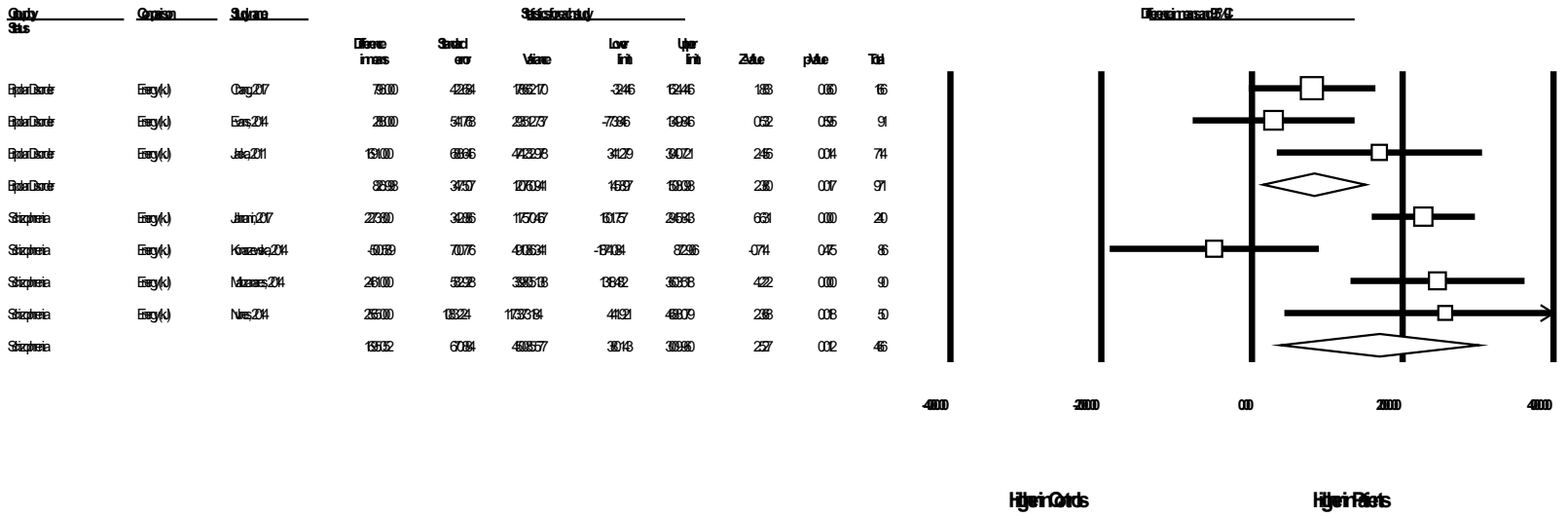


Figure 2. Meta-analysis of energy intake in bipolar disorder and schizophrenia.



PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5,6
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	7
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	7,8
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	7,8,S2
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	S2
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	7,Fig1
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	8
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	8,9
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	9,10
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	9,10
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	9,10

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	9,10
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	9,10
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	11,Fig1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	11,12,T1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	13,14
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	13,14,Fig2
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	13,14,T2
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	13,14
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	13,14,T2
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	16-20
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	18-20
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	16-20
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	20

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: **www.prisma-statement.org**.

MOOSE Checklist for Meta-analyses of Observational Studies

Item No	Recommendation	Reported on Page No
Reporting of background should include		
1	Problem definition	4
2	Hypothesis statement	-
3	Description of study outcome(s)	6-8
4	Type of exposure or intervention used	
5	Type of study designs used	6
6	Study population	5
Reporting of search strategy should include		
7	Qualifications of searchers (eg, librarians and investigators)	Title page, 5
8	Search strategy, including time period included in the synthesis and key words	5, Suppl 2.
9	Effort to include all available studies, including contact with authors	6
10	Databases and registries searched	Suppl 2.
11	Search software used, name and version, including special features used (eg, explosion)	-
12	Use of hand searching (eg, reference lists of obtained articles)	5
13	List of citations located and those excluded, including justification	9-10, Fig 1, Table 1
14	Method of addressing articles published in languages other than English	-
15	Method of handling abstracts and unpublished studies	6
16	Description of any contact with authors	-
Reporting of methods should include		
17	Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	5-6
18	Rationale for the selection and coding of data (eg, sound clinical principles or convenience)	5-6
19	Documentation of how data were classified and coded (eg, multiple raters, blinding and interrater reliability)	5-6
20	Assessment of confounding (eg, comparability of cases and controls in studies where appropriate)	7-8
21	Assessment of study quality, including blinding of quality assessors, stratification or regression on possible predictors of study results	6-7
22	Assessment of heterogeneity	7-8
23	Description of statistical methods (eg, complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated	7-8
24	Provision of appropriate tables and graphics	Tables 1-2, Figs 1-2, Suppl 1-3
Reporting of results should include		
25	Graphic summarizing individual study estimates and overall estimate	Table 2, Fig 2
26	Table giving descriptive information for each study included	9-11, Table 1
27	Results of sensitivity testing (eg, subgroup analysis)	11, Fig 2

28	Indication of statistical uncertainty of findings	11-12

Item No	Recommendation	Reported on Page No
Reporting of discussion should include		
29	Quantitative assessment of bias (eg, publication bias)	11-12, Table 2
30	Justification for exclusion (eg, exclusion of non-English language citations)	5-6
31	Assessment of quality of included studies	Suppl 3
Reporting of conclusions should include		
32	Consideration of alternative explanations for observed results	15-17
33	Generalization of the conclusions (ie, appropriate for the data presented and within the domain of the literature review)	17
34	Guidelines for future research	17
35	Disclosure of funding source	17

From: Stroup DF, Berlin JA, Morton SC, et al, for the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) Group. Meta-analysis of Observational Studies in Epidemiology. A Proposal for Reporting. *JAMA*. 2000;283(15):2008-2012. doi: 10.1001/jama.283.15.2008.

