S1. Electronic search criteria

1. cyclothymi$3.ab,ti.

2. (mania or manic or hypomania or hypomanic).ab,ti.

3. (affective adj disorder$1).ab,ti.

4. (mood adj disorder$1).ab,ti.

5. (affective adj psychosis).ab,ti.

6. ((bipolar or (bi adj polar)) adj (disorderS2 or depress$4)).ab,ti.

7. 1 or 2 or 3 or 4 or 5 or 6

8. Alcohol-Induced Disorders.ab,ti.

9. ALCOHOLISM.ab,ti.

10. (drink$ and (misuse or abuse)).ab,ti.

11. (alcohol$ and (misuse or abuse)).ab,ti.

12. (alcohol$ and (dependen$ or addicti$)).ab,ti.

13. Alcohol-Related Disorders.ab,ti.

14. 8 or 9 or 10 or 11 or 12 or 13

15. 7 and 14

16. epidemiology.ab,ti.

17. morbidit$3.ab,ti.

18. prevalence$1.ab,ti.

19. incidence.ab,ti.

20. ((co$1 adj occurrence) or cooccurrence).ab,ti.

21. (comorbidity or (coS1 adj morbidity)).ab,ti.

22. 16 or 17 or 18 or 19 or 20 or 21

23. 15 and 22

S2. List of parameter extracted from each study

* Sampling procedures:
  + Epidemiological, population based studies
  + Clinical and register based studies
* Country
* Setting
  + Academic or tertiary centres
  + General psychiatric services
  + Mixed
* Sample characteristic
  + Inpatients
  + Outpatients
  + Inpatients and outpatients
* Primary diagnosis
* Gender distribution
* Diagnostic instruments, way of ascertainment
  + Structured interview
  + Semi-structured interview
  + Unstructured interview
  + Chart review
* Time window
  + Current
  + In a specific time-frame (usually 12 months)
  + Lifetime (over the whole life-span)
* Outcome/Diagnostic criteria employed:
  + RDC alcoholism (Alc);
  + ICD-8 alcoholism (Alc);
  + ICD-10 alcoholism (Alc);
  + DSM-III alcohol use disorders (AUD): alcohol abuse (AA) or alcohol dependence (AD);
  + DSM-III-R alcohol use disorders (AUD): alcohol abuse (AA) or alcohol dependence (AD);
  + DSM-IV alcohol use disorders (AUD): alcohol abuse (AA) or alcohol dependence (AD).

**S3 Detailed studies description**

**Table S3a**

**Epidemiological studies included in the systematic review**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| FIRST AUTHOR  YEAR OF PUBLICATION | COUNTRY | STUDY NAME | STUDY POPULATION | MULTI-CENTRIC | AGE (YEARS) | NUMBER OF SUBJECTS | RESPONSE RATE | DIAGNOSTIC CRITERIA | PRIMARY DIAGNOSIS | DIAGNOSTIC INSTRUMENT | TIME WINDOW | OUTCOME | CONTROLLED VARIABLES | Years |
| Regier, 1990 (Regier et al., 1990) | US | NIMH Epidemiologic Catchment Area Program (ECA) | C+I | Y | ≥18 | 20291 | 0.76 | DSM-III | Bipolar disorder | DIS | Lifetime | P | Age, gender, race/ethnicity marital status, socio-economic status | 1980-1985 |
| Fogarty, 1994 (Fogarty et al., 1994) | Canada |  | C | N | ≥18 | 3258 | 0.75 | DSM-III | Mania | DIS | Lifetime | P | Age, gender, household size | 1983-1986 |
| Kessler, 1997 (Kessler et al., 1997) | US | National comorbidity survey (NCS) | C + students living in campus group housing | Y | 15-54 | 8098 | 0.82 | DSM-III-R | Mania | Modified CIDI2 | Lifetime | P | Several socio-demographic variables | 1990-1992 |
| Merikangas 2008 (Merikangas et al., 2008), Angst, 1998 (Angst, 1998) | Switzerland | Zurich Cohort Study | C | N | 19-38 | 4547 | NA | DSM-III-R | DSM-IV Hypomania | Non structured + SPIKE3 interview | Lifetime | P | None specified | 1979-1999 |
| 0.69 | 18 years | I |
| Grant, 2005 (Grant et al., 2005), Goldstein, 2006 (Goldstein and Levitt, 2006) | US | National epidemiologic survey on alcohol and related conditions (NESARC) | C, Black and Hispanic oversampled | Y | ≥18, aged 18-24 oversampled | 43093 | 0.81 | DSM-IV | Mania and hypomania | AUDASIS-IV | Lifetime | P | Age, gender, race/ethnicity, region | 2001-2002 |
| 12 months | I |
| Glantz 2009 (Glantz et al., 2009) | US | National comorbidity survey Replication (NCS-R) | C, English speaking | Y | 18-44 | 92822, 3199 | 0.71 | DSM-IV | Bipolar disorder | CIDI3.0 | Lifetime | P | Age, gender, race/ethnicity, education, occupation for the average expected hours of work per week | 2001-2003 |
| 12 months |
| Grant, 2009 (Grant et al., 2009) | US | NESARC, Wave 2 | C, Black and Hispanic oversampled | Y | ≥18, aged 18-24 oversampled | 34653 | 0.87 | DSM-IV | Mania and hypomania | AUDASIS-IV | 12 months | I | Age, gender, race/ethnicity, region, non response, psychiatric diagnosis |  |
| Chou, 2012 (Chou S.P. et al., 2012) | Korea | Korean Epidemiologic Catchment Area | All eligible residents listed in the updated 2000 Population Census | Y | 18-65 | 7867 | 0.80 | DSM-IV | Bipolar disorder | CIDI 2.1 | 12 months | P | Age, gender, race/ethnicity, region | 2000 |

