

Health problems and care needs in patients with Korsakoff's syndrome: A systematic review

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Accessible summary

What is known on the subject?:

- Patients with Korsakoff's syndrome suffer from a broad range of comorbid somatic and/or psychiatric conditions.
- The various health problems in patients with Korsakoff's syndrome limit their ability to perform daily activities and also negatively affect their social functioning.

What the paper adds to existing knowledge?:

- Patients with Korsakoff's syndrome have complex somatic and psychiatric comorbid conditions co-occurring with behavioural and functional problems. They are compounded by patients' poor self-awareness regarding their health status and functioning.

What are the implications for practice?:

- This review demonstrates that patients with Korsakoff's syndrome should receive integrated care.
- Integrated care for patients with Korsakoff's syndrome should be based on accurate multidimensional and multidisciplinary diagnostics in which nurses and nurse assistants have a prominent role due to their central position in the care process patients with Korsakoff's syndrome.

Abstract

Introduction: The literature shows that Korsakoff's syndrome is associated with a wide range of severe comorbid somatic and psychiatric health problems that lead to care needs in several domains of functioning.

Aim: To provide a comprehensive overview of Korsakoff patients' health conditions and related care needs.

Method: Following the PRISMA guidelines, we searched MEDLINE, PsycInfo, Cochrane Library and CINAHL up to January 2019. After applying our inclusion criteria, two reviewers independently selected the studies, extracted the data and assessed methodological quality.

Results: Twelve articles were included. The commonest somatic comorbid conditions were liver disease, cardiovascular disease, COPD and diabetes mellitus. The commonest psychiatric comorbid conditions were mood disorder, personality disorder and psychotic disorder. Anxiety, aggressive/agitated behaviour, depressive symptoms and care needs in social functioning and (instrumental) activities of daily living were also very commonly reported.

Discussion: In patients with Korsakoff's syndrome, somatic and psychiatric comorbid conditions co-occur with behavioural and functional problems. They are compounded by patients' poor self-awareness regarding their health status and functioning. Adequate responses to their care needs require high-quality integrated care.

Implications for practice: Patients with Korsakoff's syndrome should receive integrated care based on accurate multidimensional and multidisciplinary diagnostics in which nurses have a prominent role.

KEYWORDS

activities of daily living, alcohol amnesic disorder, comorbidity, delivery of health care, integrated, Korsakoff syndrome

1 | INTRODUCTION

Korsakoff's syndrome (KS) is a chronic neuropsychiatric disorder caused by thiamine (vitamin B1) deficiency. It is most common in patients with severe alcohol-use disorders and develops after self-neglect and malnutrition. It follows under-treated or untreated acute Wernicke encephalopathy (Isenberg-Grzeda, Rahane, DeRosa, Ellis, & Nicolson, 2016; Kopelman, Thomson, Guerrini, & Marshall, 2009; Thomson, Guerrini, & Marshall, 2012).

Korsakoff's syndrome is characterized by severe cognitive disorders, such as profound anterograde amnesia, and impaired recall of past events. Apart from memory difficulties, patients with KS frequently suffer a disturbed working memory and difficulties in social cognition (Arts, Walvoort, & Kessels, 2017; Brion, Pitel, & D'Hondt, 2016; Drost, Postma, & Oudman, 2018; Fama, Marsh, & Sullivan, 2004; Kopelman et al., 2009; Oscar-Berman & Marinkovic, 2003; Ridley, Draper, & Withall, 2013). Another characteristic symptom in patients with KS is confabulation, that is "false or erroneous memories arising involuntarily in the context of neurological amnesia" (Kopelman, 2015). Almost all patients with KS have at least some deficits in executive functioning (Maharasingam, Macniven, & Mason, 2013; Moerman-van den Brink et al., 2018; Van Oort & Kessels, 2009), which cause problems with higher-order organization, planning and cognitive flexibility (Van Oort & Kessels, 2009).

A majority of patients with KS are male ($\pm 70\%$), and the disorder is most prevalent in people with alcohol dependence in the 55–65-year age range (Blansjaar, Takens, & Zwinderman, 1992; Gerridzen & Goossensen, 2014; Schepers, Koopmans, & Bor, 2000). A high proportion of patients are unmarried ($\pm 71\%$) and lack any support from family or friends ($\pm 25\%$) (Blansjaar et al., 1992; Gerridzen & Goossensen, 2014; Kopelman et al., 2009; Oslin & Cary, 2003;

Oudman, van Dam, & Postma, 2018; Schepers et al., 2000). Due to their severe cognitive disorders and impaired functioning, up to 25% of them also require long-term institutionalization (Ganzevles, de Geus, Bianca, & Wester, 1994; Kopelman et al., 2009). Research indicates a median survival rate of 8 years after Wernicke encephalopathy (Sanvisens et al., 2017).

