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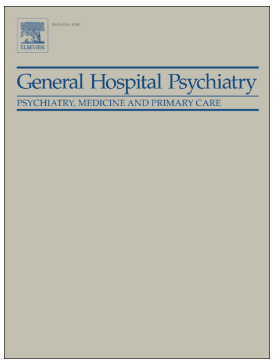


# The prevalence of diabetes mellitus and abnormal glucose metabolism in the inpatient psychiatric setting: A systematic review and meta-analysis

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Title:

# The Prevalence of Diabetes Mellitus and Abnormal Glucose Metabolism in the Inpatient Psychiatric Setting: A Systematic Review and Meta-Analysis

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Abstract:

Objective: To systematically determine the prevalence of diabetes mellitus (DM), impaired fasting glucose (IFG), and impaired glucose tolerance (IGT) in psychiatric inpatients and explore the impact of patient and study variables on prevalence estimates.

Method: We searched EMBASE, PsychINFO, Medline and CENTRAL from database inception until 1st December 2015. We included studies of any design reporting prevalence of abnormal glucose metabolism in any adult psychiatric inpatients. We conducted a random effects meta-analysis to generate pooled prevalence estimates. Chi-square tests compared differences within categorical variables (inpatient setting, continent of study and patient diagnostic category) and Spearman's correlation analyses assessed the impact of linear variables (age, year of data collection and study quality). Study quality was assessed using an adapted Newcastle-Ottawa Scale.

Results: 36 study reports representing 42 unique cohorts were included. Across all studies prevalence of unspecified type DM was 10% (95%CI: 9-12), of T1DM was 1% (0-1), of T2DM was 9% (6-13), of IFG 18% (8-28), and of IGT was 22% (16-28). These estimates were not affected by study quality.

Conclusions: All estimates are higher compared to the general population. Mental health professionals should be aware of this elevated prevalence to improve screening and management of abnormal glucose metabolism.

Keywords:

Diabetes Mellitus, Serious Mental Illness, Inpatient Psychiatry

## Introduction

The prevalence of diabetes mellitus (DM) and abnormal glucose metabolism is often reported as higher in psychiatric inpatients compared to the general population, [1] and as a co-morbidity has been associated with an increased length of stay. [2] Psychiatric patients with abnormal glucose metabolism have poorer long-term outcomes including increased tendency to relapse of mental illness, [3,4] and increased mortality secondary to an increased risk of cardiovascular disease. [5] Appropriate detection and treatment of abnormal glucose metabolism is thus an important target for interventions to improve clinical outcomes in psychiatric inpatients. Reported prevalence estimates for DM in psychiatric inpatients range from 2% to 25% and are often based on small cross-sectional studies, [6,7] which frequently are limited to subpopulations, including those with particular diagnoses or on particular psychotropic medication. [8]

Previous systematic reviews in patients with psychiatric illness have focused on the prevalence of metabolic syndrome, or of exclusively type two diabetes mellitus (T2DM). [9, 10, 11, 12, 13] Whilst rates of 30-40% [9,14] of metabolic syndrome, and 7-13% of T2DM [12,13] are commonly reported they offer no specific detail on prevalence of T1DM or impaired glucose metabolism, and do not focus on the psychiatric inpatient setting. The burden of disease of DM, impaired fasting glucose (IFG), and impaired glucose tolerance (IGT) within the inpatient setting remains uncertain despite these disease states having specific and alternative interventions available as management strategies, with the inpatient setting representing an excellent window of opportunity for both screening and intervention. Improved knowledge and screening for abnormal glucose metabolism has the potential to improve and personalise inpatient psychotropic prescribing regimens leading to fewer diabetogenic prescriptions in those with states of impaired glucose metabolism but without frank diabetes.

As yet no systematic review has provided pooled prevalence estimates of all types of DM, IFG or IGT in psychiatric inpatients despite an increase in the awareness of the need for physical health screening and management of chronic medical conditions in patients with psychiatric illness. [15] With greater emphasis being placed on improving diagnosis and management of co-morbid medical conditions within psychiatric inpatient settings, this study aims to systematically review the literature and fill this gap. We aimed to present a pooled prevalence of DM, IFG and IGT in psychiatric inpatients and to explore the impact of study populations and characteristics on prevalence estimates.

## Methods

### Data sources

We searched Embase, Medline, PsychINFO and the Cochrane Central Register of Controlled Trials, from database inception to December 1st 2015 for studies published in English. Three authors (XX, XX and XX) initially assessed the titles and abstracts identified by the search and reviewed the full text of the remaining articles for inclusion. Any discrepancy was resolved by discussion, and where agreement could not be reached a fourth author (ER) was consulted. All relevant references were checked for additional citations. The full search terms can be found in the online supplementary material eFigure one.

### Study Selection

We included full studies of adult participants (18-65) in any psychiatric inpatient setting. These were subdivided into general adult, intensive care, rehabilitation, learning disability, forensic, eating disorder and addiction inpatient units. We included studies of any design, any adult psychiatric inpatient with any diagnoses, and which reported a prevalence of diabetes mellitus T1 or T2, or IFG or IGT. We excluded those studies which were conducted in mixed inpatient and outpatient settings and prevalence estimates were unable to be calculated separately for inpatient cohorts, and those studies which only reported percentages of prevalence from which we could not calculate the absolute number of patients diagnosed with abnormal glucose metabolism. Where multiple studies reported on the same patient cohort the more conservative estimate was used for meta-analysis.

### Data Extraction

Three authors (XX, XX and XX) independently extracted diagnostic categories of patients

studied; mean patient age, psychiatric diagnoses, year of data collection, the country in which the study was conducted and method of diagnostic assessment of abnormal glucose metabolism. We planned a priori to group studies into three-year strata from the earliest year of collection, into continent on which they were conducted, and into four diagnostic categories (any inpatient, schizophrenia or schizoaffective disorder, any mood disorder and any substance use disorder) for separate analyses.

Quality assessment

A 10-point quality assessment tool was adapted from the Newcastle-Ottawa Scale [16] (available in the online supplementary material as eFigure two). This scale is used to assess the methodological quality of observational studies and has acceptable validity and reliability. The scale can be modified and was adapted to take into account the adequacy of criteria used to determine the diagnosis of diabetes or impaired glucose metabolism. A diagnosis was deemed adequate if it was based on international criteria (e.g. the American Diabetes Association criteria [17] or World Health Organization (WHO) criteria [18]). Methodological considerations in each study were scored as follows: 0-5 points for adequate selection of study subjects, 0-2 points for adequate comparability of study subjects and 0-3 points for adequate outcome assessment. Overall study quality was scored as follows: 0-3 = low quality; 4-7 = medium quality; 8-10 = high quality.

Data Synthesis and Statistical Analysis

Data were pooled according to diagnoses of IFG, IGT or DM; either undefined in individual studies or defined as type one (T1DM) or type two (T2DM). We expected heterogeneity to be moderately high between studies due to variation in data sampling, and therefore planned to conduct a random-effects meta-analyses with 95% Confidence

Intervals (CIs). Heterogeneity was assessed using $I^2$, with thresholds of ≥25%, ≥50% and ≥75% indicating low, moderate and high heterogeneity, respectively [19]. Subgroup analyses explored whether prevalence estimates of unspecified DM were influenced by type of inpatient setting, continent on which study was performed, year of data collection, diagnostic category of participants, and overall study quality. Chi-square tests were used to compare differences within categorical variables (setting, continent and diagnostic category) and Spearman's correlation analyses with adjusted $\rho^2$ assessed the impact of linear variables (age, year of data collection and study quality) on prevalence estimates with the significance level set at 0.05. Where significant differences in prevalence of unspecified DM were demonstrated within subgroups heterogeneity was explored with meta-regression analyses to investigate potential moderators. We planned to conduct sensitivity analyses using only those studies with adequate reported criteria to determine the diagnosis of diabetes or impaired glucose metabolism, and removing those studies which preselect only patients treated with antipsychotic medication. Funnel plots were produced to explore the possibility of publication bias due to preferential publication of small studies reporting high prevalence estimates; Egger's test of publication bias was also performed. All analyses were conducted with STATA version 12.0. Ethical approval was not required for the study. The study was conducted in accordance with the Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines, and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [20, 21]. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Results

The search identified 1114 abstracts. 100 full texts were examined and 36 study reports comprising 42 unique cohorts were included in the analysis. An included studies flow diagram and list of excluded studies can be found in the online supplementary material as eFigure three and eTable one respectively. Thirty one study cohorts reported the prevalence of DM of unspecified type, five reported prevalence of T1DM, thirteen of T2DM, seven of IFG and three of IGT. Across all studies prevalence of unspecified type DM was found to be 10% (95% CI: 9-12), of T1DM was 1% (0-1), of T2DM was 9% (6-13), of IFG 18% (8-28) was and of IGT was 22% (16-28). A description of included study characteristics can be found in table one, and the number of study cohorts and prevalence for each analysis can be found in table two. Forest plots for each analysis can be found in the online supplementary material as eFigure four.

Setting:

There were no studies in psychiatric intensive care, eating disorder or learning disabled inpatient settings. 31 study cohorts were reported in general adult, 3 in addiction, 4 in forensic and 4 in rehabilitation inpatient settings. The prevalence of unspecified type diabetes mellitus was found to be 10% (95%CI: 9-12) in general adult, 11% (0-23) in

addiction, 10% (6-13) in forensic and 12% (4-21) in rehabilitation inpatient settings. The prevalence of unspecified DM did not differ by setting.

Continent:

There were no studies conducted in the continents of South America, Africa or Australasia. 13 study cohorts were reported in Europe, 17 in Asia and 12 in North America. The prevalence of unspecified type diabetes mellitus was found to be 9% (95% CI: 7-12) in Europe, 11% (6-16) in Asia, and 11% (9-12) in North America.. The prevalence of unspecified DM did not differ by continent.

Diagnostic Category:

22 study cohorts reported on any inpatients, 9 on patients with schizophrenia or schizoaffective disorder, 8 on patients with any mood disorder and 3 on patients with any substance use disorder. The prevalence of unspecified type diabetes mellitus was found to be 11% (95% CI: 10-12) in any inpatients, 11% (5-17) in patients with schizophrenia or schizoaffective disorder, 8% (4-12) in patients with any mood disorder and 11% (0-23) in patients with any substance use disorder. The prevalence of unspecified DM did not differ by diagnostic category.

Mean patient age:

31 study cohorts reported mean age. The mean age of patients ranged from 33 to 54 years old. The prevalence of unspecified DM did not differ by mean patient age.

Year of data collection:

Studies were grouped into three-year strata from 1997 onwards. Two study cohort's data were collected before 1997, 4 from 1997-1999, 4 from 2000-2002, 8 from 2003-2005, 7 from 2006-2008, 5 from 2009-2011, and 2 from 2012-2014. 10 did not report period of data collection. The prevalence of unspecified type diabetes mellitus was

found to be 9% (95% CI 7-12) before 1997, 8% (7-10) from 1997-1999, 11% (10-13) from 2000-2002, 13% (11-14) from 2003-2005, 6% (3-9) from 2006-2008, 9% (6-13) from 2009-2011, and 12% (2-23) from 2012-2014. Spearman's correlation analyses demonstrated that year of data collection did not show a significant association with prevalence estimates of unspecified DM.

Quality:

16 study cohorts were rated as low, 12 were rated as medium, and 14 were rated high quality. The prevalence of unspecified type diabetes mellitus was found to be 9% (95% CI: 6-11) in low quality study cohorts, 12% (8-16) in medium quality study cohorts and 11% (9-12) in high quality study cohorts. Spearman's correlation analyses demonstrated that study quality did not show a significant association with prevalence estimates of unspecified DM.

Sensitivity Analysis:

When restricted to those studies reporting adequate criteria to determine the diagnosis of diabetes or impaired glucose metabolism there was no significant difference in the prevalence estimates of all measures of abnormal glucose metabolism. When those studies recruiting only patients treated with antipsychotic medication were removed there was no significant difference in the prevalence estimates of all measures of abnormal glucose metabolism.

We found no evidence of publication bias for all measures of abnormal glucose metabolism. Funnel plots can be found in the online supplementary material as eFigure five.

Discussion

Across all studies one in ten psychiatric inpatients has a diagnosis of diabetes mellitus, one in five has a diagnosis of impaired fasting glucose and one in five has a diagnosis of impaired glucose tolerance. The prevalence of T2DM is consistent with other reviews in patients with serious mental illness (SMI), but to our knowledge we are the first group to report a pooled prevalence of impaired glucose metabolism in psychiatric inpatients. All estimates are higher compared to the general population [58], and comparable to psychiatric patients in outpatient settings. [13, 59] Although studies varied widely in terms of quality, subgroup and Spearman's rank correlation analysis indicate that prevalence estimates were reasonably stable.

