Prevalence and severity of behavioural symptoms in patients with Korsakoff syndrome and other alcohol-related cognitive disorders: a systematic review

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Objective: Experiences from clinical practice suggest that behavioural symptoms in patients with Korsakoff syndrome (KS) are a frequent problem. Knowledge about behavioural symptoms is important in understanding and managing these symptoms. The aim of this study is to review the prevalence and severity of behavioural symptoms in KS.

Methods: Relevant articles were identified by searching Medline (PubMed), PsycINFO, Embase and CINAHL up to 4 June 2014. Two reviewers independently selected the studies, extracted their baseline data and assessed methodological quality using a standardized checklist.

Results: Fifteen studies fulfilled the inclusion criteria. A diversity of diagnoses was used indicating that KS and other alcohol-related cognitive disorders and terms were used interchangeably. None of the studies were primarily designed to estimate the prevalence or severity of behavioural symptoms in patients with KS. Most studies had serious methodological limitations. The reported prevalence estimates of behavioural symptoms in the included studies varied strongly. Most prevalent were depressive symptoms and disorders (2–50%, median 27%) and agitation and aggression (10–54%, median 27%). None of the reported, mean severity estimates met pathological thresholds. The highest severity estimates were found for apathy.

Conclusions: Good quality studies on behavioural symptoms in patients with KS are lacking. Observational research designed to provide reliable estimates of the prevalence and severity of behavioural symptoms in patients with KS is needed. This could improve understanding and managing these symptoms and help care staff to better support the needs of this specific patient group.

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Introduction

Wernicke–Korsakoff syndrome (WKS) is a symptom complex in which acute Wernicke encephalopathy (WE) proceeds, if untreated, to death in up to 20% of cases, or to the chronic Korsakoff syndrome (KS) in 85% of survivors (Thomson et al., 2012; Thomson and Marshall, 2006; Victor et al., 1989). WKS usually occurs in alcoholics and is caused by malnutrition and the associated thiamine deficiency. Only 20% recover completely and up to 25% do not show any improvement in cognitive functioning and will require long-term institutionalization (Kopelman et al., 2009; Victor et al., 1989). Studies on the prevalence and
incidence of KS are very limited. Ramayya and Jauhar (1997) reported a KS incidence in Glasgow, Scotland, of around 5 per 100,000 between 1990 and 1995. In The Hague, The Netherlands, a KS point-prevalence of 48 per 100,000 inhabitants has been found (Blansjaar et al., 1987). It is estimated that about 1200 patients with KS are residing in Dutch specialist long-term care facilities (LTCFs) (www.korsakovcentrum.nl).

Clear diagnostic criteria for KS are lacking, and KS is often used interchangeably with alcohol-related dementia (ARD) and other alcohol-related cognitive disorders. In the Diagnostic and Statistical Manual of Mental Disorders IV-TR (DSM), KS is classified as ‘alcohol-induced persisting amnestic disorder’ (American Psychiatric Association, 2000). The DSM-5 (2013) categorized KS as ‘alcohol-induced major or mild neurocognitive disorder’. Oslin et al. (1998) proposed clinical criteria for ARD, which may include cases of WKS and also other cases of dementia that appear to be alcohol-related. To reflect the heterogeneity of alcohol-related cognitive disorders, the umbrella terms ‘alcohol-related brain damage’ (ARBD) or ‘alcohol-related brain injury’ are increasingly used (Jauhar and Smith, 2009; Ridley et al., 2013). The varying terminology and conceptualizations of KS, ARD and other alcohol-related cognitive disorders hamper the possibility to identify clearly defined population studies for scientific purposes.

Korsakoff syndrome is characterized by severe deficits in long-term explicit memory, both in anterograde and retrograde memory and is often associated with confabulation. The episodic aspect of memory is specifically affected (Kessels and Kopelman, 2012). Executive functioning is also commonly impaired (Brion et al., 2014; Maharasingam et al., 2013; Van Oort and Kessel, 2009). Overall intelligence, attention and implicit or procedural memory as well as short-term memory usually remain intact (Kessels and Kopelman, 2012; Kopelman, 1995; Kopelman et al., 2009; Oscar-Berman, 2012). A lack of insight into their own disease has also been noticed in clinical practice as a characteristic of KS patients, although this has not been subject to much research (Egger et al., 2002; Thomson et al., 2012; Victor et al., 1989).

In addition to the cognitive deficits, behavioural symptoms, such as aggression and apathy or lack of initiative, have been noticed from the earliest reports of the disease and have also been mentioned in some more recent studies amongst KS patients (Blansjaar et al., 1987; Egger et al., 2002; Gerridzen and Goossens, 2014; Ridley et al., 2013; Thomson et al., 2012; Victor et al., 1989). Sergei S. Korsakoff, a Russian physician who was the first to describe KS, observed that in some KS cases, the predominant features were increased irritability and agitation (Victor and Yakovlev, 1955). In other cases, confusion predominated, either apathetic or associated with excitement (Talland, 1960; Victor et al., 1989). Egger et al. (2002) described patients with KS as follows: ‘They are often very indifferent and are lacking initiative in performing the simplest daily activities. Furthermore, they are very slow, a-practical and apathetic. Lack of insight into oneself and one’s disease often completes the picture’.

Cognitive functioning, in particular memory, and to a lesser extent executive functioning have been studied extensively in patients with KS, yet studies addressing behavioural symptoms in KS patients are scarce. Although evidence is lacking, staff caring for KS patients frequently encounter behavioural symptoms and experience these symptoms as very challenging (Blansjaar et al., 1992; Gerridzen and Goossens, 2014; Victor et al., 1989). A better insight into behavioural disturbances in KS patients may help care staff to understand and manage challenging behavioural symptoms. Therefore, the aim of this systematic review was to describe the prevalence and severity of behavioural symptoms, thereby focusing primarily on KS. However, given the controversy on diagnosis, other alcohol-related cognitive disorders were also taken into consideration, and the term KS was used as an umbrella term.

**Methods**

Data sources and search strategy

This review was conducted according to the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement (Moher et al., 2009). A comprehensive literature search was conducted in the databases Medline (PubMed), PsycINFO, Embase and CINAHL. MeSH terms (PubMed), Thesaurus terms (PsychINFO, Embase, CINAHL) and free text words were used for the search. The search strings combined two separate domains: (1) ‘Korsakoff syndrome’ or ‘alcohol amnestic syndrome’ or ‘Wernicke encephalopathy’; and (2) a wide range of behavioural symptoms. The search period was from inception of the databases up to 4 June 2014. The PubMed search strategy is presented in Appendix I. Comparable search strategies were undertaken in the other databases and are available from the authors. The results of the searches were entered into a Reference Manager database. Duplicates were
removed, and the unique references were included for further selection procedure.