Typically, patients with KS suffer from a broad range of health problems. In their descriptive study, Gerridzen and Goossensen (2014) reported that over 50% of Korsakoff patients had at least one comorbid somatic and/or comorbid psychiatric condition. The most commonly reported somatic diseases are diabetes, respiratory diseases, cardiovascular diseases, skin diseases and liver diseases (Draper, Karmel, Gibson, Peut, & Anderson, 2011; Gale, Batty, Osborn, Tynelius, & Rasmussen, 2014; Gerridzen & Goossensen, 2014; Lemke & Schaefer, 2010; Schepers et al., 2000; Wijnia, van de Wetering, Zwart, Nieuwenhuis, & Goossensen, 2012; Wilson et al., 2012). Patients with prolonged alcohol-use disorder are also at greater risk of developing cancers of the head and neck, oesophagus, liver and colorectum (Lee & Hashibe, 2014). The most commonly reported comorbid psychiatric disorders include mood disorders, psychotic disorders and personality disorders (Draper et al., 2011; Gerridzen & Goossensen, 2014; Gerridzen et al., 2018; Jervis & Manson, 2007; Lemke & Schaefer, 2010; Wijnia et al., 2012; Wilson et al., 2012). Various behavioural symptoms of emotional or psychological distress such as agitation, restlessness, disinhibition, and aggression are also reported (Draper et al., 2011; Ferran, Wilson, Doran, & Ghadiali, 1996; Schepers et al., 2000).

It is important to note that the presence of a comorbid condition increases the risk of developing subsequent comorbid conditions (Cohen, 2017). Schepers et al. (2000) showed that, upon admission to a nursing home, patients with KS had an average of 2.9 comorbid

somatic and/or psychiatric conditions, and, over 13-year follow-up, acquired an average of 1.7 new comorbid conditions (Schepers et al., 2000). These multiple comorbid conditions lead to adverse disease outcomes and reduced life expectancy (Sanvisens et al., 2017; Schepers et al., 2000).

Korsakoff patients' various health problems limit their ability to perform daily activities and also negatively affect their social functioning (Blansjaar et al., 1992; Cheon, Park, Joe, & Kim, 2008; Gerritzen et al., 2018). As those responsible for meeting their physical and emotional needs in long-term care facilities, nurses and nurse assistants play an important role in ensuring their function and quality of life (Passalacqua & Harwood, 2012); if these needs are not met, further neuropsychiatric symptoms and discomfort may result (Vasse, Vernooij-Dassen, Spijker, Rikkert, & Koopmans, 2010).

1.1 | Aim

To date, there is no systematic review available providing a comprehensive overview of health problems and associated care needs of patients with KS. Further insight into the prevalent health problems and care needs of this patient group is required for planning and delivering integrated nursing care.

2 | METHODS

2.1 | Study design

We conducted a systematic review of the literature according to the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement (Moher, Liberati, Tetzlaff, Altman, & PRISMA Group, 2010).

2.2 | Data sources and search strategy

With the assistance of a qualified librarian, we performed a comprehensive literature search in MEDLINE (PubMed and EMBASE), PsycInfo, Cochrane Library and CINAHL. The final search was carried out on 1 January 2019. There is little scientific literature on treatment and care for patients with KS. To identify all the articles relevant to this systematic review, we conducted a broad search with all search terms referring to Korsakoff's syndrome, so as to include all available studies from inception. To assess titles and abstracts, articles that seemed relevant to our research question were selected on the basis of our predefined inclusion criteria.

In PubMed, we used the following search terms:

MeSH term:

"Alcohol Amnestic Disorder"

Title/abstract search terms:

"Korsakof* OR Korsakov* OR early onset alcohol dementia* OR alcohol dementia* OR alcohol amnesia* OR alcohol brain damage* OR alcohol cognitive disorder* OR alcohol related cognitive disorder* OR alcohol related brain damage* OR amnestic confabulatory* OR polyneuritic psychos* OR alcohol amnestic disorder* OR alcoholic Korsakoff syndrome* OR alcohol induced amnestic psychos* OR alcohol induced persisting amnestic disorder* OR alcohol induced amnestic psychos* OR alcohol induced dysmnesic psychos* OR alcohol induced dysmnesic syndrome* OR alcohol induced korsakoff syndrome* OR alcohol induced amnestic syndrome* OR alcohol amnestic syndrome* OR alcohol induced persisting dementia* OR alcohol induced major neurocognitive disorder* OR alcohol major neurocognitive disorder* OR Dementia Associated with Alcoholism"