**Abbreviations:**

Diagnostic instrument: AUDASIS-IV: NIAAA alcohol use disorder and associated disabilities interview schedule – DSM-IV version;

CIDI: composite international diagnostic interview; DIS: Diagnostic Interview Schedule; C: community population; I: institutionalized population

N: no, Y: yes

Outcome: P prevalence; I incidence

**Table S3b Clinical studies included in the systematic review**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| FIRST AUTHOR, YEAR OF PUBLICATION | COUNTRY | PRO CAPITA ALCOHOL | RISKY DRINK PATTERN | SETTING | STUDY POPULATION | RECRUITMENT | MULTI CENTRIC | INCLUSION CRITERIA | AGE\* | DIAGNOSTIC CRITERIA | PRIMARY DIAGNOSIS | DIAGNOSTIC INSTRUMENTS | TIME WINDOW | OUTCOME | N | YEARS |
| Baldessarini, 2008 (Baldessarini R.J. et al., 2008) | US | D | B | GP | OUT | S, from Adelphy Bipolar Disorder DSP participants | Y | Only completed questionnaires | 42 (13.8) | DSM-IV | BD-I, BD-II, BD-NOS | Questionnaires from patients and physician | C | AA | 429 | 2005 |
| Bizzarri, 2007 (Bizzarri et al., 2007) | Italy | E | A | A | IN/ OUT | S | N | No unstable neurological and medical diseases or inability to cooperate | 18-60 | DSM-IV | BD-I | SCID-I/P, SCI-SUBS | LT | AUD | 104 | NA |
| Brown, 2005 (26); Kilbourne, 2005 (64) | US | D | B | GP | IN | S, from the VA Cooperative Study #430 | Y | Not acute intoxication, withdrawal, delirium, terminal medical illness, MMSE>26, hospitalised | 46 (10.0) | DSM-IV | BD-I, BD-II | SCID-I | LT, C | AA, AD | 330 | 1997-2003 |
| Cardoso, 2008 (Cardoso et al., 2008) | Brazil | D | C | A | OUT | S | N | Age | ≥18 | DSM-IV | BD-I, BD-II | SCID-I | LT | AA, AD | 178 | 2003-2007 |
| Cassidy, 2001 (Cassidy et al., 2001) | US | D | B | GP | IN | S | N | Accurate report of AUD | 42 (13.7) | DSM-III-R | BD-I | Unstructured check-list | LT | AUD | 392 | 1993-1999 |
| C | 353 |
| Castilla-Puentes, 2012 (18) | Argentina, Brazil, Chile, Colombia, Mexico | D | B/C | GP | E&A | S | Y | Severe illness, acute distress, cognitive disturbance, possible sexual assault, language problem | − | DSM-IV | BD | Unstructured | LT | AUD | 78 |  |
| Cha, 2009 (Cha B. et al., 2009) | South Korea | E | C | NA | OUT | NA | NA | NA | NA | DSM-IV | BD-I, BD-II | SCID-I | LT | AUD | 279 | NA |
| Chengappa, 2000 (Chengappa et al., 2000) | US | D | B | A | OUT | NS, voluntary community registry | N |  | 18-65 | DSM-IV | BD-I, BD-II | SCID-I | LT | AUD | 89 | 1995-NA |
| Dalton, 2003 (Dalton et al., 2003) | Canada | D | B | GP | OUT (almost all) | Members from 305 families recruited for a genetic study | Y | − | 16-67 | DSM-IV | BD-I, BD-II, SAD-BT | SCID-I | LT | AUD | 336 | NA |
| Escamilla, 2002 (Escamilla et al., 2002) | Costa Rica | B | D | GP | IN/ OUT | S | N | Age of onset < 50, bi-lineal Spanish surnames, Costa Rican ancestry | − | DSM-III-R | BD-I | DIGS | LT | AUD |  | NA |
| Frank, 2007 (Frank et al., 2007) | US | D | B | A | IN/ OUT | NS, majority from The Maintenance Therapies in Bipolar Disorder RCT | N | Not chronic AA in the previous 5 years, no rapid cycling, borderline/antisocial personality disorder, unstable severe medical conditions, pregnancy, >2 episode | 18-65 | DSM-IV | BD-I | SADS, SCID-P | LT | AUD | 170 | 1991-2002 |