Selection criteria

Articles were included if they met all of the following criteria:

1. The study included patients with a diagnosis of KS. Given the aforementioned diagnostic difficulties, patients with other alcohol-related cognitive disorders such as ARD and ARBD were also included.
2. The study reported primary research data on behavioural symptoms.
3. The study included at least 10 patients.
4. The study was written in the English, Dutch or German language.
5. The study was on humans.

Selection procedure

Titles and abstracts of the references retrieved from the searches were screened by two reviewers independently (I.G. and W.M.) according to the selection criteria. If the reviewers were uncertain about data from the title and abstract, the full text was obtained. After screening the full texts, both reviewers made the definitive selection independently based on the aforementioned selection criteria. Discrepancies between the two selections were discussed until consensus was reached. In case of persistent disagreement, a third reviewer (K.J.) was consulted. In addition to the search strategy, the reference lists of the selected articles were reviewed to identify any relevant publications that had not been found in the searches.

Data extraction and analysis

Full text articles of all selected studies were obtained for further examination. Both reviewers (I.G. and W.M.) extracted data from the included articles independently using a predefined data extraction form. The extracted data included diagnosis and the diagnostic criteria that were used, study design, study setting, study population, inclusion and/or exclusion criteria, method of data collection, behavioural measurement instrument and outcomes. Authors were contacted when insufficient data were provided. Given the heterogeneity of the included studies, we decided not to pool data, but to only provide medians and ranges of the estimates.

Assessment of methodological quality

For this study, both reviewers (I.G. and W.M.) assessed the methodological quality of the included studies using Boyle’s guidelines for evaluating prevalence studies (Boyle, 1998). This checklist comprises eight criteria (Appendix II). Each paper was rated according to these criteria, with one point being given if the criteria were fulfilled. Zero points were allocated if the criteria were not fulfilled, not reported or unclear. Disagreement between reviewers was resolved by discussion or the third reviewer was consulted if required.

Results

Study selection

The search strategy yielded 4163 articles. After removing duplicates, a list of 2967 articles remained of which 2873 were excluded based on title and abstract. After reading the full text of the remaining 94 articles, 13 studies fulfilled the selection criteria (Alderdice et al., 1994; Blansjaar et al., 1992; Cheon et al., 2008; Draper et al., 2011; Egger et al., 2002; Ganzevles et al., 1994; Gerridzen and Goossensen, 2014; Lennane, 1986; Oudman and Zwart, 2012; Plutchik and DiScipio, 1974; Scheipers et al., 2000; Wijnia et al., 2012; Wilson et al., 2012). Two articles, identified through reviewing the reference lists of the selected articles, also met the selection criteria (Ferran et al., 1996; Price et al., 1988). The study of Ferran et al. (1996) was not identified by the electronic search. The study of Price et al. (1988) was not identified because the journal it was published in is not included in the electronic databases. As a result, 15 articles were included for analysis in this review. Figure 1 presents the flow chart of the selection process and reasons for exclusion.

Characteristics of the included studies

Table 1 provides an overview of the characteristics of the 15 included studies. Ten of the studies had a cross-sectional design, and five studies used a longitudinal study design. Only Cheon et al. (2008) and Wilson et al. (2012) reported longitudinal data on behavioural symptoms. Samples sizes ranged from 10 (Alderdice et al., 1994) to 556 patients (Gerridzen and Goossensen, 2014), with a median of 44. Except for one study (Cheon et al., 2008), all studies were conducted in the Netherlands, the UK, the USA and Australia. The studies included were conducted in...
various settings varying from psychiatric hospitals and nursing homes to dedicated ARBD services. Seven of them involved specialist Korsakoff wards of which five are in nursing homes (Blansjaar et al., 1992; Gerridzen and Goossensen, 2014; Oudman and Zwart, 2012; Schepers et al., 2000; Wijnia et al., 2012) and two are in psychiatric hospitals (Egger et al., 2002; Ganzevles et al., 1994), all located in the Netherlands.

Participant exclusion criteria varied, with two studies excluding participants with other DSM-IV Axis I disorders (Cheon et al., 2008) and active psychotic symptoms (Plutchik and DiScipio, 1974). Three studies excluded participants aged 65 years and over (Blansjaar et al., 1992; Ferran et al., 1996; Wilson et al., 2012). The study of Draper et al. (2011) excluded participants younger than 50 years. The alcohol-abstinence period before subjects were assessed varied from ≥7 to ≥60 days or was not reported.