Supplementary File 3: Search Strategy

Databases
CINAHL
Cochrane Reviews
Cochrane Trials
Cochrane – Other Reviews
Embase
Medline
Medline In Process
PsychINFO
Scopus

CINAHL

#	**Query**
S1	(MH "Eating Behavior")
S2	(MH "Food Intake")
S3	(MH "Eating")
S4	(diet* n5 (intake or behavio?r* or quality or pattern*))
S5	"nutrition*"
S6	(MH "Coffee")
S7	(MH "Caffeine")
S8	(MH "Beverages+")
S9	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8
S10	(MH "Schizophrenia+")
S11	(MH "Psychotic Disorders+")
S12	(MH "Bipolar Disorder+")
S13	TI bipolar* OR AB bipolar*
S14	S10 OR S11 OR S12 OR S13
S15	**S9 AND S14 Limited to English and Humans**

Cochrane Library

#1	MeSH descriptor: [Feeding Behavior] this term only
#2	MeSH descriptor: [Eating] this term only
#3	food intake
#4	(diet* near/5 (intake or behavio?r* or quality or pattern*))
#5	nutrition*
#6	MeSH descriptor: [Coffee] this term only
#7	MeSH descriptor: [Caffeine] this term only
#8	MeSH descriptor: [Beverages] explode all trees
#9	{or #1-#8}
#10	MeSH descriptor: [Schizophrenia] explode all trees
#11	MeSH descriptor: [Psychotic Disorders] explode all trees
#12	MeSH descriptor: [Bipolar Disorder] this term only
#13	bipolar*:ti,ab
#14	{or #10-#13}
#15	{and #9, #13}

Embase

#	Searches
1	feeding behavior/
2	food intake/
3	eating/
4	(diet* adj5 (intake or behavio?r* or quality or pattern*)).mp
5	nutrition/
6	Coffee/
7	Caffeine/
8	exp Beverages/
9	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8
10	schizophrenia/
11	psychosis/
12	bipolar disorder/
13	10 or 11 or 12
14	9 and 13
15	**limit 14 to (human and english language)**

Medline

#	Searches
1	Feeding Behavior/
2	food intake.mp. or Eating/
3	(diet* adj5 (intake or behavio?r* or quality or pattern*)).mp.
4	nutrition*.mp.
5	Coffee/
6	Caffeine/
7	exp Beverages/
8	1 or 2 or 3 or 4 or 5 or 6 or 7
9	exp Schizophrenia/
10	exp Psychotic Disorders/
11	Bipolar Disorder/
12	bipolar*.tw.
13	9 or 10 or 11 or 12
14	8 and 13
15	**limit 14 to (english language and humans)**

Medline In-Process

#	Searches
1	feeding behavio?r*.mp.
2	food intake.mp. or Eating/
3	(diet* adj5 (intake or behavio?r* or quality or pattern*)).mp.
4	nutrition*.mp.
5	Coffee.mp.
6	Caffeine.mp.
7	Beverage*.mp.
8	(beverage* or tea or juice* or milk or energy drink* or drinking water).mp.
9	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8
10	Schizophrenia.mp.
11	(Psychotic or psychosis).mp.
12	Bipolar*.mp.
13	10 or 11 or 12
14	9 and 13
15	**limit 14 to english language**

PsychINFO

#	Searches
1	exp Eating Behavior/
2	food intake/
3	eating.mp.
4	(diet* adj5 (intake or behavio?r* or quality or pattern*)).mp.
5	nutrition*.mp.
6	Coffee.mp.
7	caffeine/
8	exp "BEVERAGES (NONALCOHOLIC)"/ or exp ALCOHOLIC BEVERAGES/
9	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8
10	exp SCHIZOPHRENIA/
11	exp Psychosis/
12	exp Bipolar Disorder/
13	bipolar*.tw.
14	10 or 11 or 12 or 13
15	9 and 14
16	**limit 15 to (human and english language)**

Scopus

(TITLE-ABS (**"feeding behavio?r*"** OR **"food intake"** OR **eating** OR (**diet*** W/5 (**intake** OR **behavio?r*** OR **quality** OR **pattern***)) OR **nutrition*** OR **coffee** OR **caffeine** OR **beverage*** OR **"drinking water"** OR **milk** OR **juice*** OR **"energy drink*"**) AND TITLE-ABS (**schizophrenia** OR **bipolar*** OR **psychosis** OR **psychotic**)) AND (LIMIT-TO (EXACTKEYWORD , **"Human"**)) AND (LIMIT-TO (LANGUAGE , **"English"**))

Supplementary File 4. Characteristics of included studies

Study	Design	Population studied	Control or Comparative Group	Nutrition Ax Method	Validated or recognised measure	Outcomes	Study Quality Score^	Main Findings
Adolfo et al, 2009 (USA)	Cross-cue reactivity	SCZ, SAD 80% receiving SGAs Outpatients n=15	Control n=18	Caffeine use history. Assessor not described	Unknown	Caffeine (mg)	⦸	SMI group had higher intake of caffeine (mg) and caffeinated drinks. Statistical trend for smokers to have greater caffeine urges.
Amani et al. 2007 (Iran)	Cross-sectional	SCZ Medications not described Inpatients n=30	Control n=30	Semi-quantitative FFQ Assessed by nutrition students	Unknown	Diet quality (score), Food groups (% of people consuming)	⦸	People with a SMI consumed more carbonated drinks & hydrogenated oils & ate less nuts & vegetable oils. Females with SMI had lower diet quality compared with controls.
Archie et al. 2007 (Canada)	Cross-sectional	SMI 100% prescribed APMs (70% SGAs, 15% FGAs, 15% combination) Outpatients n=101	General population data	Dietary Fat Screener & Fruit & Vegetable & Fibre Screener Assessor not described	Correlates with 100-item FFQ – recognized acceptable measure	Fat (g), Saturated fat (g), Fibre (g), Fruit (servings/day), Vegetables (servings/day)	+	People with SMI had a high fat, and saturated fat, intake. Intake of fruit & vegetables was higher in the SMI group compared to general population data.
Arrojo-Romero et al. 2015 (Spain)	Cross-sectional (4 arm)	SCZ, SAD Medications reported in chlorpromazine equivalents Inpatients n=145 Other SMI Medications reported in chlorpromazine equivalents Inpatients n=64	Control n=290	Standardised questionnaire Assessed by physician	Unknown	Caffeine (mg/day)	⦸	Frequency of caffeine use in SCZ inpatients was significantly higher than in SCZ outpatients. Frequency of high caffeine users among caffeine users was significantly higher in SCZ outpatients compared to SCZ inpatients. Smoking was significantly associated with caffeine. No significant difference in caffeine intake between people with SCZ and controls.
Baethge et al. 2009 (Germany)	Longitudinal	BPD Medications not described Outpatients n=352	None	Estimated daily coffee consumption. Assessed by study investigator.	Unknown	Caffeine (cups/day)	⦸	Mean 3 (+/-2) cups of coffee per day. Coffee intake higher in smokers. Coffee intake associated with suicidal ideation.
Bly et al. 2014 (USA)	Cross-sectional	SCZ 100% prescribed SGAs Outpatients n=143 BPD 100% prescribed SGAs Outpatients n=116	Matched population data n=259	24 hour recall (x3 within 10 days) Assessed by dietitian. Analysed by the Nutrition Data Systems for Research software	Recognised acceptable measure	Energy (kcal/day), Macronutrients (kcal/day), Fibre (g/day), EFAs (g/day)	⦸	SMI group had lower energy & omega-6 to omega-3 ratio & higher fibre intake compared to population data. BPD group has lower energy & mono- & polyunsaturated fat & higher fibre intake compared to population data.
Bobes et al. 2010 (Spain)	Cross-sectional	SCZ 100% prescribed APMs Outpatients n=1704	None	Series of verbal questions. Assessor not described	Unknown	Caffeine (cups/day), Salt (yes or no to meals), Fibre (freq of intake), Low caloric diet (freq of intake), Saturated fat (freq of intake)	⦸	Smokers more likely to consume daily caffeine (1 or more cups per day), & less likely to avoid salt & saturated fat, or to follow a high fibre or low caloric diet
Brown et al. 1999 (UK)	Cross-sectional	SCZ 91% prescribed	General population data	DINE Assessor not described	Validated for a study of health educators in	Fat (g), Unsaturated fat (g),	⦸	People with SCZ had diets higher fat and lower in fibre than the general population.