| Goldberg, 1999 (Goldberg et al., 1999) | US | D | B | GP | IN | S | N | Not concurrent AUD | ~40 | DSM-III-R | BD-I | Retrospective chart review, non structured clinical interview | LT | AUD | 204 | 1991-1995 |
| Gonzales Pinto, 2010 (González-Pinto et al., 2010) | Spain | E | A | GP | OUT | S, from the Vitoria long-term follow-up study | N | BD or treatment > 2 years, family member to participate in the assessments. | 44 (14.6) | DSM-III-R or DSM-IV | BD-I | SCID-P | LT | AUD | 95 | 1994-2004 |
| Hendrick, 2000 (Hendrick et al., 2000) | US | D | B | A | IN | S | N | Only completed questionnaires | ≥18 | DSM-IV | BD-I, BD-II | Structured questionnaire Retrospective chart review | LT | AUD | 123 |  |
| Kawa, 2005 (Kawa I. et al., 2005) | New Zealand | D | B | GP | IN/ OUT | NS, advertisements within mental health services and support organizations, part of South Island Bipolar Study in New Zealand genetic study | Y |  | ≥18 | DSM-IV | BD-I, BD-II | DIGS | LT | AUD | 211 | NA |
| Keck, 1998 (Strakowski et al., 1998); Strakowsky, 1998 (36) | US | D | B | A+GP | IN | S | N | No symptoms due to intoxication or withdrawal, due to medical condition, able to communicate in English, resided within Cincinnati Metropolitan Area | 15-45 | DSM-III-R | BD-I | SCID-P | LT | AUD | 134 | 1992-1995 |
| 12 months | 106 |
| Kessing, 1999 (Kessing, 1999) | Denmark | F | B | A+GP | IN/ OUT | S, national register of psychiatric admissions | Y | At 1st discharge | NA | ICD-8 | Manic-depression | Unstructured | C | Alc |  | 1970-1993 |
| Levander, 2007 (McElroy, 2001); Frye , 2003 (Frye et al., 2003); Leverich, 2002 (Leverich et al., 2002); McElroy, 2001 (McElroy, 2001) | Germany, The Netherlands, US | D | A/B | A+GP | OUT | NA, from The Stanley Foundation Bipolar Network | Y | Not severe current SUD/ current AUD, willingness to perform prospective daily mood charting/to be in treatment | 18-65 | DSM-IV | BD-I, BD-II, BD-NOS. SAD-BT | SCID-P | LT, C | AUD | 350 | NA |
| Lydall, 2011 (Lydall G.J. et al., 2011) | UK | F | C | A | OUT | Genetic study | N | Caucasian British ancestry, with a maximum of one grandparent from Western Europe | NA | RDC | DSM-III-R BD-I | SADS-LT | LT | Alc | 506 | NA |
| Maier, 1995 (Maier W. et al., 1995) | Germany | F | A | A | IN/ OUT | S | N | At least 1 first-degree available | 17-65 | RDC | DSM-III-R BD-I, BD-II | SADS-LA | LT | Alc | 82 | NA |
| Morgan, 2005 (Morgan V.A. et al., 2005) | Australia | E | B | A+GP | IN/ OUT | S, from the Australian National Study of Low Prevalence (Psychotic) Disorders | Y |  | 42-43 | ICD-10 | Bipolar disorder | CIDI | LT | Alc | 112 | 1997-1998 |
| Mueser, 2000 (Mueser et al., 2000) | US | D | B | GP | IN | S, from the Australian National Study of Low Prevalence (Psychotic) Disorders | N | A contact during the previous 6 months with a clinician in the community | ≥18 | DSM-III-R | BD | SCID, CRS | LT | AUD | 73 | NA |
| Nery, 2008 (Nery et al., 2008) | US | D | B | GP | OUT | NS, local media advertisements and flyers in the medical centres | N | No any other axis I diagnosis except anxiety disorders/alcoholism, no significant medical problems, no neurological disorders, age ≥18 | 20 (9.3) | DSM-IV | BD-I | SCID-I/P | LT | AA, AD | 73 | NA |