A diversity of diagnoses was used in the included studies, varying from KS, alcohol amnestic disorder, amnestic syndrome due to alcohol, Wernicke–
| Author/year/ country (reference number) | Design | Aim of the study | Study sample and setting | Criteria diagnosis ‘KS’ | Patient characteristics | Abstinence period | Inclusion criteria |
|----------------------------------------|--------|------------------|--------------------------|------------------------|------------------------|------------------|------------------|
| Alderdice et al. (1994), UK (#1) | Cross-sectional, observational | To identify specific subtypes of drinkers on the basis of their neuropsychological performance using cluster analysis. | N = 88 Organic brain damage related to alcohol abuse (hospital), n = 10: • KS, n = 4 • Alcoholic dementia, n = 1 • Non-specific diagnosis of chronic alcoholism, n = 5 Social drinkers, n = 20 Problem drinkers, n = 58 | Not given | Organic brain damage: Gender (M/F) 9/1 Mean age 63, SD ± 12 | Not given | |
| Blansjaar et al. (1992), the Netherlands (#2) | Longitudinal, observational | To define the course of both cognitive and social impairment of patients with alcohol amnestic disorder under different conditions over 3 years. | N = 44 Alcohol amnestic disorder: • Alcohol clinic, n = 14 • Specialist Korsakoff ward nursing home, n = 16 • Sheltered Korsakoff accommodation, n = 14 | DSM-III-R | Alcohol amnestic disorder: Gender (M/F) 29/15 Mean age 52, SD ± 8.1 | ≥1 month | ≤65 years |
| Cheon et al. (2008), Korea (#3) | Longitudinal, trial | To measure the cognitive functions of patients with alcohol-related dementia before (T0) and after 12 weeks (T1) treatment with memantine. | N = 19 Probable alcohol-related dementia (hospital, department of psychiatry) | Oslin | Alcohol-related dementia: Gender (M/F) 18/1 Mean age 57.37, SD ± 7.90 Range 35–66 | ≥60 days | No other DSM-IV Axis I disorder |
| Draper et al. (2011), Australia (#4) | Cross-sectional, observational | To document the prevalence of alcohol-related dementia, Wernicke’s encephalopathy and amnestic syndrome due to alcohol and to describe the principal reasons for admission, medical comorbidities, interventions and outcomes of patients admitted with alcohol-related cognitive impairment. | N = 462 (public hospitals) Alcohol-related dementia, n = 300 Wernicke’s encephalopathy, n = 77 Amnestic syndrome due to alcohol, n = 126 (With overlapping diagnoses) | ICD-10-AM | Alcohol-related dementia: Gender (M/F) 246/54 Mean age 65, SD ± 9.3 Range 50.4–86.6 | Not given | ≥50 years |
| Egger et al. (2002), the Netherlands (#5) | Cross-sectional, observational | To compare MMPI-2 profiles of Korsakoff patients with an alcohol-dependent non-Korsakoff group. | N = 40 (psychiatric hospital) KS, n = 20 (specialist Korsakoff ward) Alcohol-dependent non-Korsakoff, n = 20 (addiction ward) | DSM-IV | KS: Gender (M/F) 18/2 Mean age 49.9, SD ± 9.7 Early-onset dementia: Not given | Dementia-onset ≤65 years |
| Ferran et al. (1996), UK (#6) | Cross-sectional, observational | To describe clinical characteristics and service use of patients with early-onset dementia. | N = 200 Early-onset dementia service: (inpatients and outpatients) | ICD-10 | Early-onset dementia: Not given | Dementia-onset ≤65 years | |
| Author/year/country (reference number) | Design | Aim of the study | Study sample and setting | Criteria diagnosis ‘KS’ | Patient characteristics | Abstinence period | Inclusion criteria |
|--------------------------------------|--------|------------------|--------------------------|--------------------------|------------------------|-----------------|------------------|
| Ganzevles *et al.* (1994), the Netherlands (#7) | Cross-sectional, observational | To compare the effect of specialist Korsakoff wards on cognitive and behavioural aspects of patients with KS in a general psychiatric hospital. | N = 36 Alcohol amnestic disorder (n = 24) Specialist Korsakoff ward psychiatric hospital (K-group), n = 12 General ward psychiatric hospital (P-group), n = 12 Healthy subjects, n = 12 | DSM-III-R | Gender (M/F) | Not given | KS: not given |
| Gerridzen and Goossensen (2014), the Netherlands (#8) | Cross-sectional, observational | To describe baseline characteristic, comorbidity and the use of psychotropic drugs of patients with KS living in LTCFs. | N = 556 KS and other alcohol-related cognitive impairment (specialist Korsakoff wards nursing homes) | Not given | Gender (M/F) | Not given | KS: not given |
| Lennane (1986), Australia (#9) | Longitudinal, observational | Follow-up of a programme for the assessment and rehabilitation of patients with moderate to severe alcohol-related brain damage (=KS). | N = 104 Alcohol-related brain damage (=KS) (Assessment unit for alcohol-related brain damage psychiatric hospital) | Not given | Alcohol-related brain damage: Gender (M/F) | ≥7 days | KS: not given |
| Oudman and Zwart (2012), the Netherlands (#10) | Cross-sectional, observational | To compare different aspects of Quality of Life in patients with KS and compare this with patients with dementia from the same care facilities. | N = 147 KS (specialist Korsakoff ward nursing home), n = 72 Dementia (nursing home), n = 75 | DSM-IV-TR | Gender (M/F) | Not given | KS: not given |
| Plutchik and DiScipio (1974), USA (#11) | Cross-sectional, observational | To compare personality profiles between patients with chronic alcoholism (KS), patients with chronic schizophrenia, and geriatric patients with chronic brain syndrome. | N = 60 Chronic alcoholism with KS (long-term psychiatric patients in hospital), n = 10 Schizophrenia (long-term psychiatric ward), n = 30 Chronic brain syndrome (geriatric ward mental hospital), n = 20 | Not given | KS: Gender (M/F) | Not given | No active psychotic delusions or hallucinations |

(Continues)
Table 1. (Continued)

| Author/year/country (reference number) | Design                  | Aim of the study                                                                 | Study sample and setting                                                                 |
|---------------------------------------|-------------------------|----------------------------------------------------------------------------------|------------------------------------------------------------------------------------------|
| Price et al. (1988), Australia (#12)  | Longitudinal, observational | To assess the characteristics of patients with alcohol-related brain damage who do badly after discharge into the community. | N = 37  
Alcohol-related brain damage (including 21 patients with KS) (psychiatric or rehabilitation units and non-psychiatric facilities)  
Not given  
Alcohol-related brain damage: Gender (M/F) 29/8  
Mean age 55.1  
Range 40–65  
KS: Not given  
Until the sensorium was entirely clear (≥5 days and ≤5 months) |
| Schepers et al. (2000), the Netherlands (#13) | Cross-sectional, observational | To describe characteristics, comorbidity and mortality of patients with KS after admission to a nursing home.  
To examine the symptoms that preceded the KS. | N = 77  
KS or alcohol amnestic disorder (including four patients with alcohol dementia) (specialist Korsakoff ward nursing home)  
DSM-IV  
KS: Gender (M/F) 55/22  
Mean age 53, SD ± 8.9  
Range 34–73  
Not given |
| Wijnia et al. (2012), the Netherlands (#14) | Cross-sectional, observational |  
To examine the symptoms that preceded the KS. | N = 128  
KS (specialist Korsakoff ward nursing home)  
DSM-IV-TR  
KS: Gender (M/F) 105/23  
Mean age 58.7  
Range 33–87  
Not given |
| Wilson et al. (2012), UK (#15) | Longitudinal, observational | To describe the clinical presentation, course and psychosocial outcome of patients with alcohol-related brain damage referred to a tertiary service. | N = 41  
Alcohol-related brain damage (tertiary service for alcohol-related brain damage, in- and outpatients)  
Oslin  
Alcohol-related brain injury: Gender (M/F) 30/11  
Mean age 54  
Range 43–68  
Not given ≤65 years |
Korsakoff disease and WE (Alderdice et al., 1994; Blansjaar et al., 1992; Draper et al., 2011; Egger et al., 2002; Gerridzen and Goossensen, 2014; Lennane, 1986; Plutchik and DiScipio, 1974; Schepers et al., 2000; Wijnia et al., 2012). The diagnoses ARD, ARBD and alcoholic dementia (Alderdice et al., 1994; Cheon et al., 2008; Draper et al., 2011; Ferran et al., 1996; Lennane, 1986; Price et al., 1988; Schepers et al., 2000; Wilson et al., 2012) were also used with overlapping diagnoses. Lennane (1986) used the terms ARBD, alcohol-related amnestic syndrome, KS and WKS interchangeably. These diagnoses were classified using different classification systems such as DSM-III-R (Blansjaar et al., 1992; Ganzevles et al., 1994), DSM-IV (Egger et al., 2002; Schepers et al., 2000), DSM-IV-TR (Wijnia et al., 2012), ICD-10 (Ferran et al., 1996) and ICD-10-AM (Draper et al., 2011). In two studies (Cheon et al., 2008; Wilson et al., 2012), diagnosis was based on criteria according to Oslin et al. (1998). In the study of Oudman and Zwart (2012), diagnosis was based on DSM-IV-TR and criteria according to Kopelman et al. (2009). In five studies, it was unclear how the diagnosis had been established (Alderdice et al., 1994; Gerridzen and Goossensen, 2014; Lennane, 1986; Plutchik and DiScipio, 1974; Price et al., 1988).