In EMBASE, we used the following search terms:

Emtree:

Korsakoff psychosis

Wernicke Korsakoff syndrome

Title/abstract search terms:

'korsakof*':ab,ti OR 'korsakov*':ab,ti OR 'early onset alcohol dementia*':ab,ti OR 'alcohol dementia*':ab,ti OR 'alcohol amnesia*':ab,ti OR 'alcohol brain damage*':ab,ti OR 'alcohol cognitive disorder*':ab,ti OR 'alcohol related cognitive disorder*':ab,ti OR 'alcohol related brain damage*':ab,ti OR 'amnestic confabulatory*':ab,ti OR 'polyneuritic psychos*':ab,ti OR 'alcohol amnestic disorder*':ab,ti OR 'alcoholic korsakoff syndrome*':ab,ti OR 'alcohol induced persisting amnestic disorder*':ab,ti OR 'alcohol induced amnestic psychos*':ab,ti OR 'alcohol induced dysmnesic psychos*':ab,ti OR 'alcohol induced dysmnesic syndrome*':ab,ti OR 'alcohol induced korsakoff syndrome*':ab,ti OR 'alcohol induced amnestic syndrome*':ab,ti OR 'alcohol amnestic syndrome*':ab,ti OR 'alcohol induced persisting dementia*':ab,ti OR 'alcohol induced major neurocognitive disorder*':ab,ti OR 'alcohol major neurocognitive disorder*':ab,ti OR 'dementia associated with alcoholism':ab,ti

Exclusion:

Sources: *Medline (pubmed)*

In Cochrane, we used the following search terms:

MeSH terms:

MeSH descriptor: [Korsakoff Syndrome] explode all trees

MeSH descriptor: [Alcohol Amnestic Disorder] explode all trees

Title/abstract search terms:

"korsakof*":ab,ti or "korsakov*":ab,ti or "early onset alcohol dementia*":ab,ti or "alcohol dementia*":ab,ti or "alcohol amnesia*":ab,ti or "alcohol brain damage*":ab,ti or "alcohol cognitive disorder*":ab,ti or "alcohol related cognitive disorder*":ab,ti or "alcohol related brain damage*":ab,ti or "amnestic confabulatory*":ab,ti or "polyneuritic psychos*":ab,ti or "alcohol amnestic disorder*":ab,ti or "alcoholic korsakoff syndrome*":ab,ti or

"alcohol induced persisting amnestic disorder*":ab,ti or "alcohol induced amnestic psychos*":ab,ti or "alcohol induced dysmnesic psychos*":ab,ti or "alcohol induced dysmnesic syndrome*":ab,ti or "alcohol induced korsakoff syndrome*":ab,ti or "alcohol induced amnestic syndrome*":ab,ti or "alcohol amnestic syndrome*":ab,ti or "alcohol induced persisting dementia*":ab,ti or "alcohol induced major neurocognitive disorder*":ab,ti or "alcohol major neurocognitive disorder*":ab,ti or "dementia associated with alcoholism":ab,ti

In PsycInfo, we used the following search terms:

Subject Heading:

exp korsakoffs psychosis/ or exp alcoholic hallucinosis/ or exp confabulation/ or exp wernicke's syndrome/Korsakov.mp.

Title/abstract search terms:

("Korsakof*" or "Korsakov*" or "early onset alcohol dementia*" or "alcohol dementia*" or "alcohol amnesia*" or "alcohol brain damage*" or "alcohol cognitive disorder*" or "alcohol related cognitive disorder*" or "alcohol related brain damage*" or "amnestic confabulatory*" or "polyneuritic psychos*" or "alcohol amnestic disorder*" or "alcoholic Korsakoff syndrome*" or "alcohol induced amnestic psychos*" or "alcohol induced persisting amnestic disorder*" or "alcohol induced amnestic psychos*" or "alcohol induced dysmnesic psychos*" or "alcohol induced dysmnesic syndrome*" or "alcohol induced korsakoff syndrome*" or "alcohol induced amnestic syndrome*" or "alcohol amnestic syndrome*" or "alcohol induced persisting dementia*" or "alcohol induced major neurocognitive disorder*" or "alcohol major neurocognitive disorder*" or "Dementia Associated with Alcoholism").ab,ti.