There was no consistent pattern that abnormal glucose metabolism had a higher prevalence in any specific type of inpatient setting. No clear pattern of significantly

differential prevalence was found in terms of diagnostic category, however patients with schizophrenia or schizoaffective disorder had higher rates of T2DM and IFG, again a consistent finding with other studies. [60] We are unable to comment on the aetiology of this increased prevalence though hypothesise it may be linked to antipsychotic medication use in these patients. [61,62] We were unable to identify sufficient detail from reporting in included studies to stratify analyses by numbers of patients with current or past antipsychotic medication use, or patient ethnicity.

We used rigorous methods to conduct the review, with a broad search and a structured approach to data extraction. We took a comprehensive approach into the construct of inclusion criteria, including studies of all designs, and subpopulations using subgroup analysis to assess the impact of study and population variables as opposed to exclusion of such studies from the outset. Prevalence estimates are susceptible to potential publication bias based on the assumption that small studies reporting low prevalence of abnormal glucose metabolism would be less likely to be published than small studies reporting high prevalence. We explored publication bias by visual inspection of funnel plots and Egger's test, which can be found in the online supplementary material as eFigure five. We found no evidence of publication bias for all measures of abnormal glucose metabolism.

There are several limitations to the review. The number of studies included is relatively small and pooling demonstrates consistently high heterogeneity between prevalence estimates for unspecified DM, T2DM, IFG and IGT. Many studies did not report methods by which diabetes mellitus was diagnosed, and some relied on use of anti-diabetic medication as a proxy measure for diagnosis. As anti-diabetic medication may be prescribed for reasons other than frank diabetes this has the potential to overestimate the prevalence. However we conducted a sensitivity analysis restricted to only those prevalence estimates from cohorts that reported adequate criteria to determine the

diagnosis of diabetes or impaired glucose metabolism, and there was no significant difference in the prevalence estimates for all measures of abnormal glucose metabolism. A further consideration is the representativeness of the sample from which prevalence levels are estimates. No studies were conducted in psychiatric intensive care, eating disorder and learning disabled settings, or in South America, Africa or Australasia thus results cannot be generalised to these settings. There were also a number of excluded studies which were conducted in mixed inpatient and outpatient settings and prevalences were unable to be calculated separately for inpatient cohorts due either to sampling methods or lack of reporting.

The main reason for identification and clarification of the prevalence of a disease is to raise awareness of the scale of the problem and ultimately intervene to improve clinical outcome. Given the high numbers of patients with abnormal glucose metabolism, and the links to psychotropic drug use as a putative causative and exacerbating factor [61,62] there is an argument that psychiatrists and mental health professionals be better trained and empowered to detect and manage abnormal glucose metabolism. There is often a reticence of ownership of responsibility for managing co-morbid medical conditions by psychiatrists, [63] and large variation exists in provision for management of co-morbid medical conditions within psychiatric inpatient facilities. [63] There has been recognition that abnormal glucose metabolism management strategies may be unsuitable or unacceptable to some patients with psychiatric illness due to a variety of patient, provider and system factors. [64] Indeed a prevalence of one in five for IFG or IGT is higher than estimates for number of inpatients with bipolar affective disorder and some personality disorders across all inpatient settings, [65] suggesting that abnormal glucose metabolism should be an essential part of psychiatric postgraduate examination, training and expertise. [66]

Future research should focus on prevalence estimates in settings not currently reported on including eating disorders, learning disabled and psychiatric intensive care settings, and on translating the knowledge of increased prevalence of these conditions into action; emphasising their screening and management in a system that should advocate holistic care of the patient.



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All authors have completed the ICJME declarations of interest form.

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57. Wang C, Zhang Z, Sun J et al: Serum Free Fatty Acids and Glucose Metabolism, Insulin Resistance in Schizophrenia with Chronic Antipsychotics. Biological Psychiatry 60(12):1309-1313, 2006

58. Global status report on noncommunicable diseases 2014. Geneva, World Health Organization, 2012

59. Gardner-Sood P, Lally J, Smith S et al: Cardiovascular risk factors and metabolic syndrome in people with established psychotic illnesses: baseline data from the IMPaCT randomized controlled trial. Psychol Med 45(12):2619-29, 2015

60. Hsu JH, Chien IC, Lin CH et al: Incidence of diabetes in patients with schizophrenia: a population-based study. Can J Psychiatry 56(1):19-26, 2011
61. Galling B, Roldán A, Nielsen RE et al: Type 2 Diabetes Mellitus in Youth Exposed to Antipsychotics: A Systematic Review and Meta-analysis. JAMA Psychiatry 73(3):247-59, 2016
62. Leslie DL, Rosenheck RA: Incidence of newly diagnosed diabetes attributable to atypical antipsychotic medications. Am J Psychiatry 161(9):1709-11, 2004
63. Ronnis R: Best practices for co-occurring disorders: Medical co-management of psychiatric patients addressing the other dual diagnoses. Journal of Dual Diagnosis 4(4):420-425, 2008
64. Wang HF, Yeh MC: Psychological resistance to insulin therapy in adults with type 2 diabetes: mixed-method systematic review. J Adv Nurs 68(4):743-57, 2012
65. Regier DA, Narrow WE, Rae DS et al: The de facto US mental and addictive disorders service system. Epidemiologic catchment are a prospective 1-year prevalence rates of disorders and services. Arch Gen Psychiatry 50(2):85-94, 1993
66. Bringing together physical and mental health: A new frontier for integrated care. The Kings Fund. 2016. http://www.kingsfund.org.uk/publications/physical-and-mental-health (Last accessed 1/7/16)

Tables

Table one:

Included Studies
NR: Not reported; DSM: Diagnostic and Statistical Manual of Mental Disorders; ICD: International Classification of Diseases; USA: United States of America; UK: United Kingdom

| Study ID | Setting | Year/s of Data Collection | Country | Quality (0-10) | Mean Age | Abnormal Glucose Diagnosic Criteria | Psychiatric Diagnostic Criteria | Unspecified DM (Cases/Total) | T1DM | T2DM | IFG | IGT |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Blank 2010[22] | General Adult | Apr 2003 - Mar 2006 | USA | 3 | NR (Range 35-64) | NR | All inpatients aged ≥ 35 with a clinical diagnosis of Major Depressive Disorder | 201/1401 | . | . | . | . |
| Cassidy 1999[23] | General Adult | NR | USA | 3 | 42.1 | NR | DSM III -R criteria for bipolar disorder manic or mixed subtype | 36/345 | . | . | . | . |
| Citrome 2006[24] | General Adult | 1997 - 2004 | USA | 8 | 45.7<br>45.1<br>44.5<br>44.3<br>44<br>44<br>44.1<br>44.2 | Received prescriptions of antidiabetic medication or a recorded diagnosis of diabetes mellitus (ICD-9 250.xx) | Every inpatient in the 17 adult civil facilities of the New York State psychiatric hospital system. | 1997: 696/10091<br>1998: 794/9424<br>1999: 836/9008<br>2000: 842/8621<br>2001: 969/8520<br>2002: 1068/8269<br>2003: 1038/7724<br>2004: 1079/7420 | . | . | . | . |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Go 2009[25] | General Adult | Jan 2006 - Aug 2007 | Phillipines | 8 | 40 | Documented DM type II' | DSM-IV TR criteria for schizophrenia | . | . | 1/227 | . | . |
| Goethe 2006[26] | General Adult | 2003 | USA | 3 | 42.4 | Diabetes Diagnosed' | All inpatients treated with antipsychotic medication | 188/1691 | . | . | . | . |
| Hennings 2010[27] | General Adult | NR | Germany | 3 | 44.2 | IGT: Glucose > 140mg/dL 120 mins after glucose intake | Inpatients with major depression without lifetime Axis I diagnosis | . | . | . | . | 4/10 |
| Kan 2015[28] | General Adult | 2013 - 2014 | UK | 6 | 50.2 | NR | Any Inpatient | 31/411 | 2/411 | 29/411 | . | . |
| Kanzaki 2015[29] | General Adult | Jan 2012 - Dec 2013 | Japan | 4 | 54.3 | Diabetes mellitus was defined as haemoglobin A1c (HbA1c) ≥ 6.5% and fasting plasma glucose ≥ 126 mg/dL or use of hypoglycaemic agents | Any Inpatient | 28/152 | . | . | . | . |
| Kelbrick 2013[30] | General Adult | Jan 2011 - Jun 2011 | UK | 3 | 48 | DM: NR IFG: Patients without DM + BM >7 mmol/litre | Any primary affective disorder according to ICD10 criteria | 8/70 | 1/70 | 7/70 | 2/70 | . |
| Kim 2009[31] | General Adult | Jan 2005- Dec 2006 | South Korea | 3 | 38 | Anti diabetic medication | DSM-IV Bipolar I | 8/184 | . | . | . | . |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Kimijima 2011[32] | General Adult | 2007 - 2008 | Japan | 1 | 53.5 | NR | Schizophrenia included schizotypal and delusional disorders (ICD F20-F29 | . | - | 24/138 | . | . |
| Levine 2001[33] | General Adult | 1998 - 1999 | USA | 7 | 40 | T2DM: Fasting blood glucose > 140 mg/dl on two occasions or a 2 hour postprandial blood glucose ≥ 200 mg/dl; subjects with diabetes mellitus had already been diagnosed and were all receiving dietary and/or pharmacological treatment for glucose control | Any inpatient | . | | 30/414 | . | . |
| Lilliker 1980[34] | General Adult | Jan 1969 – Dec 1978 | USA | 4 | 58 | NR | DSM II Manic-depressive illness, manic type: manic-depressive illness, depressed type; manic-depressive illness, circular type | 20/203 | . | . | . | . |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Lindenmayer 2003[35] | General Adult | NR: Olanzapine arm added 1997 | USA | 9 | 40.33 | NR | DSM-IV crieria for schizophrenia or schizoaffective disorder | 7/108 | . | . | . | . |
| Luppino 2014[36] | General Adult | Jan 2007 - Dec 2009 | Netherlands | 3 | 44.8 | NR | Any inpatient with DSM IV major depressive disorder | 2/80 | . | . | . | . |
| Manu 2012[37] | General Adult | Aug 2010 - Dec 2010 | USA | 8 | 45.2 | NR | Any inpatient | 121/1000 | . | . | . | . |
| Manu 2012/13[38,39] | General Adult | Nov 2003 - Jul 2007 | Belgium | 10 | 37.6 | DM: FPG ≥125mg/dL or 2 hour OGTT >199mg/dL or HbA1c >6,4% IFG: Excludes those with DM or 'IGT' defined as a fasting plasma glucose greater than 125 mg/dL, 2-h glucose level during OGGT 140 mg/dL or greater and hemoglobin A1c 6.5% or greater | Any inpatient on Antipsychotic medication | 80/783 | . | . | 91/783 | . |
| Mookhoek 2011[40] | General Adult | NR | Netherlands | 4 | 48 | DM: used anti-diabetic medication, or had fasting serum | Any inpatient | 39/256 | 3/256 | 36/256 | 36/256 | . |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | glucose levels over 6.9 mmol/l or non-fasting serum glucose levels over 11.0 mmol/l IFG:Used no anti-diabetic medication and had fasting serum glucose levels between 6.1 and 6.9 mmol/l or non-fasting serum glucose levels between 7.0 and 11.0 mmol/l, | | | | | | |
| Ono 2013[41] | General Adult | NR | Japan | 4 | 40 | IFG: A fasting glucose level of 100-125 mg/dL IGT: A 2-hour glucose level of 140-199 mg/dL | DSM IV Schizophrenia on antipsychotic medication | . | . | . | 31/256 | 47/256 |
| Rezaei 2009[42] | General Adult | Dec 2007 - May 2008 | Iran | 8 | 48.7 | DM: Fasting blood glucose level of > 126 mg/dl, or random BM > 200 mg/dl or pharmacological therapy for diabetes. IFG:FBG ≥ 110 mg/dl; Excluding those with DM. | DSM IV Schizophrenia | 36/372 | . | . | 159/372 | . |
| Shinozaki 2012[43] | General Adult | 2005 - 2007 | USA | 4 | NR | DM:Documentation in the past medical history, current use of | Females with major depressive epsiode | 11/185 | . | . | . | . |