In addition to this, patients were at different stages of their disease varying from the onset (Ferran et al., 1996) to the chronic phase (Blansjaar et al., 1992; Gerridzen and Goossensen, 2014; Oudman and Zwart, 2012; Plutchik and DiScipio, 1974; Schepers et al., 2000; Wijnia et al., 2012).

Methodological quality

As shown in Table 2, according to the Boyle criteria (Boyle, 1998), most of the included studies received low ratings for methodological quality. Although the target population was clearly defined in 67% of the studies, most studies did not fulfil or report on the other criteria.

The prevalence of behavioural symptoms

A total of 10 studies reported on the prevalence of behavioural symptoms. Table 3 presents the prevalence estimates reported in the included studies. We distinguished the following categories: psychotic symptoms and disorders, affective symptoms and disorders, agitation and aggression and other symptoms. Two studies reporting on prevalence used an assessment instrument (Price et al., 1988; Wilson et al., 2012). In the other studies, prevalence estimates were nearly all obtained clinically. The time period during which these estimates were measured was often unknown. One study did not report how prevalence was assessed (Lennane, 1986).

Table 2 Methodological quality of the included studies (n = 15) (Boyle, 1998)

| Reference (#) | #1 | #2 | #3 | #4 | #5 | #6 | #7 | #8 | #9 | #10 | #11 | #12 | #13 | #14 | #15 | Total (%) |
|---------------|----|----|----|----|----|----|----|----|----|----|-----|-----|-----|-----|-----|----------|
| 1. Was the target population defined clearly? | 0 | 0 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 0 | 0 | 1 | 1 | 1 | 1 | 66.7 |
| 2. Was probability sampling used to identify potential respondents? | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 3. Did characteristics of respondents match the target population? | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 4. Were the data collection methods of behavioural symptoms standardized? | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 5. Was the measure of behavioural symptoms reliable? | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 6. Was the measure of behavioural symptoms valid? | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 7. Were special features of sampling design accounted for in the analysis? | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 8. Did the reports include confidence intervals for statistical estimates? | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

0, not fulfilled, not reported or unclear; 1, fulfilled.
Table 3  Prevalence estimates of behavioural symptoms amongst Korsakoff patients reported by the included studies (n = 10)

| Behavioural symptom                                      | Study reference | Reported prevalence | Behavioural measure                  | Period of time measured | Assessment instrument | Other* |
|-----------------------------------------------------------|-----------------|---------------------|--------------------------------------|-------------------------|-----------------------|--------|
| Psychotic symptoms and disorders                          |                 |                     |                                      |                         |                       |        |
| Delusions                                                 |                 |                     |                                      |                         |                       |        |
| Hallucinations                                            |                 |                     |                                      |                         |                       |        |
| Cluster alcoholic dementia                               | #1              | 25                  | Unknown                              |                         |                       | 1      |
| Cluster mild alcoholic                                   | #1              | 25                  | Unknown                              |                         |                       | 1      |
| Korsakoff                                                 |                 |                     |                                      |                         |                       |        |
|                                                          | #6              | 0                   | From onset of disease until latest   |                         |                       | 2,5    |
|                                                          |                 |                     | contact with service                 |                         |                       |        |
| Confabulations, hallucinations or delusions               |                 |                     |                                      |                         |                       |        |
|                                                          | #15             | 87                  | Within the first year of referral to | HoNOS-ABI©              |                       |        |
|                                                          |                 |                     | service                              |                         |                       |        |
|                                                          | #15             | 35                  | After an average of 24 month after   | HoNOS-ABI©              |                       |        |
|                                                          |                 |                     | referral to service                  |                         |                       |        |
| Confabulations                                           |                 |                     |                                      |                         |                       |        |
| Confabulations, hallucinations or delusions               |                 |                     |                                      |                         |                       |        |
| Psychosis / hallucinations                               |                 |                     |                                      |                         |                       |        |
| Paranoid psychosis                                       |                 |                     |                                      |                         |                       |        |
| #14                                                       | 7               | Unknown             |                                       |                         |                       |        |
| #9                                                        | 9               | Unknown             |                                       |                         |                       |        |
| #15                                                       | 5               | Unknown             |                                       |                         |                       | 1,4    |
| Mania                                                     |                 |                     |                                      |                         |                       |        |
| #6                                                        | 27              | Unknown             | From onset of disease until latest    |                         |                       | 2,5    |
|                                                          |                 |                     | contact with service                 |                         |                       |        |
| Schizophrenia                                            |                 |                     |                                      |                         |                       |        |
| Depression                                                |                 |                     |                                      |                         |                       |        |
| Cluster alcoholic dementia                               | #1              | 25                  | Unknown                              |                         |                       | 1      |
| Cluster mild alcoholic                                   | #1              | 50                  | Unknown                              |                         |                       | 1      |
| Korsakoff                                                 |                 |                     |                                      |                         |                       |        |
|                                                          | #6              | 36                  | From onset until latest contact with  |                         |                       | 2,5    |
|                                                          |                 |                     | service                              |                         |                       |        |
|                                                          |                 |                     | Around discharge from inpatient care |                         |                       |        |
| Depression or other mental health problems                |                 |                     |                                      |                         |                       |        |
| Major depression                                          | #1              | 25                  | At the start of the study            |                         |                       | 1,2,3,4|
| Depression                                                |                 |                     |                                      |                         |                       |        |
| Major depression                                          | #2              | 2                   | At the start of the study            |                         |                       | 1,2,3,4|
| Major depression                                          | #2              | 5                   | At the start of the study            |                         |                       |        |
| Depression or other mental health problems                |                 |                     |                                      |                         |                       |        |
| Major depression                                          | #9              | 7                   | Unknown                              |                         |                       | Not given|
| Depressive illness                                        |                 |                     |                                      |                         |                       |        |
| Depression or other mental health problems                |                 |                     |                                      |                         |                       |        |
| Major depression                                          | #12             | 46                  | Unknown                              | HAM-D©                  |                       |        |
| Major depression                                          | #14             | 18                  | Unknown                              |                         |                       | 1      |
| Major depression                                          | #15             | 42                  | On referral to the service           |                         |                       | 1,4    |
| Major depression                                          | #15             | 29                  | After an average of 24 months after  | HoNOS-ABI©              |                       |        |
| Major depression                                          | #15             |                     | referral to service                  |                         |                       |        |
| Major depression                                          | #15             |                     | After an average of 24 months after  | HoNOS-ABI©              |                       |        |
| Major depression                                          | #15             |                     | referral to service                  |                         |                       |        |
| Mood disorder                                             | #8              | 32                  | Unknown                              |                         |                       | 1,2    |
| Anxiety disorder                                          | #8              | 5                   | Unknown                              |                         |                       | 1,2    |
| Anxiety disorder                                          | #8              | 6                   | Unknown                              |                         |                       | 1,2    |
| Anxiety                                                  | #6              | 27                  | From onset of disease until latest    |                         |                       | 2,5    |
|                                                          |                 |                     | contact with service                 |                         |                       |        |
| Anxiety and paranoia                                      |                 |                     |                                      |                         |                       |        |
| Chronic                                                  | #13             | 12                  | Diagnosed during admission           | 2, CvZ-V®               |                       |        |
| Acute                                                     | #13             | 14                  | Diagnosed during admission           | 2, CvZ-V®               |                       |        |
| Anxiety disorder                                          | #6              | 5                   | At the start of the study            | 1,2,3,4                |                       |        |
| Agitation                                                 |                 |                     | From onset of disease until latest    |                         |                       | 2,5    |
|                                                          | #6              | 27                  | contact with service                 |                         |                       |        |
| Agitation                                                 |                 |                     | From onset of disease until latest    |                         |                       | 2,5    |
|                                                          | #6              | 27                  | contact with service                 |                         |                       |        |
| Chronic                                                  | #13             | 10                  | Diagnosed during admission           | 2, CvZ-V®               |                       |        |
| Acute                                                     | #13             | 40                  | Diagnosed during admission           | 2, CvZ-V®               |                       |        |
| Aggression and suspiciousness                             | #15             | 20                  | On referral to the service           |                         |                       | 1,4    |
Psychotic symptoms and disorders