		psychotropic medication Outpatients n=102			general practice attenders	Fibre (g), Fruit (portions/day), Vegetables (portions/day)		No SMI participants ate the recommended 5 portions of fruit or vegetables per day.
Chang et al. 2017 (USA)	Cross-sectional	BPD 63% prescribed MS 52% prescribed SGAs Outpatients n=91	Control n=75	7 day diet record Assessed by dietitian Analysed using Nutrition Data System for Research software 2011	Recognised acceptable measure	Energy (kcal), Linoleic acid (g)	+	Energy intake higher in BPD group compared to controls (statistical trend) Non-significant difference in linoleic acid intake between groups
Clayton et al. 2008 (Australia)	Cross-sectional	BPD 100% prescribed MS Outpatients n=15	Control n=15	FFQ Assessor not described	Unknown	EFAs (mg/day)	⦸	BPD had significantly lower intake of EFAs (except DPA) compared to controls
Ellingrod et al. 2011 (USA)	Cross-sectional	SCZ, SAD, SCZF 100% prescribed APMs (88% SGAs, 12% FGAs) 26% prescribed MS Setting not described n=63	APM group compared to no APM group	24 hour recall (x3 within study period). Assessor not described Analysed by the Nutrition Data Systems for Research software	Recognised acceptable method	Energy (kcals/day), Macronutrients (g/day), FA subgroups (g/day), Fibre (g/day)	⦸	Statistical trend for SMI group to have lower PUFA: SFA ratio.
Elmslie et al. 2001 (New Zealand)	Cross-sectional	BPD 87% prescribed pharmacotherapy Outpatients n=89	Matched population data n=445	24 hour recall & 4-day estimated diet record. Assessor not described Analysed by Diet Cruncher software	Recognised acceptable measure	Energy (kJ) Macronutrients (g)	⦸	BPD group consumed more total fluid & sweetened drinks. Females with BPD consumed more energy than reference group.
Evans et al. 2014 (USA)	Cross-sectional	BPD 63% prescribed MS 52% prescribed SGAs Outpatients n=47	Control n=44	7 day diet record Assessed by dietitian Analysed using Nutrition Data System for Research software 2011	Recognised acceptable measure	Energy (kCal), EFA (g), Selenium (mcg)	+	Energy, SFA, eicosanoic & docosanoic FA intake higher in BPD compared to controls. Intake of selenium, EPA, DHA, DPA & AA lower in BPD group compared to controls.
Evans et al. 2015 (USA)	Cross-sectional	BPD 63% prescribed MS 48% prescribed SGAs Outpatients n=56	Control n=46	7 day diet record Assessed by dietitian Analysed using Nutrition Data System for Research software 2011	Recognised acceptable measure	Macronutrients (% total energy), EFA (% total FA),	+	Intake of EPA, DHA, AA lower in BPD group compared to controls. No difference in intake of macronutrients as % of energy intake, SFA, PUFA, MUFA, LA or ALA
Fawzi et al. 2015 (Egypt)	Cohort	SCZ 100% prescribed APM (58% FGA, 17% SGA, 25% combination) Outpatients n=100	None	24 hour recall (x3 within study period) Assessor not described Analysed using program based on Egyptian Food Composition Tables	Recognised acceptable measure	Energy (kCal), Macronutrients (g)	⦸	Mean energy, protein, CHO & fat intake slightly higher in SCZ group with metabolic syndrome compared to SCZ group without metabolic syndrome.
Fusar-Poli et al. 2009 (Italy)	Cross-sectional	SMI Medications not described Outpatients n=123	General population data	Questionnaire Assessor not described	Unknown	Fruit, vegetables (no. per day)	⦸	Low fruit and vegetable intake.
Gothelf et al. 2002 (Israel)	Cohort	SCZ 100% prescribed OLZ Inpatients n=10	None	Weighed food record (2 consecutive days) Assessed by dietitian	Recognised acceptable measure	Energy (kCal)	⦸	People receiving OLZ had a significant increase in caloric intake coinciding with weight gain.
Gupta et al. 2009 (UK)	Cross-sectional	SCZ Medication not described Residential care	General population data	FFQ (past 7 days), responses cross-checked with staff. Assessor not described	Unknown	'Healthy' and 'unhealthy' food categories	⦸	People in both high level and medium level care made more unhealthy food choices. Provision of healthy food options may not automatically equate to healthier diets.