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| | | | | | | medication for DM, and/or documented glucose level that met criteria for the diagnosis of DM. | | | | | | |
| Siegler 1995[44] | General Adult | 1988 - 1990 | USA | 2 | NR | NR | Any inpatient with hypernatremia: Controls with non hypernatremia combined for overall prevalence | 22/256 | . | . | . | . |
| Yasui-Furukori 2009[45] | General Adult | Apr 2005 - Mar 2006 | Japan | 2 | NR | NR | DSM IV Schizophrenia | 7/130 | . | . | . | . |
| Zhang 2011[46] | General Adult | NR | China | 4 | NR | DM: Persistent FPG >126mg/dL or 2 hour OGTT > 200mg/dL | DSM IV Schizophrenia on clozapine | 46/206 | . | . | . | . |
| Jarvis 2007[47] | Addictions | NR | USA | 3 | 34.8 | IFG: FPG ≥ 100 mg/dL (range, 102-110 mg/dL) | Newly abstinent from alcohol men and women in a residential drug treatment facility | . | . | . | 6/46 | . |
| Matoo 2011[48] | Addictions | Jul 2009 - Dec 2009 | India | 7 | 37.43 | NR | Men with ICD 10 alcohol or opioid dependence | 5/110 | . | . | . | . |
| Nakamura 2004[49] | Addictions | Jun 2003 - May 2004 | Japan | 5 | NR | DM: FPG of 7.0 mmol/l (126 mg/dl) or higher on two or | ICD 10 alcohol dependence | 109/652 | . | . | 203/652 | . |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | more occasions when examined on separate days<br>IFG: FPG ≥ 6.1 and < 7.0 mmol/l). | | | | | | |
| Haw 2011[50] | Forensic | Feb 2010 - Feb 2010 | UK | 2 | 33 | NR | Any forensic rehabilitation inpatient | . | . | 20/234 | . | . |
| Kelbrick 2012[51] | Forensic | Aug 2009 - Sep 2009 | UK | 2 | NR | NR | Any forensic rehabilitation inpatient | 33/348 | 2/348 | 31/348 | . | . |
| Macfarlane 2004[52] | Forensic | Sep 2001 - Sep 2001 | UK | 8 | NR | NR | Any forensic inpatient | . | . | 35/408 | . | . |
| Vasudev 2012[53] | Forensic | Jan 2007 - Jan 2007 | UK | 1 | 34.5 | NR | Any male medium secure forensic psychiatric rehabilitation unit patient | . | . | 2/15 | . | . |
| Cohen 2006[54] | Rehabilitation | NR | Netherlands | 6 | NR | T2DM: Random BM >11.1 | DSM IV schizophrenia or schizoaffective disorder | | | 24/266 | | |
| O'Brien 2007[55] | Rehabilitation | NR | Ireland | 1 | NR | NR | Any patient on long stay ward | 3/27 | 1/27 | 2/27 | . | . |
| Udo 2011[56] | Rehabilitation | NR | Ireland | 1 | NR | NR | Any inpatient on rehabilitation ward | 4/30 | . | . | . | . |
| Wang 2006[57] | Rehabilitation | Feb 2004 - Jun 2004 | China | 4 | 49.6 | T2DM: Symptoms of diabetes, or a random fasting blood glucose level was higher than 7.1 mmol/L, or 2-hour blood | DSM IV schizophrenia on antipsychotic medication | . | . | 42/308 | . | 75/308 |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | glucose level after breakfast was higher than 11.1 mmol/ IGT: 6.1 mmol/L < FBG < 7.0 mmmol/L; (b) 7.8 mmol/L < 2-hour blood glucose after breakfast < 11.1 mmol/L | | | | | | |

Table two:

The prevalence of diabetes mellitus and impaired glucose metabolism in the adult inpatient psychiatric setting.

| | Unspecified DM | | | T1DM | | | T2DM | | | IFG | | | IGT | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Number of cohorts (n) | Prevalence % (95%CI) | $I^2$ (%) | Number of cohorts (n) | Prevalence % (95%CI) | $I^2$ (%) | Number of cohorts (n) | Prevalence % (95%CI) | $I^2$ (%) | Number of cohorts (n) | Prevalence % (95%CI) | $I^2$ (%) | Number of cohorts (n) | Prevalence % (95%CI) | $I^2$ (%) |
| All | 31 | 10 (9-12) | 95 | 5 | 1 (0-1) | 0 | 13 | 9 (6-13) | 93.4 | 7 | 18 (8-28) | 97.5 | 3 | 22 (16-28) | 55.2 |
| *Setting* | | | | | | | | | | | | | | | |

| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| IP General Adult Setting | 26 | 10 (9-12) | 95.7 | 3 | 1 (0-1) | 0 | 6 | 9 (4-14) | 95.1 | 5 | 17 (6-27) | 97.5 | 2 | 24 (5-42) | 47.5 |
| IP Addictions Setting | 2 | 11 (0-23) | 95.9 | 0 | . | . | 0 | . | . | 2 | 23 (5-40) | 91.5 | 0 | . | . |
| IP Forensic Setting | 1 | 10 (6-13) | . | 1 | 1 (0-1) | . | 4 | 9 (7-11) | 0 | 0 | . | . | 0 | . | . |
| IP Rehabilitation Setting | 2 | 12 (4-21) | 0 | 1 | 4 (0-11) | . | 3 | 11 (7-15) | 44.1 | 0 | . | . | 1 | 25 (20-29) | . |
| *Year of data collection* | | | | | | | | | | | | | | | |
| <1997 | 2 | 9 (7-12) | 0 | 0 | . | . | 1 | 9 (6-11) | . | 0 | . | . | 0 | . | . |
| 1997-1999 | 3 | 8 (7-10) | 94.8 | 0 | . | . | 1 | 7 (5-10) | . | 0 | . | . | 0 | . | . |
| 2000-2002 | 3 | 11 (10-13) | 95.2 | 0 | . | . | 0 | . | . | 0 | . | . | 0 | . | . |
| 2003-2005 | 7 | 13 (11-14) | 87.5 | 0 | . | . | 1 | 14 (10-18) | . | 2 | 21 (2-40) | 98.8 | 1 | 24 (20-29) | . |
| 2006-2008 | 4 | 6 (3-9) | 72.5 | 0 | . | . | 3 | 10 (0-24) | 93.1 | 1 | 43 (38-48) | . | 0 | . | . |
| 2009-2011 | 4 | 9 (6-13) | 74.6 | 2 | 1 (0-1) | 0 | 3 | 9 (7-11) | 93.1 | 1 | 3 (0-7) | . | 0 | . | . |
| 2012-2014 | 2 | 12 (2-23) | 90.2 | 1 | 1 (0-1) | . | 1 | 7 (5-10) | . | 0 | . | . | 0 | . | . |
| *Continent* | | | | | | | | | | | | | | | |
| Europe | 8 | 9 (7-12) | 72.2 | 5 | 1 (0-1) | 0 | 8 | 9 (7-11) | 15 | 3 | 10 (4-16) | 89.1 | 1 | 40 (10-70) | . |
| North America | 16 | 11 (9-12) | 97 | 0 | . | . | 1 | 7 (5-10) | . | 1 | 13 (3-23) | . | 0 | . | . |
| Asia | 7 | 11 (6-16) | 91.8 | 0 | . | . | 4 | 10 (2-17) | 96.8 | 3 | 29 (12-45) | 97.9 | 2 | 21(16-27) | 67 |
| *Diagnostic Category* | | | | | | | | | | | | | | | |
| Any inpatient | 18 | 11 (10-12) | 96.5 | 4 | 1 (0-1) | 0 | 8 | 9 (7-10) | 24.2 | 2 | 12 (10-14) | 0 | 0 | . | . |
| Schizophrenia/Schizoaffective Disorder | 4 | 11 (5-17) | 88.2 | 0 | . | . | 4 | 9 (11-18) | 96.5 | 2 | 27 (0-57) | 98.9 | 2 | 21 (16-27) | 67 |
| Any Mood Disorder | 7 | 8 (4-12) | 89.9 | 1 | 2 (0-4) | . | 1 | 10 (3-17) | . | 1 | 3 (0-7) | . | 1 | 40 (10-70) | . |
| Any Substance Dependence Disorder | 2 | 11 (0-23) | 95.9 | 0 | . | . | 0 | . | . | 2 | 23 (5-40) | 91.5 | 0 | . | . |

| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *Study Quality* | | | | | | | | | | | | | | | |
| Low Quality | 11 | 9 (6-11) | 84.1 | 3 | 1 (0-1) | 0 | 6 | 10 (8-13) | 25.7 | 2 | 7 (0-17) | 72.4 | 1 | 40 (10-70) | . |
| Medium Quality | 8 | 12 (8-16) | 89.4 | 2 | 1 (0-1) | 0 | 5 | 10 (7-13) | 73.9 | 3 | 19 (7-32) | 96.7 | 2 | 21 (16-27) | 67 |
| High Quality | 12 | 11 (9-12) | 97.7 | 0 | . | . | 2 | 4 (0-12) | 96.8 | 2 | 27 (3-58) | 99.2 | . | . | . |

Online Supplementary Material

eFigure 1: Search terms
[(diabet* OR glucose) AND (inpatient* OR ward OR residential) AND (psychiatr* OR SMI OR mental* OR schizo*)]

eFigure 2: Adapted Newcastle Ottawa Scale Quality Assessment Scale for Cross Sectional Studies

Selection:

1) Representativeness of the sample:
a) Truly representative of the average in the target population. (Randomised/consecutive)

b) Somewhat representative of the average in the target population. (non-random sampling)

c) Selected group of users.

d) No description of the sampling strategy.

(One point for A or B; Zero points for C or D)

2) Sample size:
a) Justified and satisfactory. (>100)
b) Not justified.

(One point for A; Zero points for B)

3) Non-respondents:
a) Comparability between respondents and non-respondents characteristics is established, and the response rate is satisfactory. (Participation rate reported)
b) The response rate is unsatisfactory, or the comparability between respondents and non-respondents is unsatisfactory. (Participation < 75%)
c) No description of the response rate or the characteristics of the responders and the non-responders.

(One point for A; Zero points for B or C)

4) Ascertainment of the diagnosis of diabetes/impaired glucose metabolism:
a) Validated measurement tool. A diagnosis based on international criteria (e.g., the American Diabetes Association criteria or World Health Organization criteria.
b) Non-validated measurement tool, Proxy measurement such as anti-diabetic medication.
c) No description of the measurement tool.

(Two points for A; One point for B; Zero points for C)

Comparability:

1) The subjects are comparable across studies based on age and gender, based on the study design or analysis.
a) Comparable
b) Non-Comparable

(Two points for A; Zero points for B)

Outcome:

1) Assessment of the outcome:
a) Independent assessment.

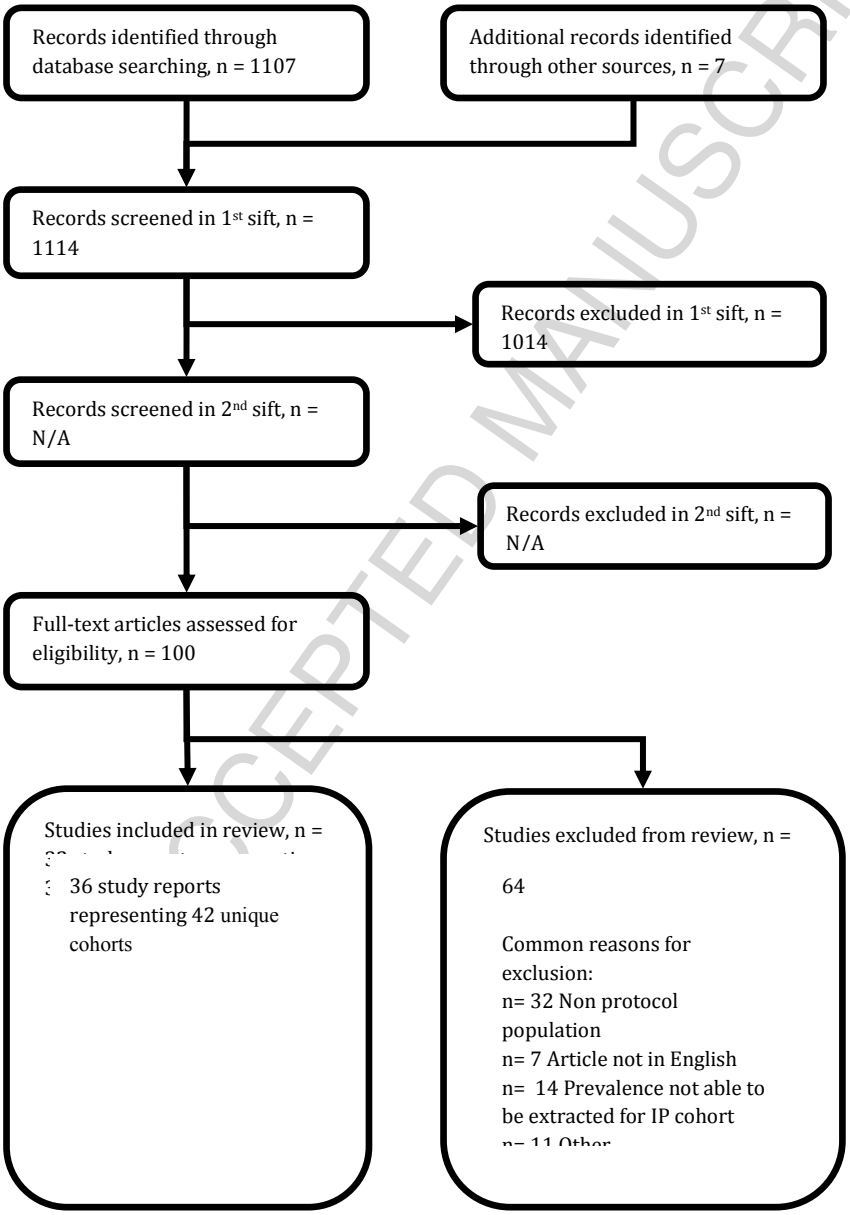
b) Documented diagnosis.
c) Self report.
d) No description.