As shown in Table 3, nine studies described 15 prevalence estimates on psychotic symptoms and disorders, ranging from 0% (Ferran et al., 1996) to 87% (Wilson et al., 2012) with a median of 10%. Some studies reported on psychiatric disorders such as schizophrenia while others reported on psychotic symptoms such as hallucinations and delusions. The study of Wilson et al. (2012) constituted an outlier with a very high prevalence estimate of 87% of confabulations, hallucinations or delusions in patients with ARBD as measured with the Health of the Nation Outcome Scale-Acquired Brain Injury (HoNOS-ABI) within the first year of referral to the ARBD service.

Affective symptoms and disorders

Nine studies reported 12 prevalence estimates on depressive symptoms and disorders ranging from 2% (Blansjaar et al., 1992; Wilson et al., 2012) to 50% (Alderdice et al., 1994) with a median of 27%. Four studies reported on anxiety and anxiety disorders with five prevalence estimates ranging from 5% (Blansjaar et al., 1992; Schepers et al., 2000) to 27% (Ferran et al., 1996) with a median of 6%. One study reported about anxiety and paranoia with a prevalence estimate of 5% (Blansjaar et al., 1992).

Agitation and aggression

Only three studies reported on agitation and aggression with five prevalence estimates ranging from 10% (Schepers et al., 2000) to 54% (Ferran et al., 1996) with a median of 27%. In one study, a prevalence estimate of 13% was found for aggression and suspiciousness (Schepers et al., 2000).

Other symptoms

Apathy was reported in one study with a prevalence estimate of 8% (Schepers et al., 2000). Disinhibition, insomnia, recklessness and wandering were reported only by Ferran (Ferran et al., 1996) with prevalence estimates of 36%, 18%, 18%, and 27%, respectively.
Table 4  Severity estimates of behavioural symptoms amongst Korsakoff patients reported by the included studies (n=6)

| Reported Severity (score ± SD) | BPRS-E (mean scores) | MMPI-2 (mean T-scores or percentile scores) | NPI* (mean scores) | GOK (mean scores) | QualIDEM (mean scores) |
|-------------------------------|----------------------|------------------------------------------|-------------------|-------------------|------------------------|
|                               | (Blansjaar et al., 1992) | (Egger et al., 2002)                      | (Cheon et al., 2008) |                   | (Oudman and Zwart, 2012) |
| Total score                   | 34.5±0.6             | Clinical scales:                         | T0*:              | Observation:      | Care relationship:      |
| Somatic concern              | 1.6±0.9              | Hypochondriasis                          | Total score:      | 5.6               | 55.2±19.9              |
| Anxiety                       | 1.4±0.7              | Depression                               | Mean score:       | 5.8               | Gregarious:            |
| Depression                    | 1.8±1.1              | Hystera                                 | Delusions:        | 1.0±1.1           | 70.0±22.4              |
| Guilt                         | 1.4±0.5              | Psychopathic deviate                     | Hallucinations:   | 5.0±0.9           | Trustful:              |
| Hostility                     | 1.2±0.4              | Masculinity/ femininity                  | Agitation/         | 0.7±1.6           | Negative affect:       |
| Suspiciousness                | 1.2±0.4              | Paranoia                                | Depression/       | 2.6±2.0           | Poorly controlled:     |
| Guilt                         | 1.2±0.6              | Psychasthenia                           | Anxiety:          | 1.1±1.4           | Controlled:            |
| Grandiosity                   | 3.1±1.1              | Schizophrenia                           | Elation/euphoria: | 0.0±0.0           | Feeling at home:       |
| Hallucinations                | 1.1±0.2              | Hypomania                               | Apathy/indifference: | 3.4±3.2         | Have some-thing to do: |
| Disorientation                | 3.5±1.3              | Social introversion                     | Disinhibition:    | 0.8±1.4           | 55.1±33.8              |
| Conceptual disorganization    | 1.2±0.5              |                                       | Irritability/lability: | 1.0±1.5          | Bias:                  |
| Excitement                    | 1.5±0.6              | Content scales:                         | Aberrant motor    | 0.0±0.0           |                        |
| Motor retardiation            | 1.0±0.1              | Anxiety                                | Sleep/night-time  | 1.7±2.0           |                        |
| Blunted affect                | 1.0±0.1              | Fears                                 | Appetite/eating   | 0.0±0.0           |                        |
| Tension                       | 1.1±0.4              | Obsessiveness                           | 55.6±11.3         |                   |                        |
| Mannerisms and posturing      | 1.2±0.4              | Depression                             | 57.9±10.0         |                   |                        |
| Uncooperativeness             | 1.5±1.0              | Health concerns                        | 52.5±13.9         |                   |                        |
| Emotional withdrawal          | 1.3±0.6              | Bizarre mentation                      | 57.3±10.1         |                   |                        |
| Suicidality                   | 1.4±0.6              | Anger                                 | 52.4±12.2         |                   |                        |
| Self-neglect                  | 1.1±0.2              | Cynicism                                | 59.5±11.7         |                   |                        |
| Bizarre behaviour             | 1.2±0.2              | Antisocial practices                    | 54.3±11.0         |                   |                        |
| Elevated mood                 | 1.1±0.4              | Type A                                 | 53.2±8.9          |                   |                        |
| Motor hyperactivity           | 1.2±0.3              | Low self-esteem                        | 54.5±13.4         |                   |                        |
| Distractibility               | 1.2±0.1              | Anxiety                                | 47.7±10.5         |                   |                        |