		n=21 (low care) n=41 (high care)						
Gurpegui et al. 2004 (Spain)	Cross-sectional	SCZ 94% taking APMs (75% FGAs, 25% SGAs) Outpatients n=250	None	Self-reported alcohol & caffeine intake. Assessor not described	Unknown	Caffeine (mg/kg/day),	-	Caffeine associated with smoking and alcohol intake. No clear association between caffeine intake and APM or symptom severity.
Gurpegui et al. 2006 (Spain)	Case control	SCZ 94% taking APMs (75% FGAs, 25% SGAs) Outpatients n=250	Control n=290	Self-reported alcohol & caffeine intake. Assessor not described	Unknown	Caffeine (mg/day),	⦸	Amongst caffeine users, high caffeine intake more frequent in SMI compared to controls.
Hahn et al. 2014 (Australia)	Cross-sectional	SMI Medications not described Setting not described n=1,286	None	Semi-structured interview using standardised questionnaire. Assessor not described	Unknown	Food intake (g), Difficulty purchasing food (shortage of $)	⦸	74% people with psychosis ate <4 servings of fruit & vegetables combined daily. Unhealthy dietary intake associated with other detrimental lifestyle factors.
Hamera et al. 1995 (USA)	Cohort	SCZ, SAD 100% prescribed APM (52.9% oral, 29.4% LAI. 17.6% combination) Outpatients n=17	None	Substance use checklist (previous 24 hours) Assessor not described	Unknown	Caffeine (cups)	-	No association between psychosis symptom severity and caffeine, but caffeine intake increased with increased tension & depression.
Hardy et al. 2012 (UK)	Cross-sectional	SCZ 100% prescribed APM (75% SGA, 12.5% FGA, 12.5% combination) Outpatients n=8	None	Food diary (1 week). Assessed by study investigator.	Recognised acceptable measure	Dietary pattern (qualitative data)	-	People with SCZ had low overall consumption and variety of consumption of fruit and vegetables with a high consumption of convenience and ready-to-eat meals. Poor diet literacy in people with SCZ.
Haruyuki et al. 2015 (Japan)	Cross-sectional	SCZ Medication not described Outpatients n=51	General population data	Photographic 3-day food record. Assessed by dietitian.	Recognised acceptable measure	Energy (kcal), Macronutrients (g), Micronutrients (mg/µg), Fibre (g)	⦸	SCZ patients had higher intake of energy, CHO, fat, calcium, phosphorus and sodium compared to general population.
Heald et al. 2017 (UK)	Cross-sectional	SCZ, SAD 100% neuroleptics (54% oral SGAs, 35% depot APM, 11% MS) Outpatients n=32	None	Dietary questionnaire. Assessor not described.	Recognised acceptable measure	Food categories (portions, days eaten)	⦸	Most participants were not eating fruit (84%) and vegetables (75%) on >5 days/week. Majority chose white bread. 62.5% had takeaway foods within the last week.
Henderson et al. 2005 (USA)	Cross-sectional	SCZ, SAD 100% prescribed SGAs Outpatients n=36	None	4-day food record Assessor not described Analysed through Minnesota Nutrient Data System	Recognised acceptable measure	Energy (kcal), Macronutrients (% EI), Sugars (g),	⦸	Mean energy intake by APM in descending order was olanzapine (2,583.6kcal/day), clozapine (2,199kcal/day), risperidone (1,921kcal/day), (p=0.33, n=12 in each group).
Henderson et al. 2006 (USA)	Cross-sectional	SCZ, SAD 98% prescribed SGAs Outpatients n=88	Matched population data n=723	4-day dietary record & block FFQ. Assessed by trained dietary interviewers. Analysed by Minnesota Nutrient Database.	Recognised acceptable measure FFQ validated against 24-hr diet recall, 3-day diet record & serum carotenoids.	Energy (kcal) Macronutrients (g, % EI) Fat subgroups (g, % EI), Micronutrients (mg, mcg), Fibre (g), Caffeine (mg),	⦸	SMI group consumed less energy, CHO, protein, fat, fibre, sodium & folate but more caffeine than the comparison group.