| Neves, 2009 (Neves et al., 2009) | Brazil | D | C | A | IN/ OUT | S | N | Euthymic based on clinical judgment |  | DSM-IV | BD-I, BD-II | MINI | LT | AUD | 239 | 2005-2007 |
| Nivoli, 2011 (44) Vieta 2001 (Vieta et al., 2001) | Spain | E | A | A+GP | OUT | S | N | Diagnostic concordance between two separate interviewers | ≥18 | DSM-IV-TR | BD | SCID | LT | AUD | 604 | 1992-NA |
| Ongur, 2009 (Öngür et al., 2009) | US | D | B | A+GP | IN/ OUT | NA for an association genetic study | N | No if symptoms due to medical illness or substance abuse, developmental disorder, head trauma | 18-65 | DSM-IV | BD-I with psychotic features | SCID-I | LT | AUD | 92 | NA |
| Ostacher, 2006 (Ostacher M.J. et al., 2006) | US | D | B | A | OUT | S | N | − | 16-74 | DSM-IV | BD | MINI, ADE | LT | AA, AD | 388 | 1999-2004 |
| Ostacher, 2010 (Ostacher et al., 2010); Baldassano, 2006(Baldassano, 2006) | US | D | B | A+GP | OUT | S, from the STEP-BD | Y | Not in need of acute detoxification | >15 | DSM-IV | BD-I, BD-II | MINI, ADE | LT, C | AUD | 2154 | 1999-2005 |
| Pini, 1999 (Pini et al., 1999) | Italy | E | A | A | IN | S | N | No acute intoxication or withdrawal | >16 | DSM-III-R | BD-I with psychotic features | SCID | LT | AA | 125 | NA |
| Salloum, 2002 (Salloum et al., 2002) | US | D | B | A | IN/ OUT | S | N | Acute | ≥18 | DSM-III, DSM-III-R | Bipolar disorder | IEF | C | Alcohol misuse | 256 | NA |
| Suzanne, 2002 (Suzanne I. et al., 2001) | France | F | A | A | IN/ OUT | S | N | − | 17-93 | ICD-10 | Bipolar disorder | Unstructured, Retrospective chart review | C | Alc | 77 | 1998 |
| Slama, 2004 (Slama et al., 2004) | France | F | A | A | IN/ OUT | Part of a genetic study | Y | Euthymic |  | DSM-IV | BD-I, BD-II | DIGS | LT | AA | 307 | 1994-2001 |
| Strakowski, 1996 (Strakowski et al., 1996) 2005 (Strakowski S.M. et al., 2005); Fleck 2006 (Fleck et al., 2006); | US | D | B | A | IN | S, from the University of Cincinnati First-Episode Mania Study | N | No intoxication or withdrawal, 1st hospitalization | 12-45 | DSM-III, DSM-III-R, DSM-IV | BD-I with psychotic features | SCID-I/P | LT | AUD | 144 | 1996-2003 |
| Suominen, 2009 (Suominen et al., 2009) | Finland | F | C | GP | IN/ OUT | S, from the Jorvi Bipolar Study | N | Current episode | 18-59 | DSM-IV | BD-I, BD-II | SCID-I/P | LT | AA, AD | 191 | 2002-2003 |
| Tsai, 1997 (Tsai et al., 1997) | Taiwan | C | B | G | IN/ OUT | S | N | Treated for more than 15y | 33-70 | DSM-III-R | BD | PDA | LT | AUD | 101 | 1995-1996 |
| Tsai, 2012 (Tsai H.-C. et al., 2012) | Taiwan | C | B | A+GP | OUT | S, part of a family study | N | No substance-induced BD |  | DSM-IV | BD-I | CIDI | LT | AUD | 306 | NA |
| Van Roy, 2010 (Van Roy et al., 2010) | Belgium | E | A | GP | OUT | NS, part of a genetic study | Y | In remission | 18-74 | DSM-IV | BD-I | MINI Plus, SCID-I/P | LT | AUD | 69 | NA |
| Winokur, 1998 (Winokur et al., 1998); Winokur, 1994 (Winokur et al., 1994) | US | D | B | A | IN/ OUT | S, part of the NIMH Collaborative Study of the Psychobiology of Depression | Y | IQ ≥ 70, language, white ethnicity, knowledge of one’s biological parents, no secondary to a general medical condition | ≥17 | RDC | BD-I, BD-II, SAD-BT | SADS | LT, C | Alc | 277 | 1978- 1981 |