In CINAHL, we used the following search terms:

MeSH terms:

"Alcohol Amnestic Disorder"

Title search terms:

"Korsakof*" or "Korsakov*" or "early onset alcohol dementia*" or "alcohol dementia*" or "alcohol amnesia*" or "alcohol brain damage*" or "alcohol cognitive disorder*" or "alcohol related cognitive disorder*" or "alcohol related brain damage*" or "amnestic confabulatory*" or "polyneuritic psychos*" or "alcohol amnestic disorder*" or "alcoholic Korsakoff syndrome*" or "alcohol induced amnestic psychos*" or "alcohol induced persisting amnestic disorder*" or "alcohol induced amnestic psychos*" or "alcohol induced dysmnesic psychos*" or "alcohol induced dysmnesic syndrome*" or "alcohol induced korsakoff syndrome*" or "alcohol induced amnestic syndrome*" or "alcohol amnestic syndrome*" or "alcohol induced persisting dementia*" or "alcohol induced major neurocognitive disorder*" or "alcohol major neurocognitive disorder*" or "Dementia Associated with Alcoholism"

Abstract search terms:

"Korsakof*" or "Korsakov*" or "early onset alcohol dementia*" or "alcohol dementia*" or "alcohol amnesia*" or "alcohol brain

damage*" or "alcohol cognitive disorder*" or "alcohol related cognitive disorder*" or "alcohol related brain damage*" or "amnestic confabulatory*" or "polyneuritic psychos*" or "alcohol amnestic disorder*" or "alcoholic Korsakoff syndrome*" or "alcohol induced amnestic psychos*" or "alcohol induced persisting amnestic disorder*" or "alcohol induced amnestic psychos*" or "alcohol induced dysmnesic psychos*" or "alcohol induced dysmnesic syndrome*" or "alcohol induced korsakoff syndrome*" or "alcohol induced amnestic syndrome*" or "alcohol amnestic syndrome*" or "alcohol induced persisting dementia*" or "alcohol induced major neurocognitive disorder*" or "alcohol major neurocognitive disorder*" or "Dementia Associated with Alcoholism"

2.3 | Selection criteria

The following inclusion criteria were applied:

- Types of participant: All types of patient with an alcohol-induced neurocognitive disorder. Patients with acute Wernicke encephalopathy were excluded due to the specific nature of care problems associated with this acute delirium.
- Types of outcome measure: Health problems and care needs in patients with KS in all areas of functioning.
- Types of study: Baseline data from experimental research, cohort studies and cross-sectional studies.
- Publication language and date: published in English or Dutch. Since it is not likely that comorbidities in patients with KS change over time, we did not apply publication data restrictions.

2.4 | Selection procedure

On the basis of our inclusion criteria, two authors (M.D. and E.O.) independently screened the articles retrieved from the searches for titles and abstracts. If they were uncertain about selection, the article was included provisionally. Next, all articles selected in this first round of selection were studied in the full-text version. A definitive selection of articles for review was then made. If there was no consensus, discrepancies were discussed until consensus was reached. In addition to the formal search strategy, we also screened the reference lists of the included articles for relevant references. The reference management software RefWorks was used.

2.5 | Data extraction and analyses

A data extraction form was used to extract data from the selected studies. The data extracted included authors, year of publication, country, research design, setting, study sample, data collection methods and findings (see Table 1). If possible, data were pooled

TABLE 1 Study characteristics of the included studies (*n* = 12)