Jacka et al. 2011 (Australia)	Cross-sectional	BPD Medications not described Setting not described n=23	Control n=691	Dietary Questionnaire for Epidemiological Studies. Assessor not described.	Validated against weighted food records in healthy Australian-, Greek- and Italian-born adults living in Australia.	Energy (kJ), Glycaemic load, Dietary patterns: 'western', 'modern', & 'traditional'	+	BPD group had higher glycaemic load, & higher scores on the 'western' & 'modern' diet scores. Higher 'western' & 'modern' score positively associated, & 'traditional' score negatively associated, with BPD.
Jahrami et al. 2017 (Bahrain)	Case control	SCZ, SAD, SCZF Medications not described Outpatients n=120	Control n=120	FFQ (past 1 month). Assessor not described.	Pilot study with 15 patients with SCZ (unpublished data)	Energy (kcal), Macronutrients (g), Fat subgroups (g), Micronutrients (mg), Fibre (g), Caffeine (mg), Individual foods (g/ml)	+	SMI group had excessive dietary intakes (energy, macronutrients, high energy/nutrient poor foods) when compared to controls.
Kilbourne et al. 2007 (USA)	Cross-sectional	SCZ 80% prescribed APM Setting not described n=1720 BPD 32% prescribed APM Setting not described n=1925	Control n=3065	Questionnaire (3 nutrition & 3 eating habits questions). Assessor not described.	Unknown	Eating habits, Fruit juice (# servings), Fruit (# servings), Vegetables (# servings),	⦸	BPD & SCZ groups more likely to report suboptimal eating behaviours and report difficulties obtaining or cooking food.
Killan et al. 2006 (Germany)	Cross-sectional	SMI Medications not described Inpatients n=363	General population data n=7124	Standardised questionnaire. Assessor not described.	Unknown	'Unhealthy nutrition behaviour' (based on consumption of fruit, vegetables, salty snacks, sweets, fast food & ready-to-eat meals – not quantified)),	⦸	SMI group had higher levels of unhealthy lifestyle practices including 'unhealthy nutrition behaviour'.
Konarzewska et al. 2014 (Poland)	Cross-sectional	SCZ 100% prescribed APM Setting not described n=52	Control n=45	24-hour recall (3 consecutive days using food images) Assessor not described. Analysed by Diet 5 software	Recognised acceptable measure	Energy (kcal), Macronutrients (g), Micronutrients (mg & µg), Fibre (mg)	⦸	Male SCZ group reported lower energy, glucose, protein and fibre, vitamins B2+C, & minerals zinc, magnesium, iron, copper, calcium compared to control. While D3, folic acid, calcium & magnesium did not meet recommended intakes. Female SCZ group reported higher saturated fat intakes. D3, C, folic acid, calcium and magnesium did not meet requirements.
Manzaneres et al. 2014 (Spain)	Cross-sectional	SMI 86% prescribed APM Outpatients n=65	Control n=25	24-hour recall. Assessed by dietitian Analysed by CESNID, Barcelona University software	Recognised acceptable measure	Energy (kcal) Macronutrients (%EI) Refined sugar (%EI) Sodium (mg)	⦸	SMI & high risk for psychoses groups had higher energy & saturated fat (% of total energy) intakes compared to controls. Symptom severity positively associated with energy intake.
McCreadie et al. 2003 (Scotland)	Cross-sectional	SCZ 94% prescribed APM Outpatients n=102	General population data	FFQ (part of Scottish Health Survey, modelled on the Health Survey for England). Assessed by research nurse Analysis program not required	Unknown	Selected foods: fruit, vegetables, legumes, oily fish, cereal, wholemeal bread (% of intake)	⦸	Mean weekly fruit & vegetables consumed by SCZ group was 16 (recommended intake is 35 per week). More males in SCZ group consumed inadequate fruit, vegetables, milk, potatoes & pulses compared to general population. More females with SCZ consumed inadequate milk & potatoes compared to general population.
Mucheru et al. 2017 (Australia)	Cross-sectional	SMI Medications not described Outpatients n=221	None	Short Diet Questions derived from 1995 National Nutrition Survey. Assessor not described. Analysis program not required	Unknown	Fruit, vegetables, breakfast consumption, meal frequency (frequency of intake)	⦸	Most participants did not meet recommendations for vegetables (86.9%) or fruits (70.6%). Average number of meals per day was 3.72, breakfast was consumed on average 4.27 times per week.
Nenke et al. 2015 (Australia)	Cross-sectional	SMI 85% prescribed APM 34% prescribed MS	General population data	Dietary Questionnaire for Epidemiological Studies. Assessed by trained researcher	Validated against weighted food records in healthy Australian-,	Energy (kJ) Macronutrients (g) Micronutrients (mg/ug)	⦸	SMI group consumed more fat and less fibre and vitamin E compared to general population. SMI group did not achieve RDIs for fruit & vegetables (98%),

		Setting not described n=184		Analysed using nutrient table for use in Australia (NUTTAB95) database	Greek- and Italian-born adults living in Australia.	Fibre (g) Selected foods (g)		fibre (89%), fish (61%), magnesium (73%) & folate (86%) and 58% exceeded RDIs of saturated fat and sodium.
Noguchi et al. 2013 (Japan)	Cross-sectional	Bipolar Depression Medications not described Outpatients n=75 Unipolar Depression Medications not described Outpatients n=91	None	Brief self-administered diet history questionnaire (BDHQ). Assessor not described. Analysed by a computer algorithm using the Standard Tables of Food Composition in Japan.	Validated against 16-day diet records in Japanese adults.	Dietary patterns: 'plant foods & fish products', 'fish' & 'western/meat' Energy (kcal) Macronutrients (%EI) EFAs (%EI) Micronutrients (mg, ug/1000kcal)	⦸	No difference in energy (kJ), nutrient intakes or dietary pattern scores between bipolar depression and unipolar depression. In men, psychiatric symptoms more pronounced with infrequent intakes of vegetables, mayonnaise, potatoes, soy products, seaweed and fish products. No correlations between dietary pattern scores and symptom scores in women.
Nunes et al. 2014 (Brazil)	Case control	SCZ 100% prescribed APM (68% SGAs, 28% FGAs, 4% combination) Outpatients n=25	Control n=25	FFQ (previous 1 month) Assessor not described. Analysed by NUTRIBASE Software	Validated against two-consecutive 24hr recalls in a Brazilian adult sample	Energy (kcal) Macronutrients (%EI) Fat subgroups (g/1000kcal, %EI) Micronutrients (mg, ug/1000kcal) Fibre (g/1000kcal)	⦸	SCZ group had higher intake of energy, energy per kg of body weight, % of CHO & TFAs but lower intakes of other types of fat, phytosterols & vitamin A compared to controls.
Osborn et al. 2007 (UK)	Cross-sectional	SMI 74% prescribed APM (64% SGAs, 35% LAI) Outpatients n=74	Control n=148	DINE Assessed by a 'rater' Analysis program not required	Validated against a 4-day diet record in 206 factory workers in the UK.	Fat, saturated fat, fibre (score) Health/dietary knowledge (score)	⦸	SMI group had lower fibre and higher saturated fat diets compared to controls. SMI group had lower knowledge on the health benefits of diet on cardiovascular risk.
Ratliff et al. 2012 (USA)	Cross-sectional	SCZ, SAD 100% prescribed APM (69% SGAs, FGAs 31%) Outpatients n=130	Matched population data n=250	24-hour recall (using food models) Assessed by trained personnel. Analysis program not described	Recognised acceptable measure.	Energy (kcal) Macronutrients (g) Sodium (mg) Caffeine (mg)	⦸	SMI group consumed higher sugar, fat, saturated fat & protein compared to controls. Both groups exceeded sodium upper limits.
Roick et al. 2007 (Germany)	Cross-sectional	SCZ 60% prescribed SGAs Inpatients n=194	General population data n=2,419	Eating & drinking section of German national health survey. Assessor not described. Analysis program not required	Unknown	Eating & drinking habits, dietary choices	-	SCZ group more frequently consumed instant meals, calorie-reduced food & supper snacks, and less frequently consumed breakfast & healthy groceries compared to general population.
Ryan et al. 2003 (UK)	Cross-sectional	FEP Medication Naïve Inpatients n=26	Control n=26	DINE Assessor not described Analysis program not required	Validated against a 4-day diet record in 206 factory workers in the UK.	Monounsaturated fat, saturated fat, fibre (score)	⦸	FEP group consumed more saturated fat compared to controls. No difference between groups for fibre and monounsaturated fat intakes
Ryan et al. 2004 (UK)	Cohort	FEP Medication Naïve Inpatients n=19	Control n=19	DINE Assessor not described. Analysis program not required	Validated against a 4-day diet record in 206 factory workers in the UK.	Monounsaturated fat, saturated fat, fibre (score)	+	FEP group consumed more saturated fat and less fibre compared to controls.
Samele et al. 2007 (UK)	Case control	FEP 89% prescribed psychotropic medication Mixed settings n=89	Control n=89	Health & lifestyle questionnaire (includes FFQ). Assessed by study researcher Analysis program not required	Unknown	'High-fat/fast-food diet', 'high in fruit & vegetables diet'	⦸	FEP group more likely to consume high fat, fast food and less likely to consume fruit and vegetables.
Saarni et al. 2009 (Finland)	Cross-sectional	SMI APM prescription ranges: 69% in SCZ, 35% in ONP, 32% in affective psychosis Setting not described n=208	General population data (Health 2000 study)	Standardised dietary questions from Finnish Health Examination Survey Assessor not described. Analysis program not required.	Unknown	Healthfulness of diet (based on vegetable & saturated fat intake)	-	No significant difference in diet healthfulness between SMI group and population data.