(Continues)
### Table 4. (Continued)

| Severity                        | BPRS-E (mean scores) (Blansjaar et al., 1992) | MMPI-2 (mean T-scores or percentile scores) (Egger et al., 2002) | NPI* (mean scores) (Cheon et al., 2008) | GOK (mean scores) (Ganzevles et al., 1994) | QUALIDEM (mean scores) (Oudman and Zwart, 2012) | EPI (mean percentile scores) (Plutchik and DiScipio, 1974) |
|--------------------------------|-----------------------------------------------|------------------------------------------------------------------|----------------------------------------|--------------------------------------------|------------------------------------------------|------------------------------------------------|
| Social discomfort              |                                               |                                                                   |                                  1.7±1.9                                  |                                           |                                           |                                           |
| Family problems                |                                               |                                                                   |                                  0.3±0.7                                   |                                           |                                           |                                           |
| Work interference              |                                               |                                                                   |                                  0.7±1.3                                   |                                           |                                           |                                           |
| Negative treatment indicators  |                                               |                                                                   |                                  0.0±0.0                                   |                                           |                                           |                                           |
| Total score T0*                | 42.2±5.1                                      |                                                                   |                                           |                                           |                                           |                                           |
| Total score T1**               | 35.5±4.9                                      |                                                                   |                                           |                                           |                                           |                                           |
| Scores each item are not given |                                               |                                                                   |                                           |                                           |                                           |                                           |

Abbreviations:

BPRS (-E) = Brief Psychiatric Rating Scale (-Expanded): 18-24 items on psychiatric symptoms, ranging 1 “not present” to 7 “extremely severe”. Score ≥4 = pathologic. Total score 24-168.

MMPI-2 = Minnesota Multiphasic Personality Inventory-2: a variety of scales with a total of 567 items on personality and psychopathology. Individual scores (=T-score) together represent a profile. T-score 40-59 = the mean, T-score ≥ 60 = pathologic.

NPI = Neuropsychiatric Inventory: 12 domains on behaviour symptoms. Frequency (ranging 1 “rarely” to 4 “very often”), severity (ranging 1 “mild” to 3 “severe”) and total score (frequency x severity) can be calculated of each individual symptom. Total score ≥4 indicates the presence of a clinically relevant symptom. Total NPI score 0-144. Possible, the author has recoded the scoring.

GOK = Behaviour Observation Scale for patients with KS: a Dutch, non-validated instrument, that has been used once with 7 subscales and a total of 118 items on behaviour. Max score on subscale = 7 indicating less problem behaviour.

QUALIDEM = Dementia specific quality of life instrument: 9 subscales with a total of 37 items (item ranging 0 “never” to 3 “often”). Scores are linearly transformed from 0 to 100 by the author, higher scores indicate a better quality of life.

EPI = Emotions Profile Index: 8 subscales representing personality traits with a total of 62 items. Mean percentile scores are given. Fiftieth percentile represents the average score for the EPI standardization group (normal population) = *Baseline tests.*

**After 12-week treatment with memantine

*Specialised Korsakoff ward in psychiatric hospital.

General ward in psychiatric hospital.
The severity of behavioural symptoms

A total of six studies reported on the severity of behavioural symptoms. Table 4 presents the severity estimates reported in the included studies. Different assessment instruments were used to measure severity. Of these, only the Neuropsychiatric Inventory (NPI) (Cummings et al., 1994) and the Behaviour Observation Scale for patients with KS (GOK) (Ganzevles et al., 1994) were primarily developed to assess behavioural symptoms. The GOK is a Dutch, non-validated instrument, which has been used once (Ganzevles et al., 1994).

Psychotic symptoms

In the study of Blansjaar et al. (1992), none of the mean scores of the Brief Psychiatric Rating Scale-Expanded (BPRS-E) items on psychotic symptoms were above the pathological thresholds (score of ≥4) (Table 4). The items ‘grandiosity’ and ‘disorientation’ scored highest. Lack of insight into the disease was also covered in the item ‘grandiosity’. Blansjaar et al. (1992) reported that on the item ‘grandiosity’, pathological scores were reached in 47% of all ratings. In the study of Cheon et al. (2008), the NPI domains ‘delusions’ and ‘hallucinations’ scored also low. In this study, the cut-point indicating the presence of clinically relevant symptoms (usually ≥4) was not clear. Also, Egger et al. (2002) found no pathological mean scores on the Minnesota Multiphasic Personality Inventory-2 (MMPI-2). In the study of Plutchik and DiScipio (1974), the mean percentile score on the Emotions Profile Index (EPI) item ‘distrustful’ was also low.

Affective symptoms

Affective symptom scores above pathological thresholds on the individual items of the BPRS-E were mainly observed on the items ‘anxiety’ and ‘depression’ (Blansjaar et al., 1992). However, none of the mean scores of the BPRS-E items on affective symptoms were pathological. In the other studies, mean scores were also low or not pathological.

Agitation and aggression

In the study of Blansjaar et al. (1992), the mean scores on the BPRS-E items ‘hostility’, ‘uncooperativeness’ and ‘tension’ again scored not pathological. The authors noted that the rating on ‘uncooperativeness’ was remarkably higher on patients residing in nursing homes. The NPI domain ‘agitation/aggression’ scored low in the study of Cheon et al. (2008). The mean percentile on the item ‘aggressive’ scored also low on the EPI (Plutchik and DiScipio, 1974).

Other symptoms

Severity estimates on apathy varied widely. In the study of Blansjaar et al. (1992), the item ‘blunted affect’ on the BPRS-E scored low in contrast to the relatively high scores on the NPI item ‘apathy’ (Cheon et al., 2008) and QUALIDEM item ‘having something to do’ (Oudman and Zwart, 2012). In the study of Plutchik and DiScipio (1974), the mean percentile on ‘timid’ on the EPI scored high. Items concerning other behavioural symptoms often scored low on severity.

Discussion

This is the first systematic review of the literature to examine behavioural symptoms in patients with KS. A total of 15 studies reporting on a variety of symptoms were included. Prevalence estimates varied widely across studies. Severity estimates were more consistent and all below pathological thresholds. Because the studies had serious methodological limitations and were very heterogeneous, these results have to be interpreted with caution.

Main findings and interpretation

Low quality and heterogeneity of the included studies

According to guidelines to assess the methodological quality of prevalence studies, the included studies scored poorly on almost all criteria. None of the studies were primarily designed to estimate the prevalence or severity of behavioural symptoms. With regard to the prevalence estimates, the occurrence of behavioural symptoms was mostly reported as a comorbid condition and obtained clinically. The definition of these conditions was often not reported and terms varied from diagnoses based on psychiatric nosology to clinical symptoms across studies. Also, the time period during which the prevalence of the behavioural symptoms was measured was often unknown or differed widely across studies. Regarding the severity estimates, a wide variety of assessment instruments

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was used. Most studies did not provide information on the validity and reliability of the used assessment instruments.

Besides the poor methodological quality, study heterogeneity hindered pooling and interpretation of the data. Most studies involved small, selective samples, which differed widely across studies with respect to many features. For example, a wide variety of definitions of KS and other alcohol-related cognitive disorders was used, based on different classification systems. Also, patients were included from different settings and during different stages of their disease.