Reference number/ Author/Year/ Country	Research design	Setting/Study sample	Data collection method	Findings
#1. Blansjaar et al. (1992) Netherlands	Longitudinal study	Alcohol rehabilitation clinic, nursing home and sheltered Korsakoff accommodation N = 44 Patients with alcohol amnesic disorder	Proxy ratings of the Brief Psychiatric rating Scale (BPRS), a screening instrument for psychiatric conditions (Overall & Gorham, 1962) Proxy ratings of the Groningen Social Disabilities Schedule (GSDS), a social dysfunctioning scaling instrument (Wiersma, DeJong, & Ormel, 1988)	Behavioural symptoms (BPRS): <ul style="list-style-type: none"> • 22 (50%) disorientation • 21 (47%) grandiosity (KS patients' common lack of perception of their disease and handicapped function was rated on this item) • anxiety • depression Social dysfunction (GSDS): <ul style="list-style-type: none"> • 40 (90%) had disabled social role functioning • Functioning was compromised in complex roles such as the occupational role or role as citizen.
#2. Cheon et al. (2008) Korea	Trial	Hospital N = 19 Patients with alcohol-related dementia (ARD) according to the criteria for ARD established by Oslin et al. (1998)	Clinical data Proxy ratings of the Neuropsychiatric Inventory (NPI), an observation scale for behavioural and psychiatric symptoms (Cummings, 1997) Proxy ratings of the Seoul Activities of Daily Living (S-ADL), an assessment of daily function (Ku et al., 2004) Proxy ratings of the Seoul Instrumental Activities of Daily Living (S-IADL), an assessment of the abilities to perform instrumental and social activities of daily living (Ku et al., 2004)	Somatic conditions: <ul style="list-style-type: none"> • 8 (42%) hepatic diseases • 5 (26%) diabetes mellitus • 4 (21%) hypertension • 3 (15%) respiratory diseases NPI (mean scores, range 0–36): <ul style="list-style-type: none"> • 12.32 total • 3.42 apathy/indifference • 2.58 depression/dysphoria • 1.68 sleep/night-time behaviour • 1.05 anxiety • 1.00 irritability/lability • 0.79 disinhibition • 0.68 agitation/aggression • 0.68 agitation/aggression • 0.58 delusions • 0.58 delusions • 0.21 hallucinations S-ADL (mean score, range 0–24): <ul style="list-style-type: none"> • Mean score in KS was 3.37, reflecting minor issues in basic ADL. S-IADL (mean score, range 0–45): <ul style="list-style-type: none"> • Mean score in KS was 21.74, reflecting issues in instrumental activities of daily living
#3. Draper et al. (2011) Australia	Cross-sectional study	Public and private NWS hospitals N = 462 Patients with alcohol-related dementia, alcohol-related Wernicke's encephalopathy, or alcohol-related amnesic syndrome	ICD10-AM codes (International coding system for diagnoses) (World Health Organization, 2004)	Somatic conditions (N = 881): <ul style="list-style-type: none"> • 397 (45.1%) digestive system <ul style="list-style-type: none"> a. 307 (34.8%) liver disease • 168 (19.1%) injuries <ul style="list-style-type: none"> a. 49 (5.6%) fractures b. 53 (6.0%) head injury • 385 (43.7%) nervous system <ul style="list-style-type: none"> a. 48 (5.4%) epilepsy • 409 (46.4%) symptoms, signs and ill-defined conditions • 361 (41.0%) circulatory system <ul style="list-style-type: none"> a. 13 (1.5%) stroke • 173 (19.6%) respiratory system <ul style="list-style-type: none"> a. 59 (6.7%) lower respiratory tract infection • 353 (40.1%) endocrine, nutritional, metabolic and immune • 47 (5.3%) neoplasms • 99 (11.2%) skin and subcutaneous tissue • 155 (17.6%) genitourinary system <ul style="list-style-type: none"> a. 62 (7.0%) urinary tract infection • 119 (13.5%) infectious diseases <ul style="list-style-type: none"> a. 20 (2.3%) septicaemia Psychiatric conditions (N = 881): <ul style="list-style-type: none"> • 678 (77%) mental and behavioural disorders • 91 (10.3%) psychotic disorder

(Continues)

TABLE 1 (Continued)

Reference number/ Author/Year/ Country	Research design	Setting/Study sample	Data collection method	Findings
#4. Ferran et al. (1996) UK	Cross-sectional study	Hospital-based early-onset dementia service N = 200 Patients with presenile or early-onset dementia. N = 11 Alcohol-related dementia	Aggression was defined as behaviour resulting in or liable to result in actual physical harm to another person (Burns, Jacoby, & Levy, 1990). Anxiety, depression and mania were defined according to ICD guidelines (World Health Organization, 2004) and the rest of the psychiatric symptoms were defined according to Sims (1988) (Sims, 1988).	Behavioural symptoms (N = 11): <ul style="list-style-type: none"> • 10.5 (97%) alcohol misuse • 6 (55%) fire hazard • 6 (54%) aggression • 4.5 (40%) poor mobility • 4 (36%) depression • 4 (36%) disinhibition • 3 (27%) anxiety • 3 (27%) wandering • 3 (27%) agitation • 3 (27%) delusions • 3 (27%) mania • 2 (18%) insomnia • 2 (18%) recklessness • 2 (16%) incontinence
#5. Ganzevles et al. (1994) Netherlands	Cross-sectional study	Korsakoff clinic N = 12 Korsakoff patients	Proxy ratings of the Behavioural Observation List for Korsakov patients (in Dutch; GOK), an experimental observation list for behavioural symptoms (Verstraten, 1988)	GOK (mean scores, range 0–7): <ul style="list-style-type: none"> • 4.68 planning • 4.79 affection/emotion • 4.95 social behaviour • 5.62 perception • 5.65 memory • 5.76 ADL • 6.95 dementia Lower scores (max 7) indicate stronger behavioural problems.
#6. Gerritzen and Goossensen (2014) Netherlands	Cross-sectional study	Ten specialized long-term care units for Korsakoff patients N = 556 Patients with Korsakoff syndrome	Medical chart review	Somatic conditions: <ul style="list-style-type: none"> • 167 (30.0%) COPD • 137 (24.6%) cardiovascular disease • 90 (16.2%) hypertension • 90 (16.2%) diabetes mellitus • 79 (14.2%) cerebrovascular accident • 79 (14.2%) epilepsy • 72 (13.0%) malignancy <ul style="list-style-type: none"> a. 22 (4.0%) malignancy of the oropharynx b. 4 (1.0%) lung carcinoma Psychiatric conditions: <ul style="list-style-type: none"> • 177 (31.8%) mood disorders • 100 (18.0%) psychotic disorders • 84 (15.1%) personality disorders • 52 (9.4%) suicide attempts • 39 (7.0%) other substance use disorders • 37 (6.7%) intellectual Disabilities • 35 (6.3%) anxiety disorders • 11 (2.0%) somatoform disorders • 11 (2.0%) eating disorders