(Two points for A or B; One point for C; Zero points for D)

2) Statistical test:
a) The statistical test used to analyze the data is clearly described and appropriate, and the measurement of the association is presented, including confidence intervals and the probability level (p value).
b) The statistical test is not appropriate, not described or incomplete.

(One point for A; Zero points for B)

eFigure 3: Included studies flow diagram



eTable 1: Excluded Studies

| | |
|---|---|
| Fan, Xiaoduo, Liu, Emily, Pristach, Cynthia, Goff, Donald C., Henderson, David C.Higher fasting serum insulin levels are associated with a better psychopathology profile in acutely ill non-diabetic inpatients with schizophrenia. Schizophrenia Research, Sep 2006, vol. 86, no. 1-3, p. 30-35, 0920-9964 (Sep 2006) | Preselected population with normal blood glucose a priori |
| Grover S., Nebhinani N., Chakrabarti S., Avasthi A., Kulhara P., Basu D., Mattoo S.K., Malhotra S.Comparative study of prevalence of metabolic syndrome in bipolar disorder and schizophrenia from North India. Nordic Journal of Psychiatry, January 2014, vol./is. 68/1(72-77), 0803-9488;1502-4725 (January 2014) | No individual number of DM or IFG or IGT reported |
| Massey E.W., Massey J.M. Peroneal palsy in depressed patients. Psychosomatics, 1987, vol./is. 28/2(93-94), 0033-3182 (1987) | Prevalence in inpatients receiving neurological consultations |
| Nguyen, Dang, Brakoulias, Vlasios, Boyce, Philip. An evaluation of monitoring practices in patients on second generation antipsychotics. Australasian Psychiatry, Aug 2009, vol. 17, no. 4, p. 295-299, 1039-8562 (Aug 2009) | No individual number of DM or IFG or IGT reported |
| Shiloah, Eli, Witz, Shula, Abramovitch, Yehuda, Cohen, Ohad, Buchs, Andreas, Ramot, Yoram, Weiss, Mordechai, Unger, Abraham, Rapoport, Micha J Effect of acute psychotic stress in nondiabetic subjects on beta-cell function and insulin sensitivity. Diabetes care, May 2003, vol. 26, no. 5, p. 1462-1467, 0149-5992 (May 2003) | Population excludes abnormal serum glucose level a priori |
| Lindenmayer, Jean Pierre, Tedeschi, Frank, Yusim, Anna, Khan, Anzalee, Kaushik, Saurabh, Smith, Robert C, Parakadavil, Mohan Ziprasidone's effect on metabolic markers in patients with diabetes and chronic schizophrenia. Clinical schizophrenia & related psychoses, Jan 2012, vol. 5, no. 4, p. 185-192, 1935-1232 (January 2012) | Preselected population patients with patients with DM |
| Chiu C-C. Chen C.-H., Chen B.-Y., Yu S.-H., Lu M.-L. The time-dependent change of insulin secretion in schizophrenic patients treated with olanzapine. Progress in Neuro-Psychopharmacology and Biological Psychiatry, August 2010, vol./is. 34/6(866-870), 0278-5846 (August 2010) | Preselected population with normal blood glucose a priori |
| Citrome, Leslie, Jaffe, Ari, Levine, Jerome, Allingham, Baerbel, Robinson, James. Relationship between antipsychotic medication treatment and new cases of diabetes among psychiatric inpatients. Psychiatric services (Washington, D.C.), Sep 2004, vol. 55, no. 9, p. 1006-1013, 1075-2730 (September 2004) | Double counting with Citrome 2006; Collected data 2000-2002 |
| Ladea M., Barbu C.M., Rosu D.P.Metabolic imbalance in affective disorders Journal of medicine and life, March 2013, vol./is. 6/1(45-49), 1844-3117 (15 Mar 2013) | Preselected population patients with patients with DM |
| Manu, Peter, Correll, Christoph U, Wampers, Martien, van Winkel, Ruud, Yu, Weiping, Shiffeldrim, Daphna, Kane, John M, De Hert, Marc Insulin secretion in patients receiving clozapine, olanzapine, quetiapine and risperidone. Schizophrenia research, Feb 2013, vol. 143, no. 2-3, p. 358-362 (February 2013) | Data already included; Double counting with Manu 2012/13 |
| Mookhoek E.J., Van De Kerkhof P.C.M., Hovens J.E.J.M., Brouwers J.R.B.J., Loonen A.J.M. Skin disorders in chronic psychiatric illness. Journal of the European Academy of Dermatology and Venereology, October 2010, vol./is. 24/10(1151-1156), 0926-9959;1468-3083 (October 2010) | Prevalence in inpatients seeking dermatological consultations; Collection data of data NR potential overlap with included cohort |

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|---|---|
| | Mookhoek 2011. |
| Basu, Anirban, Meltzer, Herbert Y. Differential trends in prevalence of diabetes and unrelated general medical illness for schizophrenia patients before and after the atypical antipsychotic era. Schizophrenia Research, Sep 2006, vol. 86, no. 1-3, p. 99-109, 0920-9964 (Sep 2006) | Not psychiatric IP setting; Schizophrenia in all hospitals including general hospitals |
| Chen Q., Cai Z.-j., Mao P.-x., Zhai Y.-M., Mitchell P.B., Tang Y.-l. Effects of risperidone on glucose metabolism in Chinese patients with schizophrenia: A prospective study. Journal of Psychiatric Research, December 2008, vol./is. 43/2(124-128), 0022-3956 (December 2008) | No individual number of DM or IFG or IGT reported |
| Hansen, Otto. Blood uridine diphosphate glucose in mental disease. The British Journal of Psychiatry, Jan 1969, vol. 115, no. 522, p. 557-562, 0007-1250 (1969) | Unable to calculate number of people with IGT; Uses non OGTT method to derive IGT |
| Regenold W.T., Thapar R.K., Marano C., Gavirneni S., Kondapavuluru P.V. Increased prevalence of type 2 diabetes mellitus among psychiatric inpatients with bipolar I affective and schizoaffective disorders independent of psychotropic drug use. Journal of Affective Disorders, 2002, vol./is. 70/1(19-26), 0165-0327 (2002) | Older Adult population |
| Rittmannsberger, Hans, Fellinger, Johannes, Foff, Christian, Walli, Gertraud, Zaunmüller, Thomas Deterioration of metabolic parameters during short-term psychiatric inpatient treatment: a prospective naturalistic study. International journal of psychiatry in clinical practice, Mar 2012, vol. 16, no. 1, p. 8-17 (March 2012) | No individual number of DM or IFG or IGT reported |
| Munshi T., Patel A., Mazhar M.N., Hassan T., Siddiqui E.U.Frequency of metabolic syndrome in psychiatric patients, is this the time to develop a standardized protocol to reduce the morbidity from an acute care psychiatry unit. Journal of the Pakistan Medical Association, 2015, vol./is. 65/1(54-58), 0030-9982 (2015) | 11/50 FBG>100 mg/dl of Non Met-S cant calculate for whole sample |
| Reist C., Mintz J., Albers L.J., Jamal M.M., Szabo S., Ozdemir V. Second-generation antipsychotic exposure and metabolic-related disorders in patients with schizophrenia: An observational pharmacoepidemiology study from 1988 to 2002. Journal of Clinical Psychopharmacology, February 2007, vol./is. 27/1(46-51), 0271-0749 (February 2007) | No individual number of DM or IFG or IGT reported |
| Ojala K., Niskanen L., Tiihonen J., Paavola P., Putkonen A., Repo-Tiihonen E. Characterization of metabolic syndrome among forensic psychiatric inpatients. Journal of Forensic Psychiatry and Psychology, March 2008, vol./is. 19/1(33-51), 1478-9949;1478-9957 (March 2008) | No individual number of DM or IFG or IGT reported |
| Lindenmayer J.-P., Khan A., Wance D., Maccabee N., Kaushik S. Outcome evaluation of a structured educational wellness program in patients with severe mental illness. Journal of Clinical Psychiatry, October 2009, vol./is. 70/10(1385-1396), 0160-6689 (October 2009) | T2DM/IFG or IGT reported combined at baseline unable to calculate prevalence of each |
| Lyness J.M., Caine E.D., Cox C., King D.A., Conwell Y., Olivares T. Cerebrovascular risk factors and later-life major depression: Testing a small-vessel brain disease model. American Journal of Geriatric Psychiatry, December 1998, vol./is. 6/1(5-13), 1064-7481 | Older Adult inpatients |
| Zeugmann S., Quante A., Heuser I., Schwarzer R., Anghelescu I. Inflammatory biomarkers in 70 depressed inpatients with and without the metabolic syndrome Journal of Clinical Psychiatry, August 2010, vol./is. 71/8(1007-1016), 0160-6689 (August 2010) | No individual number of DM or IFG or IGT reported |
| Susce, Margaret T, Villanueva, Noemi, Diaz, Francisco J, de Leon, Jose Obesity and associated complications in patients with severe mental illnesses: a cross-sectional survey. The Journal of clinical psychiatry, Feb 2005, vol. 66, no. 2, p. 167-173, 0160-6689 (February 2005) | Mixed IP and OP; NR separately |
| Carney, Caroline P, Jones, Laura, Woolson, Robert F .Medical | Mixed IP and OP; NR |