Furthermore, inclusion criteria varied across studies. The alcohol abstinence period before subjects were assessed varied or was not reported. Certain alcohol-related cognitive impairment is reversible with abstinence (Gupta and Warner, 2008), and the alcohol abstinence period that is required before KS or other alcohol-related cognitive disorders can be diagnosed has to be at least 6 weeks (Walvoort et al., 2013). When measured in the initial stage of the illness, symptoms like hallucinations, agitation or anxiety could also be attributed to alcohol withdrawal delirium or the acute Wernicke phase (Wijnia et al., 2012). This could have resulted in an overestimation of the prevalence and severity.

In some studies, patients were excluded based on their age. For example, in the study of Draper (Draper et al., 2011), patients were excluded below the age of 50 years, while KS can also appear in this age group. The effect of age on behavioural symptoms in KS patients is unclear. Other studies excluded patients in the presence of active psychotic symptoms, which may lead to underestimation of rates.

Lastly, about half of the studies were on KS patients in institutionalized settings from the Netherlands, which has a long-standing tradition of long-term care for KS patients in specialist Korsakoff wards. This could also influence the generalizability of the results.

Prevalence of behavioural symptoms

In view of the serious methodological limitations, results should be interpreted with caution. Based on the extracted data, depressive symptoms and disorders and agitation and aggression were most prevalent. This was followed by psychotic symptoms and disorders and anxiety and anxiety disorders. The wide range in rates of psychiatric disorders, and psychiatric and behavioural symptoms we found, is probably partly the result of the heterogeneity of the included studies.

Severity of behavioural symptoms

With regard to severity of the behavioural symptoms, scores were all below pathological thresholds. Scores on apathy were highest. The relatively low severity scores conflict with experiences from clinical practice, as reported by several previous studies amongst KS patients (Egger et al., 2002; Gerridzen and Goossens, 2014; Ridley et al., 2013; Thomson et al., 2012; Victor et al., 1989). These authors and other professionals involved in the daily care of KS patients noticed from their own clinical experience that behavioural symptoms occur frequently and are difficult to manage. Gerridzen and Goossens (2014) suggested an overuse of psychotropics to manage challenging behavioural symptoms such as agitation and aggression.

Most of the current knowledge on behavioural symptoms is based on dementia research (Brodaty et al., 2015; Zuidema et al., 2007). Behavioural symptoms in dementia often have serious adverse consequences and cause distress to both patients and their caregivers (Ornstein and Gaugler, 2012; Zwijsen et al., 2014). Moreover, challenging behavioural symptoms in dementia often contribute to institutionalization (Gaugler et al., 2009). Knowledge about behavioural symptoms in dementia has been found important to understand and manage these symptoms. However, behavioural symptoms in KS are hardly studied yet and their consequences for caregivers are unclear. We hypothesize that a better insight in the type of behavioural symptoms that are particularly prevalent and severe in KS patients, could, for example, help care staff to determine which approach or intervention might work best, and ultimately may lower distress to patients and caregivers.

There are several reasons that could explain the discrepancy between the relatively low severity estimates found in our study and the experiences from clinical practice. First, care staff who completed the assessment instruments in most studies could have underestimated the severity of symptoms, because they might have become used to the challenging behaviours. In studies using self-report instruments completed by the patients, such as the MMPI-2 and EPI, the lack of insight into their disease might have resulted in low severity estimates. Lack of insight into disease is another typical characteristic of this patient group that is frequently observed in practice by care staff. Patients often do not have any care demands themselves and are reluctant to receive care, or as Egger states ‘the patient believes that nothing is wrong with him’ (Egger et al., 2002). Little has been reported
on this feature in the included studies, but the two studies that did include items covering this domain presented relatively high scores (on the BPRS-E item ‘grandiosity’ and on the QUALIDEM subscale ‘positive self image’), indicating an impairment in awareness of their disease (Blansjaar et al., 1992; Oudman and Zwart, 2012). Egger et al. (2002) found differences between the severity ratings of care staff and patients for some behavioural symptoms. These findings suggest that lack of insight into the disease affects behaviour in KS patients.

Impaired awareness, or lack of insight into the disease, can be observed in a wide variety of neuropsychiatric disorders (Prigatano, 2014). From research in dementia, it is known that impaired awareness is associated with behavioural symptoms and caregiver burden (Aalten et al., 2006; Starkstein et al., 2010; Turró-Garriga et al., 2013). To the best of our knowledge, the association between impaired awareness and behavioural symptoms in KS patients has not been studied yet.

Furthermore, the studies included were not primarily designed to assess behaviour. Therefore, it is possible that the used assessment instruments did not correctly detect behavioural symptoms.

Next, most patients in the included studies were admitted to specialist psychiatric hospitals or LTCFs, which provide intensive support and structure to patients. Dutch care staff has experienced that these specialist wards seem to have a positive effect on the behaviour of KS patients (Ganzevles et al., 1994; Kopelman et al., 2000; Schepers et al., 2000).

Finally, it could have been possible that the use of psychotropics has influenced the severity of symptoms. On the one hand, psychotropics can mask emotional functioning and therefore have lowered estimates. On the other hand, these drugs could have increased certain symptoms, such as apathy due to side-effects (Zuidema et al., 2006).

Strengths and limitations

This is the first systematic review of the literature on behavioural symptoms in patients with KS. Our review has several strengths. Recommended guidelines from the PRISMA statement were carefully followed. An extensive search strategy was used to identify relevant studies in multiple electronic databases. Two reviewers independently selected the studies and extracted their data. Finally, the methodological quality of included studies was assessed with existing guidelines.

Limitations of this review are related to the poor quality and heterogeneity of the included studies. We provided only medians and ranges of the estimates. As no high-quality observational studies could be identified, we were limited in drawing conclusions about the prevalence and severity of behavioural symptoms in KS patients.

Directions for future research

High-quality observational studies designed to study the prevalence and severity of behavioural symptoms in KS patients are warranted to develop a better insight. The results of our review indicate that defining a target population clearly will be a challenge given the diagnostic difficulties and the heterogeneity of alcohol-related cognitive disorders. Therefore, consensus on diagnostic criteria for KS is strongly recommended. Furthermore, future studies should use an abstinence period of at least 6 weeks before the diagnosis of KS is assessed.

To increase the generalizability of findings, efforts should be made to recruit a sufficiently sized and heterogeneous sample of KS patients. KS patients can be recruited from a variety of settings such as psychiatric hospitals, assisted living facilities and nursing homes. Furthermore, to study behavioural symptoms in KS patients, established, reliable and validated assessment instruments, such as the NPI, should be used. As lack of insight into the disease may underlie behavioural symptoms, it would be interesting if future studies cover this domain in their measurement instruments to enable a better insight in this relationship.