(Continues)

TABLE 1 (Continued)

Reference number/ Author/Year/ Country	Research design	Setting/Study sample	Data collection method	Findings
#7. Gerritzen et al. (2018) Netherlands	Cross-sectional study	Nine specialized long-term care units for Korsakoff patients N = 281 Residents with Korsakoff syndrome	The elderly care physician completed a survey to obtain the medical information Proxy ratings of the Neuropsychiatric Inventory Questionnaire (NPI-Q), an assessment of 12 domains on behavioural and psychological symptoms (Cummings, 1997) Proxy ratings of the Activities of Daily Living Hierarchy Scale (ADLH), which measures performance on 4 self-care tasks (Morris, Fries, & Morris, 1999) Proxy ratings of the Instrumental Activities of Daily Living Performance Scale (I-ADL), which measures performance on 8 instrumental activities of daily living (Morris et al., 1999) Proxy ratings of the Revised Index for Social Engagement (RISE), which measures involvement in social activities (Gerritsen et al., 2008)	Somatic conditions: <ul style="list-style-type: none"> • 109 (38.8%) cardiovascular diseases <ul style="list-style-type: none"> a. 35 (12.5%) cerebrovascular accident b. 33 (11.7%) coronary heart disease c. 19 (6.8%) peripheral artery disease d. 13 (4.6%) cardiac arrhythmia e. 9 (3.2%) chronic heart failure f. 4 (1.4%) valvular disease • 80 (28.5%) COPD • 78 (27.8%) neurological diseases <ul style="list-style-type: none"> a. 43 (15.3%) epilepsy b. 21 (7.5%) traumatic brain injury • 46 (16.4%) diabetes mellitus • 37 (13.2%) hypertension • 33 (11.7%) malignancy Psychiatric conditions: <ul style="list-style-type: none"> • 86 (30.6%) mood disorder • 62 (22.1%) psychotic disorder • 34 (12.1%) personality disorder • 33 (11.7%) obsessive-compulsive disorder <ul style="list-style-type: none"> a. 14 (5.0%) hoarding • 26 (9.3%) anxiety disorder NPI scores (mean scores, range 0–36, n = 281): <ul style="list-style-type: none"> • 8.7 total severity score • 1.4 irritability/lability (n = 192 (68.3%)) • 1.2 agitation/aggression (n = 165 (58.7%)) • 1.0 disinhibition (n = 148 (52.7%)) • 0.9 apathy/indifference (n = 139 (49.5%)) • 0.9 dysphoria/depression (n = 122 (43.4%)) • 0.6 appetite/eating abnormalities (n = 93 (32.6%)) • 0.7 delusions (n = 90 (32.0%)) • 0.5 night-time behaviour disturbance (n = 86 (30.6%)) • 0.6 anxiety (n = 70 (24.9%)) • 0.4 euphoria/elation (n = 70 (24.9%)) • 0.5 aberrant motor behaviour (n = 63 (22.4%)) • 0.2 hallucinations (n = 25 (8.9%)) 138 (49.1%) had at least 1 severe (score = 3) NPS.271 (96.4%) had at least 1 NPS 251 (89.3%) had 2 or more NPS 129 (45.8%) had 5 or more NPS On average, these residents presented with 4.5 NPS. ADLH (mean score, range 0–6, N = 281): Mean score in KS was 1.2, reflecting minor issues in basic ADL. <ul style="list-style-type: none"> • 209 (74.4%) independent or supervision • 72 (25.6%) impaired IADL ordinary housework (N = 278): <ul style="list-style-type: none"> • 64 (22.8%) independent, set-up only, supervision • 214 (76.2%) impaired IADL managing finances (N = 274): <ul style="list-style-type: none"> • 4 (1.4%) independent, set-up only, supervision • 270 (96.1%) impaired More help was required in instrumental activities of daily living. RISE (range 0–6, N = 281): Mean score: 4.1 <ul style="list-style-type: none"> • 56 (19.9%) low engagement (0–2) • 97 (34.5%) moderate engagement (3–4) • 128 (45.6%) high engagement (5–6) 54.4% of the patients had low-to-moderate social engagement.