Simonelli-Munoz et al. 2012 (Spain)	Cross-sectional	SCZ, SAD, SCZF 100% prescribed APM (64% SGAs, 4% FGAs, 32% combination) Outpatients n=159	None	Quality of dietary habits questionnaire. Assessed by nurse. Analysis program not required.	Unknown	'Healthy/unhealthy' diet score	-	Mean diet score for SMI group was in the 'unhealthy' category, with only 22% of SMI group scoring in the 'healthy' category. Key reasons included fast eating and poor consumption of fruits, vegetables & fish.
Stokes et al. 2004 (UK)	Cross-sectional	SCZ 100% prescribed APM (55% clozapine, 45% FGA) Outpatients/residential n=20	General population data	7-day WFR (meals) & diet history/nursing observation (snacks). Assessed by nutritionist. Analysed by NETWISP program	Recognised acceptable measure.	Energy (kcal) Fat (g) Sugar (g)	⦸	SCZ group consumed more energy, sugar & fat compared to general population.
Strassnig et al. 2003 (USA)	Cross-sectional	SCZ, SAD, PNOS Medications not described Outpatients n=146	General population data	24-hour recall (using food models) Assessor not described. Analysed by ESHA Food Processor Nutrition Software 7.5	Recognised acceptable measure.	Energy (kcal) Macronutrients (g, %EI) Fibre (g) Caffeine (mg)	⦸	SMI group consumed more energy, CHO, fat & caffeine compared to general population data. Higher caffeine intake in smokers.
Strassnig et al. 2005 (USA)	Cross-sectional	SCZ, SAD, PNOS Medications not described Outpatients n=146	General population data	24-hour recall (using food models). Assessed by trained researcher. Analysed by ESHA Food Processor Nutrition Software 7.5	Recognised acceptable measure.	Total fat & fat subgroups (g) Vitamins A, C & E (mg)	⦸	SMI group consumed more fat, saturated fat & polyunsaturated fat compared to general population data.
Strassnig et al. 2006 (USA)	Cross-sectional	SCZ, SAD, PNOS Medications not described Outpatients n=146	General population data	24-hour recall (with food models). Assessor not described. Analysed by ESHA Food Processor Nutrition Software 7.5	Recognised acceptable measure.	Caffeine (mg)	⦸	SMI group consumed more caffeine than general population data. Caffeine intake positively associated with smoking, but not associated with BMI or dietary factors.
Sugawara et al. 2014 (Japan)	Cross-sectional	SCZ, SAD Medications not described Outpatients n=338	None	Brief self-administered diet history questionnaire (BDHQ). Assessor not described. Analysed by a computer algorithm using the Standard Tables of Food Composition in Japan.	Validated against 16-day diet records in Japanese adults.	Energy (kcal) Macronutrients (g/1000kcal) EFAs (g/1000kcal) Fibre (g/1000kcal) Micronutrients (mg, ug/1000kcal)	⦸	Those following a 'healthy dietary pattern' were less likely to be obese. Healthy pattern was positively associated with intake of protein, fat, dietary fibre, n-3 polyunsaturated fatty acids (PUFA), n-6 PUFA, folate, riboflavin, pyridoxine, cobalamin, and ascorbic acid & was inversely associated with the intake of carbohydrates.
Sugawara et al. 2016 (Japan)	Cross-sectional	SCZ Medications not described Mixed settings n=22,072	None	Brief survey questionnaire. Assessor not described. Analysis program not required.	Unknown	Soft drink, cakes or other sweets (frequency of intake)	⦸	27.9% of inpatients & 27.8% consumed soft drink everyday. 34.6% of inpatients & 28.5% of outpatients consumed soft drink >1x week. 39.3% of inpatients & 36.3% of outpatients consumed cakes or other sweets more than once per day.
Suvusaari et al. 2007 (Finland)	Cross-sectional	SMI 100% prescribed APM Setting not described n=118	General population data (Health 2000 study)	Standardised diet-related questions on intake of specific foods from Finnish Health Examination Survey Assessor not described. Analysis program not required.	Unknown	Healthfulness of diet (based on vegetable & saturated fat intake)	⦸	No difference for healthfulness of diet between SMI group and general population. No difference of healthfulness of diet between diagnoses within SMI group.
Treur et al 1999 (Multinational)	Cohort	SCZ 100% prescribed SGA Outpatients n=527 BPD 100% prescribed SGA Outpatients n=93 * 17% of total sample prescribed MS	None	Series of questions on the frequency of consumption of specific food groups Assessed by physician. Analysis program not required.	Unknown	Specific food categories (frequency of intake)	⦸	25.5% reported increased in sweet foods & sweetened beverage consumption, 23.6% reported decrease in sweet food/drink consumption. Higher weight gain in those who reported increased consumption of sweet food/drinks.