Conclusion

The studies included in this review provide some indication that various behavioural symptoms occur—sometimes very frequently—in KS patients. Good quality studies are needed to acquire reliable estimates of the prevalence and severity of behavioural symptoms in KS. This could improve understanding and managing behavioural symptoms in patients with KS and help both informal and professional caregivers to better support the needs of this specific patient group.

Conflict of interest

None declared.
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Key points
• Good quality observational studies on behavioural symptoms in patients with Korsakoff syndrome are lacking.
• There are indications that various behavioural symptoms occur—sometimes very frequently—in patients with Korsakoff syndrome.
• Prevalence estimates vary widely, likely due to the heterogeneity of the included studies. Severity estimates did not meet pathological thresholds.
• Knowledge about behavioural symptoms in patients with Korsakoff syndrome is important to better understand and manage these symptoms.

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Korsakoff syndrome

Method: #6 AND #7 = #8

Korsakoff syndrome

(#1 OR #2 = #6)

#1 Korsakoff (mesh terms):

"korsakoff syndrome"[mesh] OR "alcohol amnestic disorder"[mesh] OR "wernicke encephalopathy"[mesh]

#2 Korsakoff (tiab or ot):

Korsakoff[tiab] OR Korsakoff[ot] OR alcohol amnestic disorder[tiab] OR alcohol amnestic disorder[ot] OR wernicke encephalopathy[tiab] OR wernicke encephalopathy[ot] OR wernicke-Korsakoff[tiab] OR wernicke-Korsakoff[ot]

Behavioural symptoms

(#3 OR #4 OR #5 = #7)

#3 behavioural symptoms (mesh terms):

"affect"[mesh] OR "affective symptoms"[mesh] OR "aggression"[mesh] OR "apathy"[mesh] OR "awareness"[mesh] OR "anxiety disorders"[mesh] OR "anxiety"[mesh] OR "behaviour"[mesh] OR "behavioural symptoms"[mesh] OR "delusions"[mesh] OR "depression"[mesh] OR "depressive disorder"[mesh] OR "eating disorders"[mesh] OR "emotions"[mesh] OR "euphoria"[mesh] OR "executive function"[mesh] OR "hallucinations"[mesh] OR "irritable mood"[mesh] OR "mood disorders"[mesh] OR "negativeism"[mesh] OR "neuropsychology"[mesh] OR "neuropsychiatry"[mesh] OR "obsessive compulsive disorder"[mesh] OR "obsessive compulsive disorder"[mesh] OR "obsessive hoarding"[mesh] OR "obsessive hoarding"[mesh] OR "personality"[mesh] OR "personality disorders"[mesh] OR "psychiatry"[mesh] OR "psychomotor agitation"[mesh] OR "psychotic disorders"[mesh] OR "sexual behaviour"[mesh] OR "sleep disorders"[mesh] OR "wandering behaviour"[mesh]

#4 behavioural symptoms [tiab] or [ot] (mesh terms):

affect[tiab] OR affect[ot] OR affective sympt*[tiab] OR affective sympt*[ot] OR asymmetric[tiab] OR asymmetric[ot] OR awareness[tiab] OR awareness[ot] OR anxiety[tiab] OR anxiety[ot] OR behaviour[tiab] OR behaviour[ot] OR behavioural sympt*[tiab] OR behavioural sympt*[ot] OR delusion*[tiab] OR delusion*[ot] OR depression[tiab] OR depression[ot] OR depressive disorder*[tiab] OR depressive disorder*[ot] OR eating disorder*[tiab] OR eating disorder*[ot] OR emotion*[tiab] OR emotion*[ot] OR euphoria[tiab] OR euphoria[ot] OR executive funct*[tiab] OR executive funct*[ot] OR hallucination*[tiab] OR hallucination*[ot] OR irritable mood*[tiab] OR irritable mood*[ot] OR mood disorder*[tiab] OR mood disorder*[ot] OR negativeism*[tiab] OR negativeism*[ot] OR neuropsychology*[tiab] OR neuropsychology*[ot] OR psychomotor agitation*[tiab] OR psychomotor agitation*[ot] OR psychotic disorder*[tiab] OR psychotic disorder*[ot] OR sexual behaviour*[tiab] OR sexual behaviour*[ot] OR sleep disorder*[tiab] OR sleep disorder*[ot] OR wandering behaviour*[tiab] OR wandering behaviour*[ot]

#5 behavioural symptoms [tiab] or [ot] (free text words):

affective disorder*[tiab] OR affective disorder*[ot] OR...
agitation[tiab] OR agitation[ot] OR aggressive behav*[tiab] OR aggressive behav*[ot] OR anosognosia[tiab] OR anosognosia[ot] OR behaviour disinhibition[tiab] OR behaviour disinhibition[ot] OR behaviour probl*[tiab] OR behaviour probl*[ot] OR behaviour probl*[tiab] OR behaviour probl*[ot] OR behaviour disorder*[tiab] OR behaviour disorder*[ot] OR behaviour disorder*[tiab] OR behaviour disorder*[ot] OR behaviour sympt*[tiab] OR behaviour sympt*[ot] OR behaviour sympt*[tiab] OR behaviour sympt*[ot] OR dis inhibition[tiab] OR disinhibition[ot] OR eating disturban*[tiab] OR eating disturban*[ot] OR emotional disturb*[tiab] OR emotional disturb*[ot] OR hoarding[tiab] OR hoarding[ot] OR hoarding behav*[tiab] OR hoarding behav*[ot] OR impulsiveness[tiab] OR impulsiveness[ot] OR irritability[tiab] OR irritability[ot] OR neuropsychiatric sympt*[tiab] OR neuropsychiatric sympt*[ot] OR psychiatric sympt*[tiab] OR psychiatric sympt*[ot] OR psychologic sympt*[tiab] OR psychologic sympt*[ot] OR psychosexual behav*[tiab] OR psychosexual behav*[ot] OR psychosis[tiab] OR psychosis[ot] OR psychotic sympt*[tiab] OR psychotic sympt*[ot] OR repetition [tiab] OR repetition[ot] OR repetitive behav*[tiab] OR repetitive behav*[ot] OR restlessness[tiab] OR restlessness[ot] OR screaming[tiab] OR screaming [ot] OR sexual disinhibition[tiab] OR sexual disinhibition[ot] OR sexual dysfunct*[tiab] OR sexual dysfunct*[ot] OR sleep disturb*[tiab] OR sleep disturb*[ot] OR wandering[tiab] OR wandering[ot]

Appendix II: Boyle’s guidelines for evaluating prevalence studies (Boyle, 1998)

Sampling:
1) Was the target population clearly defined?
2) Was probability sampling used to identify potential respondents?
3) Did characteristics of respondents match the target population?

Measurement:
4) Were the data collection methods of behavioural symptoms standardized?
5) Was the measure of behavioural symptoms reliable?
6) Was the measure of behavioural symptoms valid?

Analysis:
7) Were special features of sampling design accounted for in the analysis?
8) Did the reports include confidence intervals for statistical estimates?