(Continues)

TABLE 1 (Continued)

Reference number/ Author/Year/ Country	Research design	Setting/Study sample	Data collection method	Findings
#8. Horton et al. (2015) UK	Cross-sectional study	Abstinence-based ARBD residential rehabilitation service for independent living N = 20 Alcohol-related brain damage (ARBD)	Self-ratings of the Profile of Mood States (POMS), which assess mood status on the day of administration only, without relying on intact memory function (McNair, Lorr, & Droppleman, 1971) Self-ratings of the Hospital Anxiety and Depression Scale (HADS), which assess mental health status (Smith & Zigmond, 1994) Self-ratings of the Depression, Anxiety and Stress Scales (DASS), which measures depression, anxiety and physiological stress (Lovibond & Lovibond, 1995) Proxy ratings of the Assessment of Motor and Process Skills (AMPS), a standardized, observational assessment tool comprising a set of universal motor and process-performance skills that can be observed during any activity (Fisher & Jones, 1999)	<p>POMS (mean score, normal range 40–60):</p> <ul style="list-style-type: none"> • 52.85 total mood disturbance (slightly above average) • 51.75 tension-anxiety (slightly above average) • 52.15 depression dejection (slightly above average) • 46.25 anger hostility (below average) • 43.00 vigour activity (below average, indicating that participants reported having less vitality, or energy, than the normative population) • 48.90 fatigue-inertia (slightly below average) • 56.90 confusion-bewilderment (above average, indicating that participants reported a higher level of confusion than the normative average) <p>HADS (mean score, range (0–21):</p> <ul style="list-style-type: none"> • 6.80 anxiety (0–7 is normal) • 4.9 depression - (0–7 is normal) <p>The mean HADS anxiety and depression scores lay within the normal range.</p> <p>DASS (mean score, range 0–34):</p> <ul style="list-style-type: none"> • 11.35 depression - (10–13 is mild) • 8.10 anxiety - (10–13 is mild) • 10.80 stress - (0–9 is normal) <p>The mean anxiety and depression scores on the DASS were in the mild range, and stress was in the normal range</p> <p>AMPS (mean score):</p> <p>(competence cut-off 2, risk zone 1.7–2.3)</p> <ul style="list-style-type: none"> • 1.74 motor ability, indicating a risk of compromised task performance <p>(competence cut-off 1, risk zone 0.7–1.3)</p> <ul style="list-style-type: none"> • 1.03 process ability, indicating a risk for compromised task performance <p>Participants demonstrated increased clumsiness or physical effort, as well as reduced efficiency while performing tasks</p>
#9. (Sanvisens et al. 2017) Spain	Longitudinal study	A tertiary hospital N = 10 Korsakoff syndrome	ICD-9-CM (International coding system for diagnoses) (World & Practice Management, 1998)	<p>Somatic conditions indicating the cause of death in four of the included patients with KS:</p> <ul style="list-style-type: none"> • 1 (10%) died of bacterial infection in the context of pharyngeal carcinoma • 1 (10%) died of respiratory tract infections • 1 (10%) died of liver disease • 1 (10%) died of cancer
#10. Schepers et al. (2000) Netherlands	Cross-sectional study	Nursing home N = 77 Patients with Korsakoff syndrome	ICD-10 (international coding system for diagnoses) (World Health Organization, 2004)	<p>Somatic conditions:</p> <ul style="list-style-type: none"> • 15 (6.5%) cardiovascular system <ul style="list-style-type: none"> a. 6 (7.8%) cerebrovascular accident b. 4 (5.2%) myocardial infarction c. 4 (5.2%) decompensatio cordis • 13 (16.9%) neurological disorders <ul style="list-style-type: none"> a. 4 (5.2%) epilepsy • 9 (11.7%) digestive system <ul style="list-style-type: none"> a. 4 (5.2%) alcoholic liver diseases • 8 (10.4%) endocrine <ul style="list-style-type: none"> a. 8 (10.4%) diabetes mellitus • 4 (5.2%) chronic obstructive pulmonary disease <p>Psychiatric conditions:</p> <ul style="list-style-type: none"> • 21 (27.3%) mental disorders • 19 (24.7%) behavioural disorders <p>Behavioural symptoms</p> <ul style="list-style-type: none"> • 8 (10.4%) restlessness/agitation • 4 (5.2%) nervousness/anxiety

(Continues)

TABLE 1 (Continued)