Abbreviations

Per capita consumption (litres): A <2.5; B 2.5-4.9; C 5-7.4; D 7.5-9.9; E 10-12.4; F **≥** 12.5

Drinking patterns: A Least risky drinking pattern > C Most risky drinking pattern

Setting: A academic or tertiary centre; GP general psychiatric services, general practice

Population: IN inpatients, O outpatiens

Recruitment: S systematic NS non systematic, RCT randomized controlled trials

Time window: LT lifetime, C current

Primary diagnosis: BD: bipolar disorder, BD-I: Bipolar I disorder, BD-II: bipolar II disorder, BD-NOS: bipolar disorder not otherwise specified

Diagnostic instrument: ADE: affective disorder evaluation; DIGS: Diagnostic interview for genetic studies; DIP: diagnostic interview for psychosis; IEF: initial evaluation form; PDA: psychiatrist diagnostic assessment; SCI-SUBS: structured clinical interview for the spectrum of substance use; SCID: Structured Clinical Interview for DSM-IV

Outcome: AA: alcohol abuse, AD: alcohol dependence, AUD: alcohol use disorders, Alc: alcoholism

NA information not available

**S4**

**Figure S4** Part A Freeman-Tukey double arcsine transformed proportions of lifetime AUD among clinical populations (N=31), according to geographical location are included. Part B Gender ratio among participants by geographical location. Gender ratio is here presented as the logarithm of the number of male participants divided by the number of female participants. Information on gender was provided in 20 studies. Part C. Freeman-Tukey double arcsine transformed proportions of lifetime AUD among clinical populations, according to geographical location, only studies with a gender ratio arbitrarily chosen between 0.5-2 are included (N=17).

**Part A**

**ALCMAP**

**Part B**

**SEXRATIO**

**Part C**

**ALCMAP, GENDER RATIO**

**S5 Figure S5**

Lack of effect of secular trends on comorbidity of alcohol use disorders in clinical studies on bipolar disorder. Only studies reporting the years in which the data were gathered were included (N=15). The proportion of participants affected is expressed as the Freeman-Tukey double arcsine transformed proportions of participants with BD affected by lifetime AUD.

SECULARTRENDS19