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| comorbidity in women and men with schizophrenia: a population-based controlled study. Journal of general internal medicine, Nov 2006, vol. 21, no. 11, p. 1133-1137 (November 2006) | separately |
| Cohen D., Puite B., Dekker J., De Wied C.G.Diabetes Mellitus in 93 chronic schizophrenic inpatients European Journal of Psychiatry, January 2003, vol./is. 17/1(38-47), 0213-6163 (January/March 2003) | Article in Spanish |
| Rothbard A.B., Blank M.B., Staab J.P., Tenhave T., Young D.S., Berry S.D., Eachus A.A.S. Previously undetected metabolic syndromes and infectious diseases among psychiatric inpatients. Psychiatric Services, April 2009, vol./is. 60/4(534-537), 1075-2730;1557-9700 (April 2009) | Unable to calculate accurate n for diabetes. Differing measures reported. |
| Krakowski M., Czobor P., Citrome L. Weight gain, metabolic parameters, and the impact of race in aggressive inpatients randomized to double-blind clozapine, olanzapine or haloperidol. Schizophrenia Research, May 2009, vol./is. 110/1-3(95-102), 0920-9964 (May 2009) | No individual number of DM or IFG or IGT reported only serum glucose levels given |
| Chien I.-C., Hsu J.-H., Lin C.-H., Bih S.-H., Chou Y.-J., Chou P. Prevalence of diabetes in patients with schizophrenia in Taiwan: A population-based National Health Insurance study. Schizophrenia Research, June 2009, vol./is. 111/1-3(17-22), 0920-9964 (June 2009) | Mixed OP and IP. IP data not reported separately |
| Lin C.-C., Bai Y.-M., Wang Y.-C., Chen T.-T., Lai I.-C., Chen J.-Y., Chen S.-Y., Gau S.S.F., Liou Y.-J. Improved body weight and metabolic outcomes in overweight or obese psychiatric patients switched to amisulpride from other atypical antipsychotics. Journal of Clinical Psychopharmacology, December 2009, vol./is. 29/6(529-536), 0271-0749 (December 2009) | No individual number of DM or IFG or IGT reported only serum glucose level given |
| De Hert M, van Winkel R, Van Eyck D et al. Prevalence of the metabolic syndrome in patients with schizophrenia treated with antipsychotic medication. Schizophr Res 2006; 83: 87-93. | Mixed OP and IP data. IP date not reported separately |
| van Winkel R, De Hert M, Van Eyck D, et al. Prevalence of diabetes and the metabolic syndrome in a sample of patients with bipolar disorder. Bipolar Disord. 2008;10(2):342–348. | Mixed OP and IP data. IP date not reported separately |
| Meyer J.M., Pandina G., Bossie C.A., Turkoz I., Greenspan A.Effects of switching from olanzapine to risperidone on the prevalence of the metabolic syndrome in overweight or obese patients with schizophrenia or schizoaffective disorder: Analysis of a multicenter, rater-blinded, open-label study. Clinical Therapeutics, December 2005, vol./is. 27/12(1930-1941), 0149-2918;1879-114X (December 2005) | Mixed OP and IP data. IP date not reported separately |
| Teixeira P.J.R., Rocha F.L.The prevalence of metabolic syndrome among psychiatric inpatients in Brazil. Revista de Psiquiatria do Rio Grande do Sul, December 2007, vol./is. 29/4(330-336), 0101-8108 (December 2007) | No individual number of DM or IFG or IGT reported |
| Lieberman J.A., Phillips M., Gu H., Stroup S., Zhang P., Kong L., Ji Z., Koch G., Hamer R.M. Atypical and conventional antipsychotic drugs in treatment-naive first-episode schizophrenia: a 52-week randomized trial of clozapine vs chlorpromazine. Neuropsychopharmacology : official publication of the American College of Neuropsychopharmacology, May 2003, vol./is. 28/5(995-1003), 0893-133X (May 2003) | No individual number of DM or IFG or IGT reported only serum glucose level given |
| Gupta S., Steinmeyer C., Frank B., Madhusoodanan S., Lockwood K., Lentz B., Keller P. Hyperglycemia and hypertriglyceridemia in real world patients on antipsychotic therapy. American journal of therapeutics, September 2003, vol./is. 10/5(348-355), 1075-2765 (2003 Sep-Oct) | Mixed OP and IP data. IP date not reported separately |
| Lu M.L., Lane H.Y., Lin S.K., Chen K.P., Chang W.H. Adjunctive fluvoxamine inhibits clozapine-related weight gain and metabolic disturbances. The Journal of clinical psychiatry, June 2004, vol./is. 65/6(766-771), 0160-6689 (Jun 2004) | No individual number of DM or IFG or IGT reported only serum glucose level given |

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| Simpson G.M., Glick I.D., Weiden P.J., Romano S.J., Siu C.O.. Randomized, controlled, double-blind multicenter comparison, of the efficacy and tolerability of ziprasidone and olanzapine in acutely III inpatients with schizophrenia or schizoaffective disorder. American Journal of Psychiatry, October 2004, vol./is. 161/10(1837-1847), 0002-953X (October 2004) | No individual number of DM or IFG or IGT reported only serum glucose level given |
| Straker D., Correll C.U., Kramer-Ginsberg E., Abdulhamid N., Koshy F., Rubens E., Saint-Vil R., Kane J.M., Manu P.. Cost-effective screening for the metabolic syndrome in patients treated with second-generation antipsychotic medications. American Journal of Psychiatry, June 2005, vol./is. 162/6(1217-1221), 0002-953X (June 2005) | No calculable n for DM or IFG only glucose level given, only calculable for MS population not total. |
| De Leon J., Susce M.T., Diaz F.J., Rendon D.M., Velasquez D.M. Variables associated with alcohol, drug, and daily smoking cessation in patients with severe mental illnesses. Journal of Clinical Psychiatry, November 2005, vol./is. 66/11(1447-1455), 0160-6689 (November 2005) | Mixed OP and IP data. IP date not reported separately |
| Desai M.M., Rosenheck R.A., Druss B.G., Perlin J.B. Mental disorders and quality of diabetes care in the veterans health administration. American Journal of Psychiatry, September 2002, vol./is. 159/9(1584-1590), 0002-953X (September 2002) | Not psychiatric IP sample. |
| Goethe J.W., Szarek B.L., Caley C.F. Metabolic syndrome in psychiatric inpatients treated for depression. Metabolic Effects of Psychotropic Drugs, 2009, vol./is. 26/(90-104), 1662-2685;1662-4505 (2009) | Reports individual number for criteria of MetS FBG >110 or diagnosis of DM combined |
| Greco, Maria Isabella, Gallotti, Paolo Maria, Magnolfi, Valeria, Alberti, Giorgio Gabriele Esiste un'associazione tra patologie psichiatriche e diabete mellito? Risultati di uno studio su una popolazione psichiatrica ospedaliera.. Psichiatria e Psicoterapia, Dec 2006, vol. 25, no. 4, p. 346-353, 1724-4919 (Dec 2006) | Article in Italian |
| Usta, Evrim, Metin, Özen, Birsöz, Sunar Şizofreni ve diyabet: Yeni kuşak antipsikotiklerin yol açtiği diyabet veya metabolik sendrom. Klinik Psikofarmakoloji Bülteni / Bulletin of Clinical Psychopharmacology, Dec 2007, vol. 17, no. 4, p. 207-216, 1017-7833 (Dec 2007) | Article in Turkish |
| Leonard, Hasse, Hoheneck, Dagmar. Metabolic side effects of the atypical antipsychotic olanzapine in an inpatient population of adults with developmental disabilities. Mental Health Aspects of Developmental Disabilities, Jan 2006, vol. 9, no. 1, p. 18-22, 1057-3291 (Jan-Mar 2006) | No individual number of DM or IFG or IGT reported |
| Kelly, Deanna L., Kreyenbuhl, Julie, Love, Raymond C., Van-Duong, Quynh, Conley, Robert R.Six-Month Review of Weight and Metabolic Parameters in Patients Receiving Clozapine, Risperidone, Olanzapine, or Quetiapine. Journal of Clinical Psychiatry, Sep 2003, vol. 64, no. 9, p. 1133-1134, 0160-6689 (Sep 2003) | No number of DM or IFG or IGT reported only serum glucose levels. |
| Campbell, E Cabrina, DeJesus, Melissa, Herman, Barry K, Cuffel, Brian J, Sanders, Kafi N, Dodge, William, Dhopesh, Vasant, Caroff, Stanley N A pilot study of antipsychotic prescribing decisions for acutely-Ill hospitalized patients. Progress in neuro-psychopharmacology& biological psychiatry, Jan 2011, vol. 35, no. 1, p. 246-251 (January 15, 2011) | No number of DM or IFG or IGT reported only serum glucose levels. |
| Suzuki, Yutaro, Sugai, Takuro, Fukui, Naoki, Watanabe, Junzo, Ono, Shin, Tsuneyama, Nobuto, Saito, Mami, Someya, Toshiyuki Low prevalence of metabolic syndrome and its prediction in Japanese inpatients with schizophrenia. Human Psychopharmacology: Clinical and Experimental, Mar 2013, vol. 28, no. 2, p. 188-191, 0885-6222 (Mar 2013) | FBG >100 mg/dl prevalence reported. Nil distinction between IFG and DM. Nil indiviusal number reported. |
| Deuschle, M., Paul, F., Brosz, M., Bergemann, N., Franz, M., Kammerer-Ciernioch, J., Lautenschlager, M., Lederbogen, F., Roesch-Ely, D., Weisbrod, M., Kahl, K. G., Reichmann, J., Gross, J., | IP and OP cohort; Not reported separately |

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| Umbreit, J.Assessment of cardiovascular disease risk in patients with schizophrenia spectrum disorders in German psychiatric hospitals: Results of the pharmacoepidemiologic CATS study. Social Psychiatry and Psychiatric Epidemiology, Aug 2013, vol. 48, no. 8, p. 1283-1288, 0933-7954 (Aug 2013) | |
| Schimmelbusch, Werner H., Mueller, Peter S., Sheps, Jack The positive correlation between insulin resistance and duration of hospitalization in untreated schizophrenia. The British Journal of Psychiatry, Apr 1971, vol. 118, no. 545, p. 429-436, 0007-1250 (Apr 1971) | No number of DM or IFG or IGT reported only serum glucose levels. |
| Marsay, C., Szabo, C. P. Screening for metabolic syndrome-adherence to guidelines. African Journal of Psychiatry, Mar 2011, vol. 14, no. 1, p. 64-66, 1994-8220 (Mar 2011) | OP cohort |
| Wehring, Heidi J., Liu, Fang, McMahon, Robert P., Mackowick, Kristen M., Love, Raymond C., Dixon, Lisa, Kelly, Deanna L.Clinical characteristics of heavy and non-heavy smokers with schizophrenia. Schizophrenia Research, Jul 2012, vol. 138, no. 2-3, p. 285-289, 0920-9964 (Jul 2012) | No number of DM or IFG or IGT reported only serum glucose levels. |
| Caemmerer, Jacqueline, Correll, Christoph U., Maayan, Lawrence Acute and maintenance effects of non-pharmacologic interventions for antipsychotic associated weight gain and metabolic abnormalities: A meta-analytic comparison of randomized controlled trials. Schizophrenia Research, Sep 2012, vol. 140, no. 1-3, p. 159-168, 0920-9964 (Sep 2012) | Meta-analysis with 3 IP trials. No number of DM or IFG or IGT reported only serum glucose levels. |
| Mitchell, Alex J., Vancampfort, Davy, Sweers, Kim, van Winkel, Ruud, Yu, Weiping, De Hert, Marc Prevalence of metabolic syndrome and metabolic abnormalities in schizophrenia and related disorders—A systematic review and meta-analysis. Schizophrenia Bulletin, Mar 2013, vol. 39, no. 2, p. 306-318, 0586-7614 (Mar 2013) | MA for MetS prevalence. Cross-checked for references. |
| Hjorth P., Davidsen A.S., Kilian R., Pilgaard Eriksen S., Jensen S.O., Sorensen H.O., Munk-Jorgensen P.Improving the physical health of long-term psychiatric inpatients Australian and New Zealand Journal of Psychiatry, September 2014, vol./is. 48/9(861-870), 0004-8674;1440-1614 (September 2014) | No number of DM or IFG or IGT reported only serum glucose levels. |
| Wetterling, Tilman, Schneider, Barbara, Weber, Bernhard. Blood glucose in chronic schizophrenic patients treated with antipsychotics. Psychiatrische Praxis, Mar 2007, vol. 34, no. 2, p. 76-80, 0303-4259 (March 2007) | Article in German |
| Hallahan, Brian, Lyons, Declan, Doyle, Patrick Bone mineral density and general health of long-term residential psychiatric inpatients. Irish Journal of Psychological Medicine, Sep 2008, vol. 25, no. 3, p. 95-99, 0790-9667 (Sep 2008) | No number of DM or IFG or IGT reported only serum glucose levels. |
| Abdullah, Anwar K, Khan, Salman, Mustafa, Shaheen F, Qutubuddin, Abu A, Davis, Charles M Vitamin d status and cardiometabolic risk factors in long-term psychiatric inpatients. The primary care companion for CNS disorders, Jan 2012, vol. 14, no. 1 (2012) | Reports number of MetS criteria elevated fasting glucose or DM; No separation of DM and IFG numbers able to be calculated. |
| The Bermudes, Richard A, Keck, Paul E, Welge, Jeffrey A prevalence of the metabolic syndrome in psychiatric inpatients with primary psychotic and mood disorders. Psychosomatics, Nov 2006, vol. 47, no. 6, p. 491-497, 0033-3182 (2006 Nov-Dec) | Reports number of MetS criteria elevated fasting glucose or DM; No separation of DM and IFG numbers able to be calculated. |
| Boke O., Aker S., Sarisoy G., Saricicek E.B., Sahin A.R.Prevalence of metabolic syndrome among inpatients with schizophrenia. International Journal of Psychiatry in Medicine, 2008, vol./is. 38/1(103-112), 0091-2174;1541-3527 (2008) | Reports number of MetS criteria elevated fasting glucose or DM; No separation of DM and IFG numbers able to be calculated. |
| Coakley C., Bolton P., Flaherty L., Kopeski L.M., Slifka K., Sutherland M.A. The incidence of metabolic risk factors in an inpatient psychiatric setting. Journal of Psychosocial Nursing and | Reports number of MetS criteria elevated fasting glucose or DM; No separation |