Tsuruga et al. 2015 (Japan)	Cross-sectional	SCZ, SAD 100% prescribed APM (38% APM polypharmacy) Outpatients n=237	Control n=404	Brief self-administered diet history questionnaire (BDHQ). Assessor not described. Analysed by a computer algorithm using the Standard Tables of Food Composition in Japan.	Validated against 16-day diet records in Japanese adults.	'Vegetable' & 'Cereal' (bread, rice, confectionary) dietary patterns	⦸	Cereal dietary pattern was positively associated with SCZ. Vegetable dietary pattern was not associated with SCZ.
Wallace & Tennant 1998 (Australia)	Cross-sectional	SMI 95% prescribed APM Outpatients n=170	None	24-hour recall (with food models) Assessed by 'researcher' Analysis program not described.	Recognised acceptable measure.	Food groups (servings per day)	-	All respondents ate less than the five food group recommendations. Only 5% of respondents consumed recommended amounts of fruit and vegetables.
Williamson et al. 2015 (UK)	Prospective Cohort	FEP Medication not described Outpatients n=143	General population data n=1186	4-day food diary. Assessor not described. Analysed by NetWISP dietary analysis software.	Recognised acceptable measure.	Energy (kJ) Macronutrients (g) Non-milk extrinsic sugar (g) Micronutrients (mg, ug)	⦸	FEP group consumed more fat, saturated fat & non-milk extrinsic sugar (statistical trend), & less vitamin D, folate & selenium compared to general population data. No sig. difference in energy intake.
Winstead 1976 (Germany/USA)	Cross-sectional	Psychosis Inpatients n=24 Other mental illness Inpatients n=11 * 30% of total sample prescribed FGA or antidepressant.	None	Inpatients recorded daily intake of coffee Reviewed by inpatient staff & subsequently interview for accuracy Analysis program not utilised	Unknown	Coffee ('high' users defined as ≥5 cups of coffee per day)	-	People with psychosis had a higher incidence of 'high' coffee users compared to other mental illnesses.

* SCZ = Schizophrenia, SAD = Schizoaffective disorder, SCZF = Schizophreniform disorder, BAD = Bipolar affective disorder, PNOS = Psychosis not otherwise specified, SMI = Severe mental illness, FEP = First-episode psychosis, APM = Antipsychotic medication, SGA = Second Generation Antipsychotic, FGA = First Generation Antipsychotic, LAI = Long Acting Injectable antipsychotic, MS = Mood Stabiliser, FFQ = Food Frequency Questionnaire, FA = fatty acids, EFA = essential fatty acids, Fe = iron, Se = selenium, Zn = zinc, CHO = carbohydrate, TFAs = trans fatty acids.
^ Study design quality scores were based on 10 criterion according the American Academy of Nutrition and Dietetics Quality Criteria Checklist: Primary Research [1]

Supplementary File 5.

Studies (report: Y/N/U/NA)	Adolfo 2009	Amani 2007	Archie 2007	Arrojo-Romero 2015	Baethge 2009	Bly 2013	Bobes 2010	Brown 1999	Chang 2017	Clayton 2008	Ellingrod 2011
Relevance questions	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Validity questions 1. Was the research question clearly stated?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
2. Was the selection of study subjects/patients free from bias?	Y	N	Y	Y	Y	Y	Y	U	Y	Y	Y
3. Were study groups comparable?	Y	Y	Y	Y	Y	N	Y	U	y	Y	N
4. Was method of handling withdrawals described?	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	N
5. Was blinding used to prevent introduction of bias?	U	U	U	U	Y	Y	Y	U	U	U	U
6. Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were intervening factors described?	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	N
7. Were outcomes clearly defined and the measurements valid and reliable?	N	Y	Y	N	N	Y	N	Y	Y	U	Y
8. Was the statistical analysis appropriate for the study design and type of outcome indicators?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
9. Are conclusions supported by results with biases and limitations taken into consideration?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
10. Is bias due to study's funding or sponsorship unlikely?	Y	Y	Y	Y	Y	Y	Y	U	Y	U	Y
ALL OF Q2, 3, 6, 7 "YES"? (0 = NO, 1 = YES)	0	0	1	1	0	0	0	0	1	0	0
NUMBER OF "Y" OUT OF 10	7	7	9	8	9	9	9	6	9	7	6
Overall judgement	Neutral	Neutral	Positive	Neutral	Neutral	Neutral	Neutral	Neutral	Positive	Neutral	Neutral

Studies (report: Y/N/U/NA)	Elmslie 2001	Evans 2014	Evans 2015	Fawzi 2015	Fusar-Poli 2009	Gothelf 2002	Gupta 2009	Gurpegui 2004	Gurpegui 2006	Hahn 2014	Hamera 1995
Relevance questions	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Validity questions 1. Was the research question clearly stated?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
2. Was the selection of study subjects/patients free from bias?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N
3. Were study groups comparable?	Y	Y	Y	N	N	N	N	N	N	N	N
4. Was method of handling withdrawals described?	Y	Y	Y	N	Y	N	Y	Y	N	N	N
5. Was blinding used to prevent introduction of bias?	U	U	U	Y	U	U	U	U	U	U	U
6. Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were intervening factors described?	N	Y	Y	Y	N	Y	Y	N	Y	N	Y
7. Were outcomes clearly defined and the measurements valid and reliable?	U	Y	Y	Y	N	Y	N	N	N	N	N
8. Was the statistical analysis appropriate for the study design and type of outcome indicators?	Y	Y	Y	Y	Y	y	Y	Y	Y	Y	Y
9. Are conclusions supported by results with biases and limitations taken into consideration?	Y	Y	Y	Y	Y	U	Y	N	Y	Y	Y
10. Is bias due to study's funding or sponsorship unlikely?	Y	Y	Y	Y	U	U	U	Y	Y	Y	U
ALL OF Q2, 3, 6, 7 "YES"? (0 = NO, 1 = YES)	0	1	1	0	0	0	0	0	0	0	0
NUMBER OF "Y" OUT OF 10	7	9	9	8	5	5	6	4	5	5	3
Overall judgement	Neutral	Positive	Positive	Neutral	Neutral	Neutral	Neutral	Negative	Neutral	Neutral	Negative