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| Mental Health Services, March 2012, vol./is. 50/3(24-30), 0279-3695 (March 2012) | of DM and IFG numbers able to be calculated. |
| Gossell-Williams M., Martin J., Neita S., Gibson R.C., Abel W., Sewell C., McGrowder D. Prevalence of the metabolic syndrome in patients presenting to the university hospital of the West Indies: a need to adopt proactive screening and specific management policy The West Indian medical journal, November 2012, vol./is. 61/8(802-808), 0043-3144 (Nov 2012) | Reports number of MetS criteria elevated fasting glucose or DM; No separation of DM and IFG numbers able to be calculated. |
| Lin C.-C., Yu S.-C., Wu B.-J., Chang D.-J. Measurement of waist circumference at different sites affects the detection of abdominal obesity and metabolic syndrome among psychiatric patients. Psychiatry Research, May 2012, vol./is. 197/3(322-326), 0165-1781;1872-7123 (30 May 2012) | Reports number of MetS criteria elevated fasting glucose or DM; No separation of DM and IFG numbers able to be calculated. |
| Marthoenis M., Aichberger M.C., Puteh I., Syahrial S., Schouler-Ocak M.Metabolic syndrome among psychiatric inpatients with schizophrenia in Indonesia Asian Journal of Psychiatry, June 2015, vol./is. 15/(10-14), 1876-2018;1876-2026 (01 Jun 2015) | Reports number of MetS criteria elevated fasting glucose or DM; No separation of DM and IFG numbers able to be calculated. |
| Kai G. Kahl, Wiebke Greggersen, Ulrich Schweiger et al. Prevalence of the metabolic syndrome in men and women with alcohol dependence: results from a cross-sectional study during behavioural treatment in a controlled environment. Addiction 2010105, 1921–1927 | Reports number of MetS criteria elevated fasting glucose or DM; No separation of DM and IFG numbers able to be calculated. |
| Nagamine, Takahiko Hyperlipidemia in psychiatric inpatients. Seishin Igaku (Clinical Psychiatry), Nov 2001, vol. 43, no. 11, p. 1263-1268, 0488-1281 (Nov 2001) | Article in Japanese |
| Suzuki Y., Mikami T., Tajiri M., Kunizuka T., Abe H., Someya T.Effects of hospitalization in a psychiatric ward on the body weight of Japanese patients with schizophrenia. International Journal of Psychiatry in Medicine, January 2013, vol./is. 45/3(261-268), 0091-2174;1541-3527 (01 Jan 2013) | No number of DM or IFG or IGT reported only serum glucose levels. |
| Sugai T., Suzuki Y., Fukui N., Watanabe J., Ono S., Tsuneyama N., Someya T.Excessive insulin secretion in japanese schizophrenic patients treated with antipsychotics despite normal fasting glucose levels. Journal of Clinical Psychopharmacology, December 2012, vol./is. 32/6(750-755), 0271-0749;1533-712X (December 2012) | Reports serum glucose conentration following OGTT. Nil number of individuals with IGT reported. |
| Shafer, Alan B, Ray, Ryan Kumar, Becker, Emilie A General medical care external hospitalizations for patients in Texas state mental health hospitals. Texas medicine, Mar 2013, vol. 109, no. 3, p. e1. (March 2013) | No DM prevalence in inpatient psychiatric cohort reported. |
| Konarzewska, Beata, Waszkiewicz, Napoleon, Galińska, Beata, Szulc, Agata. Fasting insulin serum levels and psychopathology profiles in male schizophrenic inpatients treated with olanzapine or risperidone. Neuro endocrinology letters, Jan 2013, vol. 34, no. 4, p. 322-328, 0172-780X (2013) | Excludes DM patients a priori. No DM or IFG/IGT number reported only serum glucose levels. |
| Bahtiyar, Gül, Weiss, Karolina, Sacerdote, Alan S Novel endocrine disrupter effects of classic and atypical antipsychotic agents and divalproex: induction of adrenal hyperandrogenism, reversible with metformin or rosiglitazone. Endocrine practice : official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists, Oct 2007, vol. 13, no. 6, p. 601-608 (October 2007) | Included patients were those patients with known metabolic abnormalities referred to an endocrine service. |
| Correll CU, Frederickson AM, Kane JM, Manu P. Metabolic syndrome and the risk of coronary heart disease in 367 patients treated with second-generation antipsychotic drugs. J Clin Psychiatry 2006;67:575–583. | Unable to calculate number of patients with DM |
| Chien IC, Wu EL, Lin CH, Chou YJ, Chou P. Prevalence of | Prevalence reported for both |

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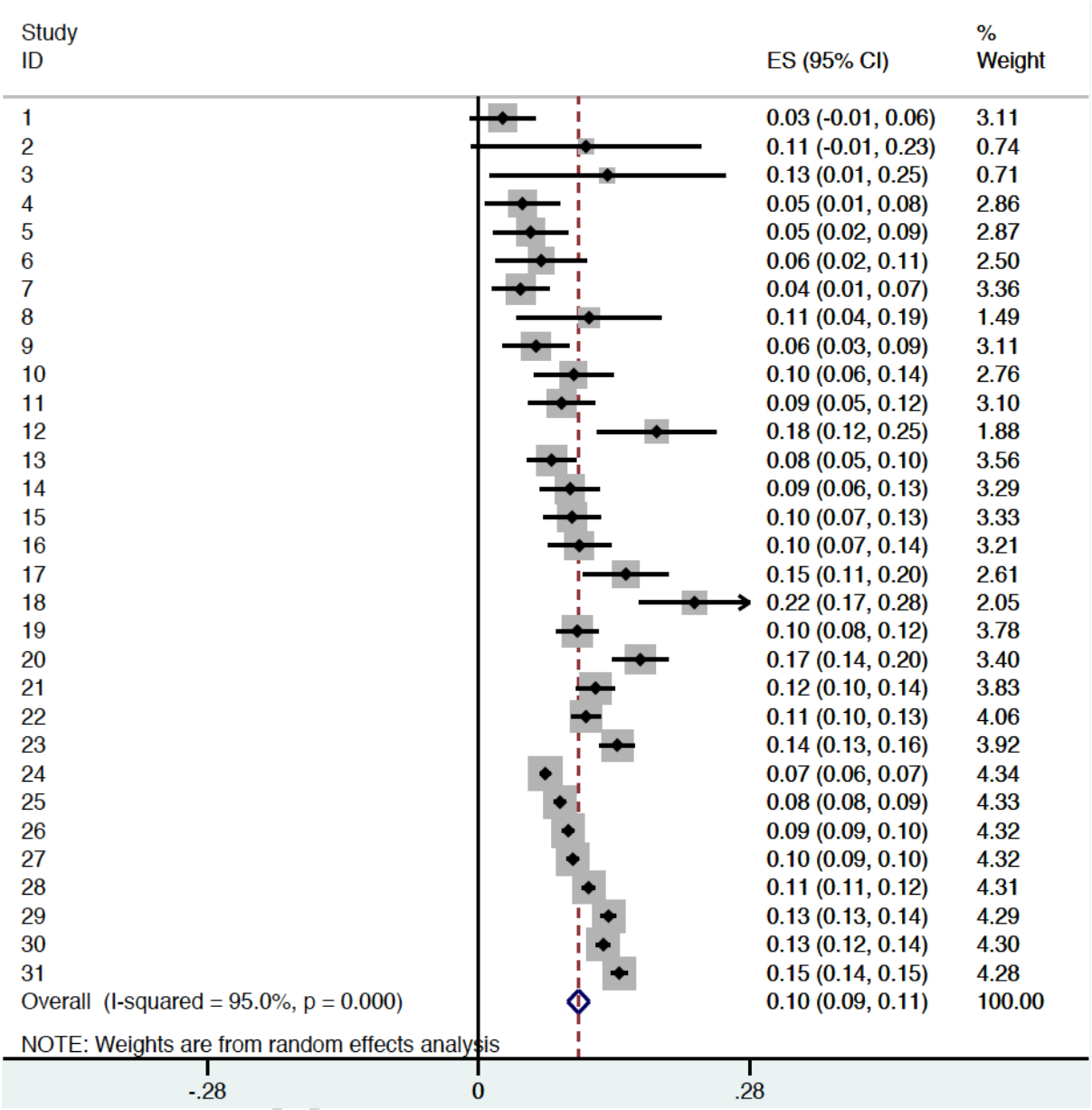
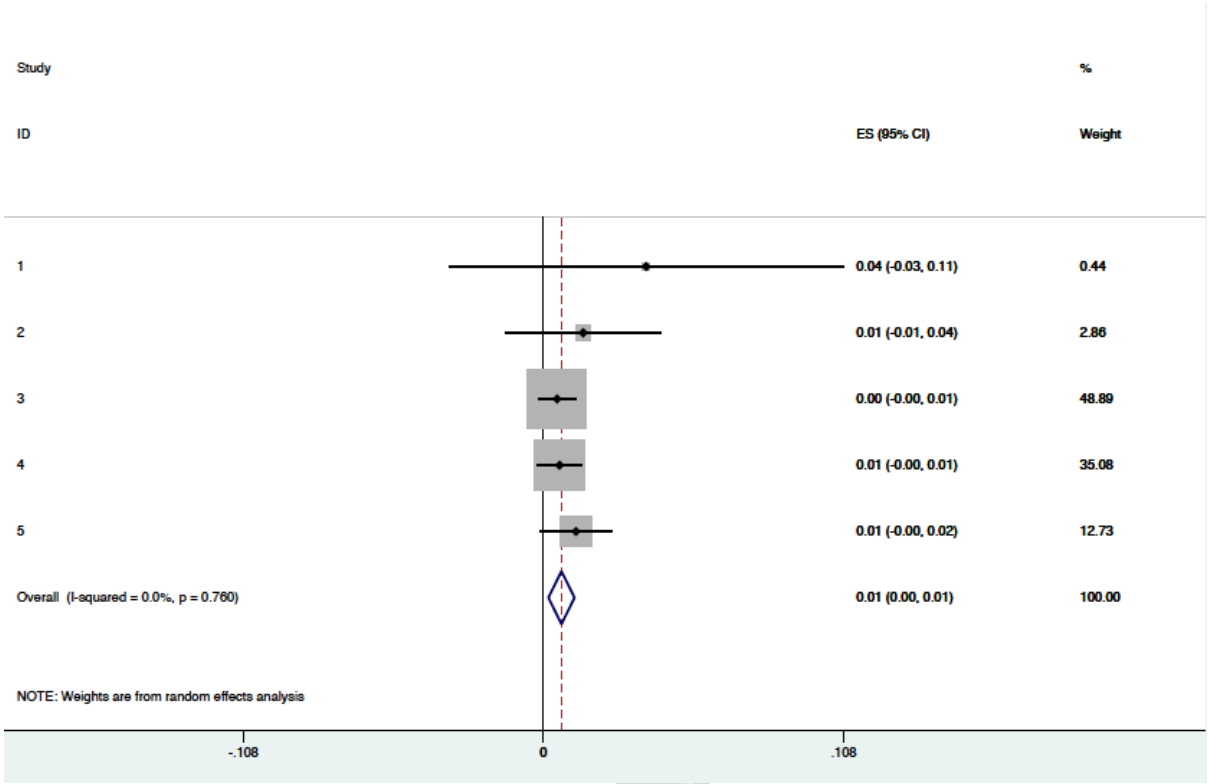
| diabetes in patients with major depressive disorder: a population based study. Compr Psychiatry 2012;53(5):569–575. | in and outpatients, unable to extract inpatient data alone. |
| Amital D, Fostick L, Silberman A, et al. Physical co-morbidity among treatment resistant vs. treatment responsive patients with major depressive disorder. Eur Neuropsychopharmacol 2013;23(8):895–901. | Prevalence reported for both in and outpatients, unable to extract inpatient data alone |
| Schoepf D, Uppal H, Potluri R, Chandran S, Heun R. Comorbidity and its relevance on general hospital based mortality in major depressive disorder: a naturalistic 12-year follow-up in general hospital admissions. J Psychiatr Res 2014;52:28–35. | General hospital inpatients not psychiatric inpatients |
| Schoepf D, Heun R. Bipolar disorder and comorbidity: increased prevalence and increased relevance of comorbidity for hospital-based mortality during a 12.5-year observation period in general hospital admissions. J Affect Disord. 2014;169:170–178. | General hospital inpatients not psychiatric inpatients |
| McElroy SL, Frye MA, Suppes T, et al. Correlates of overweight and obesity in 644 patients with bipolar disorder. J Clin Psychiatry. 2002;63(3):207–213. doi:10.408/JCP.v63n0306 PubMed | Outpatient sample |
| Kilbourne AM, Cornelius JR, Han X, et al. Burden of general medical conditions among individuals with bipolar disorder. Bipolar Disord. 2004;6(5):368–373. | Mixed inpatient and outpatient sample, inpatient sample not reported separately. |
| Birkenaes AB, Opjordsmoen S, Brunborg C, et al. The level of cardiovascular risk factors in bipolar disorder equals that of schizophrenia: a comparative study. J Clin Psychiatry. 2007;68(6):917–923. | Not psychiatric hopistal inpatients, general University hopistal |
| Hsieh MH, Tang CH, Hsieh MH, et al. Medical costs and vasculometabolic comorbidities among patients with bipolar disorder in Taiwan—a population-based and matchedcontrol study. J Affect Disord. 2012;141(2–3):449–456. | Mixed inpatient and outpatient sample, inpatient sample not reported separately. |
| Sylvia LG, Shelton RC, Kemp DE, et al. Medical burden in bipolar disorder: findings from the Clinical and Health Outcomes Initiative in Comparative Effectiveness for Bipolar Disorder study (Bipolar CHOICE). Bipolar Disord. 2015;17(2):212–223. doi:10.1/bdi.1243 PubMed | Mixed inpatient and outpatient sample, inpatient sample not reported separately. |
| Foley DL, Mackinnon A, Morgan VA, et al. Predictors of type 2 diabetes in a nationally representative sample of adults with psychosis. World Psychiatry. 2014;13(2):176–183. doi:10.102/ | Mixed inpatient and outpatient sample, inpatient sample not reported separately. |
| Perugi G, Quaranta G, Belletti S, et al. General medical conditions in 347 bipolar disorder patients: clinical correlates of metabolic and autoimmune-allergic diseases. J Affect Disord. 2015;170:95–103. doi:10.1016/j.jad.2014.08.052 PubMed | Mixed inpatient and outpatient sample, inpatient sample not reported separately. |

eFigure 4: Forest Plots:

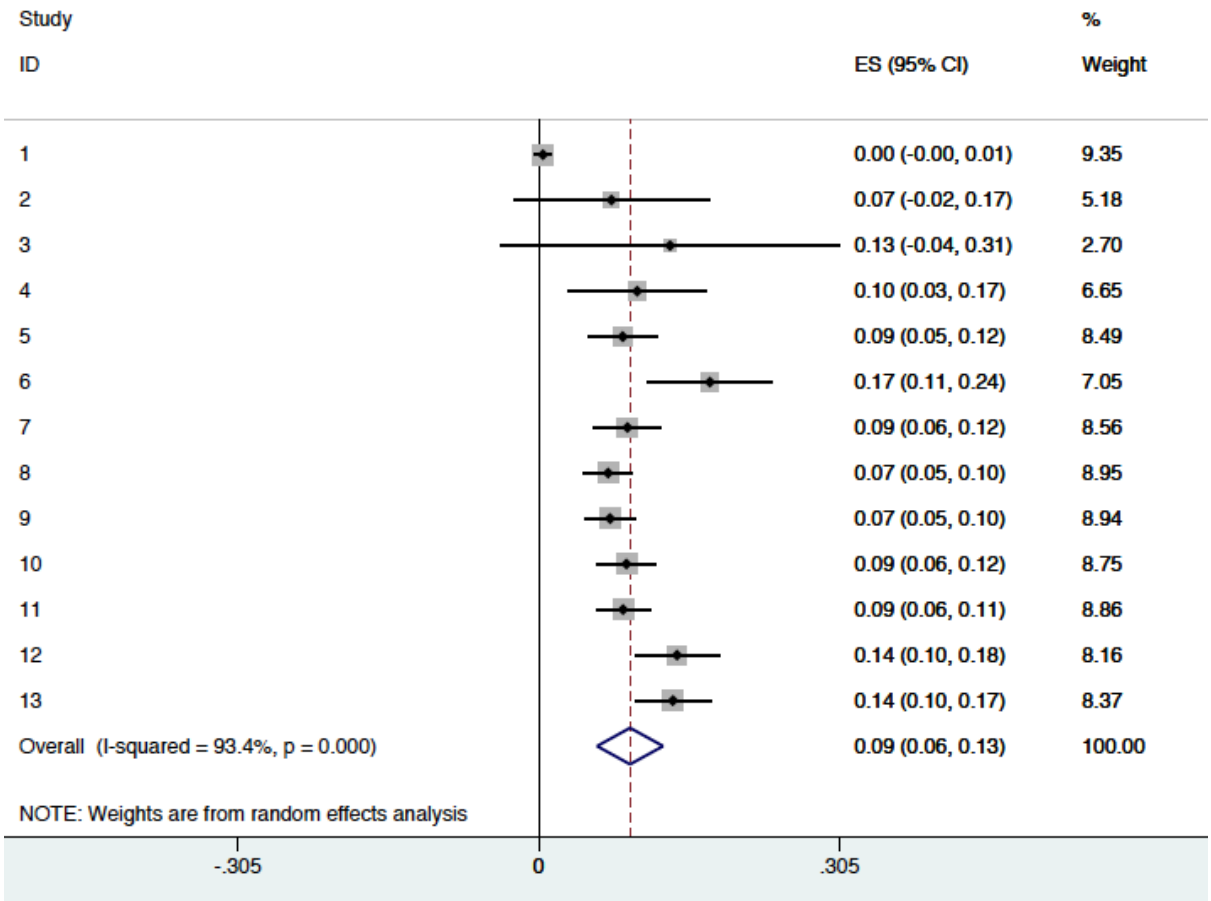
a) Prevalence of unspecified DM



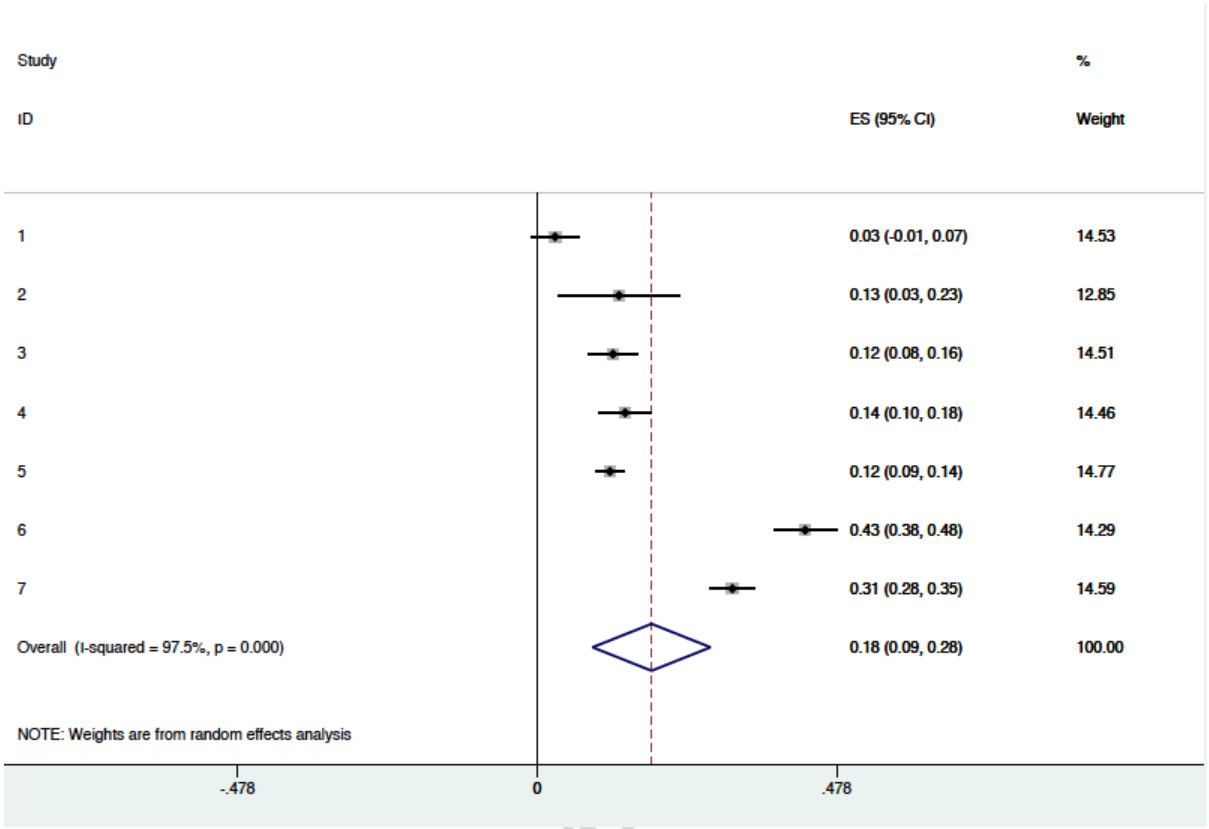

b) Prevalence of T1DM



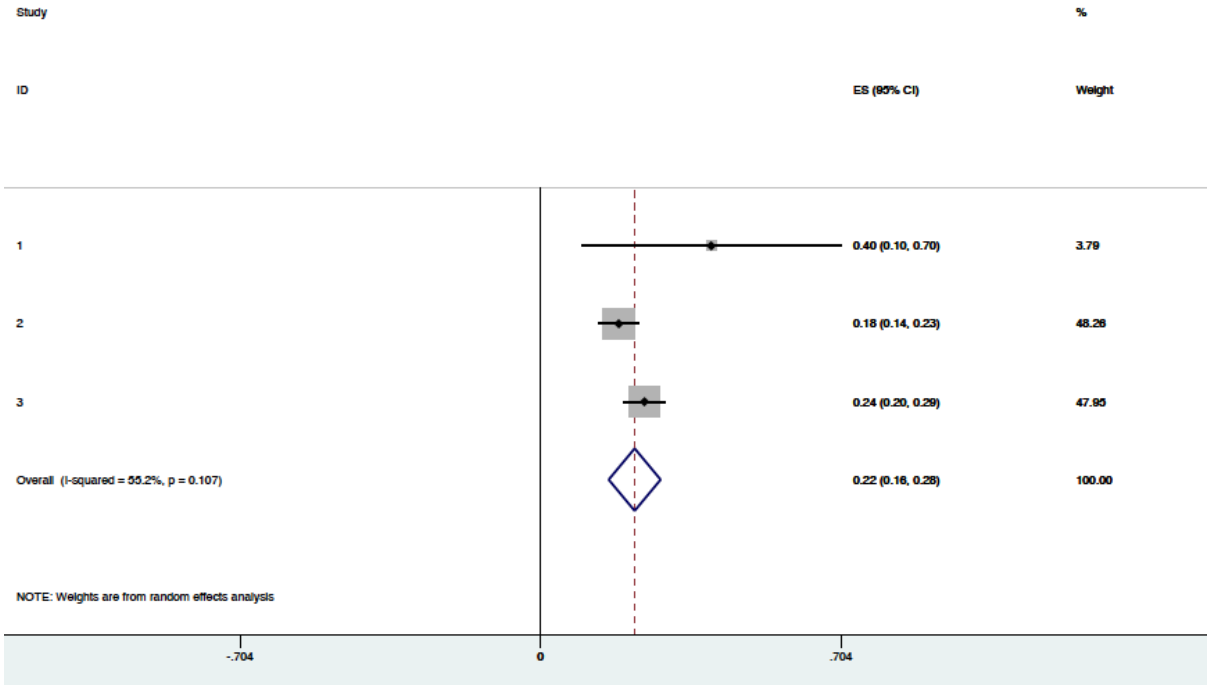

c) Prevalence of T2DM




d) Prevalence of IFG

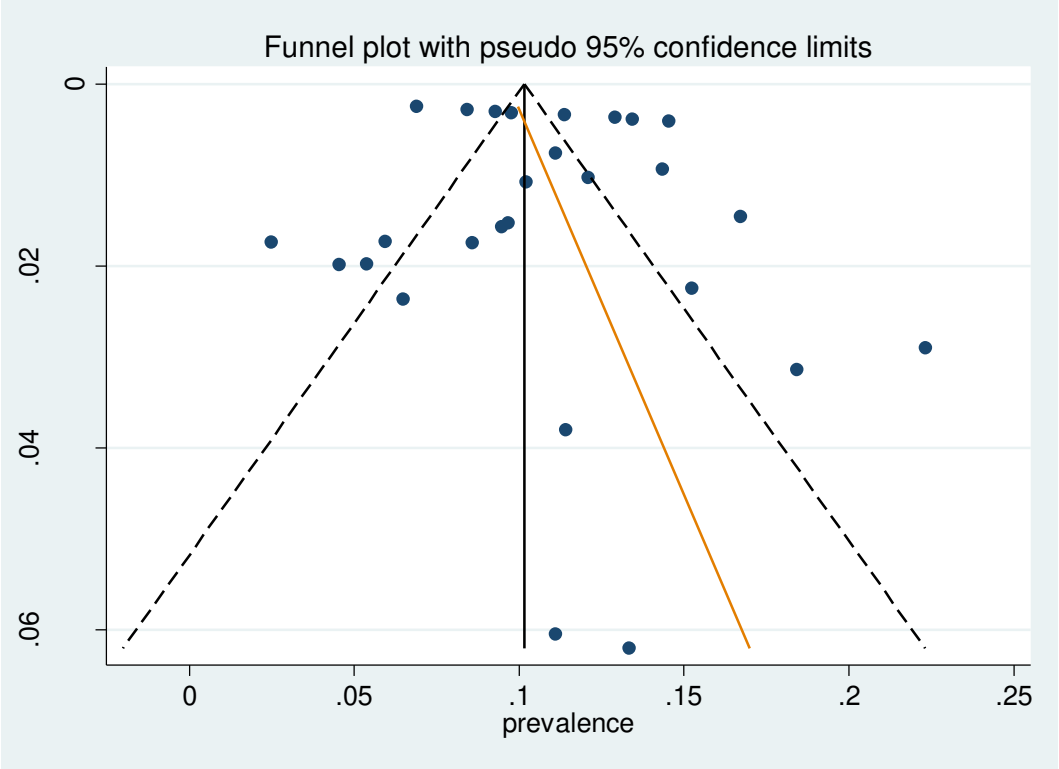



e) Prevalence of IGT

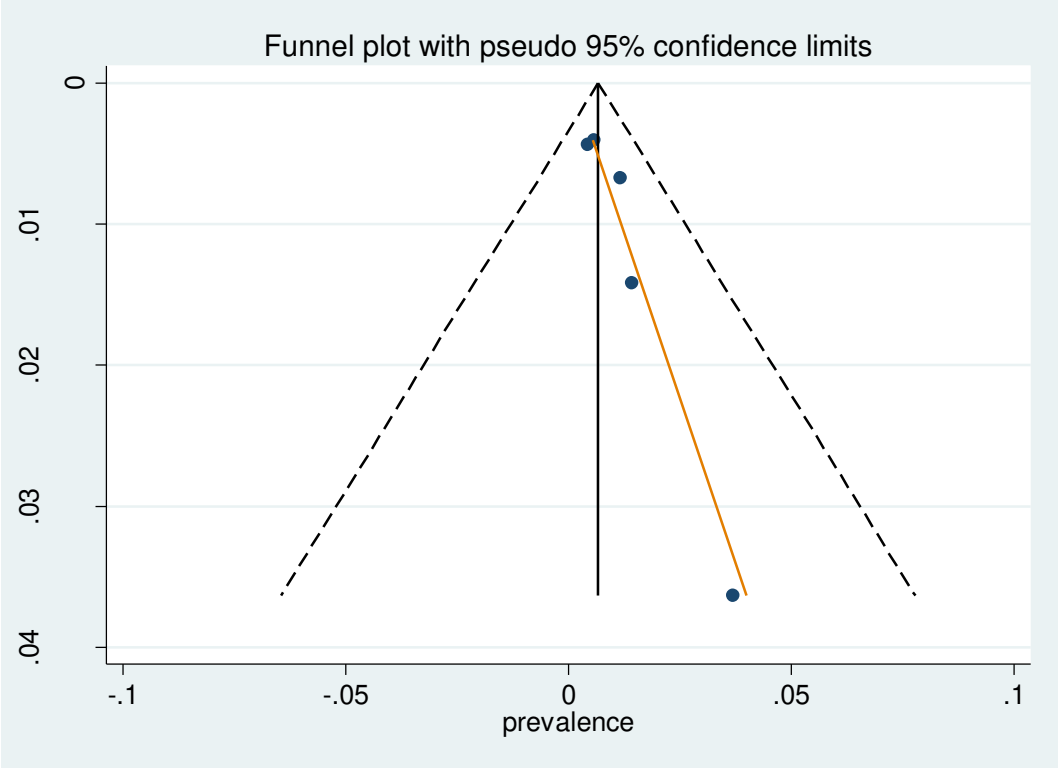


eFigure 5: Funnel Plots:

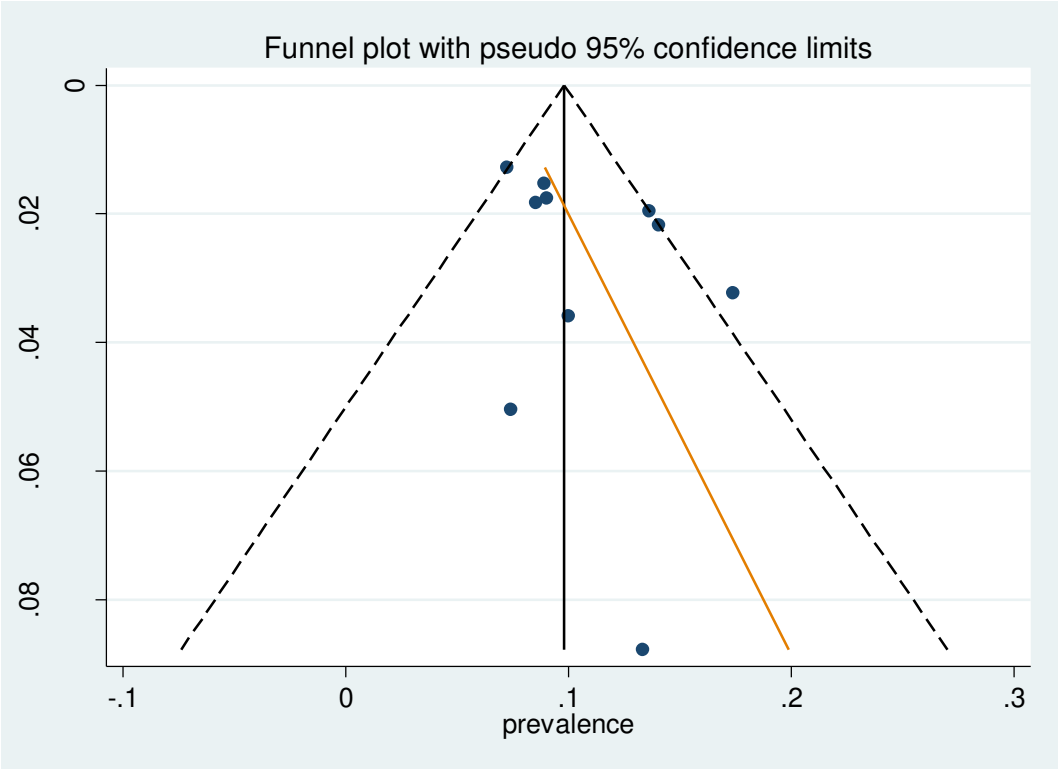
a) Unspecified DM: Eggers Test: No small-study effects; P = 0.397



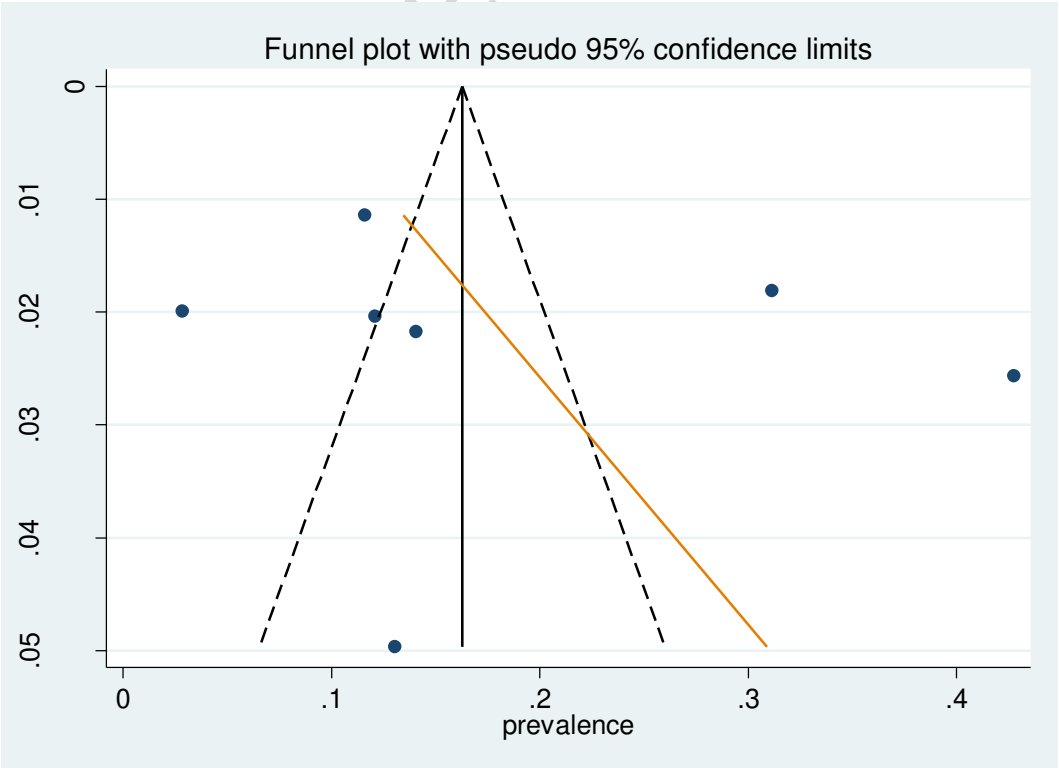

b) T1DM: Eggers Test: No small-study effects P = 0.044



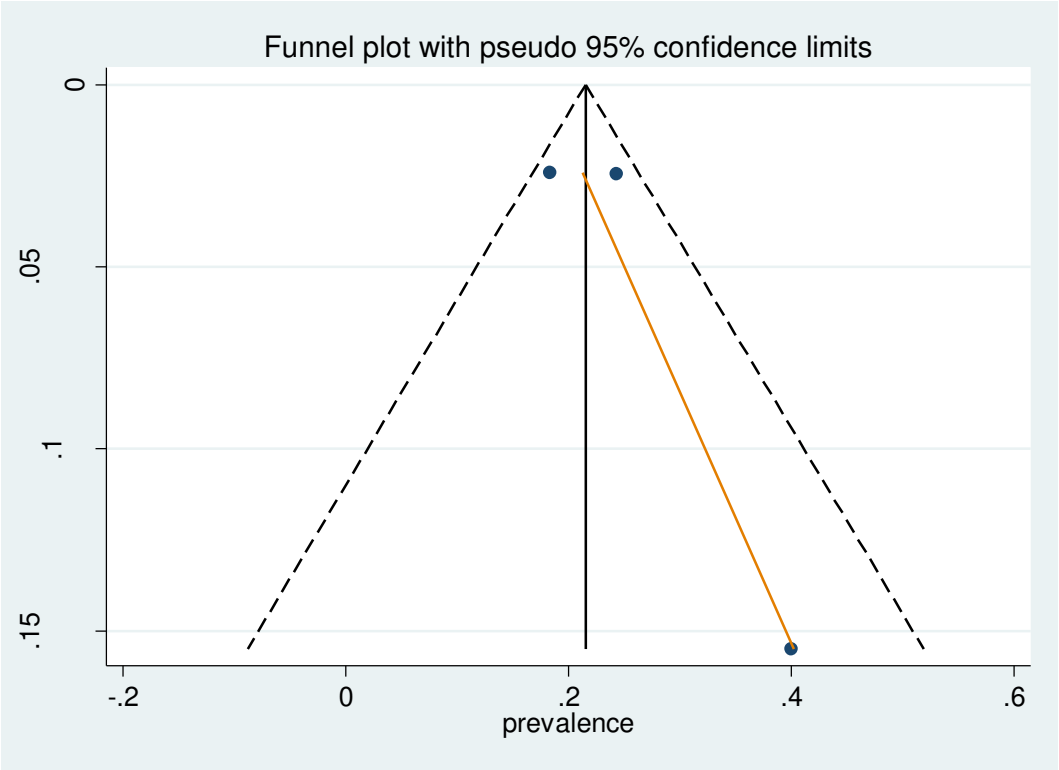

c) T2DM: Eggers Test: no small-study effects P = 0.200




d) IFG: Eggers Test: no small-study effects P = 0.551



e) IGT: Eggers Test: No small-study effects P = 0.611



| 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. | 4 |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | 5 |
| **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. | 5 |
| 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. | 5 |
| 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. | 5 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | Online supplement |
| 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). | 5 |
| 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. | 5 |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | 5/6 |
| 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. | 5 |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | 6 |

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| 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. | 6 |



| 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). | 5/6 |
| Additional analyses | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | 6 |
| **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. | 7 |
| 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. | Table 1 |
| 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). | Table 1 |
| 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. | Table 2 |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | Table 2 |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | Table 2 |
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | 7/ Table 2 |
| **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). | 9 |
| 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). | 9 |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | 9 |
| **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. | 6 |

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