Studies (report: Y/N/U/NA)	Hardy 2012	Haruyuki 2015	Heald 2017	Henderson 2005	Henderson 2006	Jacka 2011	Jahrami 2017	Kilbourne 2007	Killan 2006	Konarzewska 2014	Manzaneres 2014
Relevance questions	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Validity questions 1. Was the research question clearly stated?	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
2. Was the selection of study subjects/patients free from bias?	N	Y	Y	Y	N	Y	Y	Y	Y	Y	Y
3. Were study groups comparable?	N	N	N	N	Y	Y	Y	Y	N	U	N
4. Was method of handling withdrawals described?	Y	Y	N	Y	N	Y	Y	Y	Y	Y	Y
5. Was blinding used to prevent introduction of bias?	U	U	U	U	U	U	Y	U	U	U	U
6. Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were intervening factors described?	Y	Y	N	N	Y	Y	Y	Y	N	N	Y
7. Were outcomes clearly defined and the measurements valid and reliable?	Y	Y	Y	Y	Y	Y	Y	U	N	Y	Y
8. Was the statistical analysis appropriate for the study design and type of outcome indicators?	N	Y	N	Y	Y	Y	Y	Y	Y	Y	Y
9. Are conclusions supported by results with biases and limitations taken into consideration?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
10. Is bias due to study's funding or sponsorship unlikely?	U	Y	Y	Y	U	Y	Y	Y	U	Y	Y
ALL OF Q2, 3, 6, 7 "YES"? (0 = NO, 1 = YES)	0	0	0	0	0	0	0	0	0	0	0
NUMBER OF "Y" OUT OF 10	4	8	5	7	6	9	9	8	5	7	8
Overall judgement	Negative	Neutral	Neutral	Neutral	Neutral	Positive	Positive	Neutral	Neutral	Neutral	Neutral

Studies (report: Y/N/U/NA)	McCreadie 2003	Mucheru 2017	Nenke 2015	Noguchi 2013	Nunes 2014	Osborn 2007	Ratliff 2012	Roick 2007	Ryan 2003	Ryan 2004	Samele 2007
Relevance questions	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Validity questions 1. Was the research question clearly stated?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
2. Was the selection of study subjects/patients free from bias?	Y	Y	N	Y	N	Y	N	N	Y	Y	Y
3. Were study groups comparable?	N	N	N	N	N	Y	Y	N	Y	Y	U
4. Was method of handling withdrawals described?	Y	Y	Y	U	N	Y	N	Y	Y	Y	Y
5. Was blinding used to prevent introduction of bias?	U	U	U	U	U	U	U	U	U	U	U
6. Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were intervening factors described?	Y	Y	N	Y	Y	Y	N	N	N	Y	Y
7. Were outcomes clearly defined and the measurements valid and reliable?	N	N	Y	Y	Y	Y	N	U	Y	Y	U
8. Was the statistical analysis appropriate for the study design and type of outcome indicators?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
9. Are conclusions supported by results with biases and limitations taken into consideration?	Y	Y	Y	Y	Y	Y	Y	Y	N	N	Y
10. Is bias due to study's funding or sponsorship unlikely?	Y	Y	Y	Y	Y	Y	U	U	U	U	U
ALL OF Q2, 3, 6, 7 "YES"? (0 = NO, 1 = YES)	0	0	0	0	0	1	0	0	0	1	0
NUMBER OF "Y" OUT OF 10	7	7	6	8	7	9	5	4	5	7	6
Overall judgement	Neutral	Neutral	Neutral	Neutral	Neutral	Positive	Neutral	Negative	Neutral	Positive	Neutral

Studies (report: Y/N/U/NA)	Saarni 2009	Simonelli-Munoz 2012	Stokes 2004	Strassnig 2003	Strassnig 2005	Strassnig 2006	Sugawara 2014	Sugawara 2016	Suvusaari 2007	Treur 1999	Tsuruga 2015	Wallace 1998
Relevance questions	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Validity questions 1. Was the research question clearly stated?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
2. Was the selection of study subjects/patients free from bias?	Y	N	Y	N	N	N	N	Y	Y	Y	Y	N
3. Were study groups comparable?	Y	N	N	N	N	N	N	N	Y	N	Y	N
4. Was method of handling withdrawals described?	N	N	Y	Y	Y	Y	Y	Y	U	U	U	N
5. Was blinding used to prevent introduction of bias?	U	U	U	U	U	U	U	Y	U	U	U	U
6. Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were intervening factors described?	N	Y	Y	N	Y	N	N	Y	N	Y	N	N
7. Were outcomes clearly defined and the measurements valid and reliable?	N	N	Y	Y	Y	Y	Y	N	N	N	Y	Y
8. Was the statistical analysis appropriate for the study design and type of outcome indicators?	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N
9. Are conclusions supported by results with biases and limitations taken into consideration?	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N
10. Is bias due to study's funding or sponsorship unlikely?	Y	U	U	U	U	U	Y	Y	Y	Y	Y	Y
ALL OF Q2, 3, 6, 7 "YES"? (0 = NO, 1 = YES)	0	0	0	0	0	0	0	0	0	0	0	0
NUMBER OF "Y" OUT OF 10	4	4	7	4	6	4	6	7	6	6	7	3
Overall judgement	Negative	Negative	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Negative

Studies (report: Y/N/U/NA)	Williamson 2015	Winstead 1976
Relevance questions	Y	Y
Validity questions 1. Was the research question clearly stated?	Y	Y
2. Was the selection of study subjects/patients free from bias?	Y	Y
3. Were study groups comparable?	Y	N
4. Was method of handling withdrawals described?	N	U
5. Was blinding used to prevent introduction of bias?	U	N
6. Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were intervening factors described?	N	N
7. Were outcomes clearly defined and the measurements valid and reliable?	Y	U
8. Was the statistical analysis appropriate for the study design and type of outcome indicators?	Y	U
9. Are conclusions supported by results with biases and limitations taken into consideration?	Y	U
10. Is bias due to study's funding or sponsorship unlikely?	Y	Y
ALL OF Q2, 3, 6, 7 "YES"? (0 = NO, 1 = YES)	0	0
NUMBER OF "Y" OUT OF 10	7	4
Overall judgement	Neutral	Negative