Reference number/ Author/Year/ Country	Research design	Setting/Study sample	Data collection method	Findings
#11. Wijnia et al. (2012) Netherlands	Cross-sectional study	Nursing home N = 128 Korsakoff patients	Medical chart review	<p>Somatic conditions:</p> <ul style="list-style-type: none"> • 40 (31%) liver cirrhosis/alcoholic hepatitis • 19 (15%) diabetes mellitus • 16 (12%) COPD/pneumonia • 15 (11.5%) stroke/subdural haematoma • 9 (7%) vascular disease, including heart attack • 9 (7%) carcinoma • 7 (5%) pancreatitis • 5 (4%) peptic ulcers/oesophageal stenosis <p>Psychiatric conditions:</p> <ul style="list-style-type: none"> • 23 (18%) depression • 20 (16%) personality disorder • 9 (7%) psychosis/hallucinosi
#12. Wilson et al. (2012) UK	Longitudinal study	A tertiary service designed to cater for patients with severe ARBD. N = 41 Patients with alcohol-related brain damage (ARBD)	Medical chart review Proxy ratings of the Health of the Nation Outcome Scales for Acquired Brain Injury (Honos-ABI), a measure of neuropsychiatric sequelae following brain injury (Fleminger et al., 2005)	<p>Somatic conditions:</p> <ul style="list-style-type: none"> • 8 (20%) unspecified encephalopathy • 10 (24%) convulsions • 8 (20%) peripheral neuropathy • 3 (7%) upper motor neurone signs • 4 (10%) cerebella signs • 4 (10%) history of portal hypertension/oesophageal varices • 4 (10%) deep venous thrombosis • 4 (10%) diabetes • 4 (10%) chronic urinary incontinence/renal disease • 2 (5%) hepatitis C positive • 5 (12%) heart failure/fibrillation • 2 (5%) pancreatic disease • 5 (12%) duodenitis/gastritis/ulcers • 6 (15%) history of significant fractures/dislocations • 9 (22%) cerebral ischaemic/infarcts • 6 (15%) subdurals or significant head trauma or anoxic brain damage • 1 (2%) polydipsia <p>Psychiatric conditions:</p> <ul style="list-style-type: none"> • 17 (41%) depression • 1 (2%) bipolar affective disorder • 1 (2%) hoarding • 1 (2%) post-traumatic stress disorder • 1 (2%) heroin dependency (on methadone) <p>Behavioural symptoms:</p> <ul style="list-style-type: none"> • 8 (20%) aggression <p>Levels of functioning in Activities of Daily Living (range 0–4, N = 17):</p> <ul style="list-style-type: none"> • 2 (12%) do not have any significant problems in self-care (0) • 4 (24%) experience minor problems, with evidence of some disorganization and decline from premorbid levels of functioning (1) • 8 (47%) require prompting in basic self-care and have difficulty in more complex skills (2) • 3 (18%) require supervision and constant prompting in everyday activities and self-care (3–4)

to estimate the overall percentage, range and median of comorbid somatic and psychiatric conditions. The overall estimated percentages were calculated by aggregating the patients with the comorbid condition and determining their proportion in relation to all patients

included in the studies. The range of the comorbid somatic and psychiatric conditions was determined on the basis of the lowest and highest percentages in the studies included, the median being the percentage lying midway between the two.

2.6 | Methodological quality

The methodological quality of each article was evaluated independently by two authors (M.D and E.O.) on the basis of "Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies" (von Elm et al., 2014). The STROBE Statement is a checklist of 22 items that relate to an article's title and abstract (item 1); its introduction (items 2 and 3); its methods (items 4–12); its results (items 13–17); discussion section (items 18–21); and other information, the final item being funding. Discrepancies in scores were discussed by the authors until consensus was reached. To assess the quality of the included articles, we decided that a score of 0–7 items is referred to as low quality, 8–14 items as moderate quality and 15–22 items as high quality, see Gonzalez-Alzaga et al. (2014) for a more elaborate description of this rating system (Gonzalez-Alzaga et al., 2014).

3 | RESULTS

Our search generated 5,252 titles. After their titles and abstracts had been screened, 34 articles met the inclusion for further assessment. After the full-text version of these articles had been assessed, 12 articles met the inclusion criteria and were eligible for inclusion in this review (see Figure 1).

3.1 | Study characteristics

Table 1 provides an overview of the main characteristics of the studies included. Almost all of the studies had been conducted in Europe (6 Netherlands, 3 UK and 1 Spain) except for that by Cheon

et al. (2008) (Korea) and Draper et al. (2011) (Australia). Eight studies had used a cross-sectional study design and three had used a longitudinal study design. Only Cheon et al., 2008 had conducted a randomized controlled trial, whose baseline data were used for this review. The included studies were published between 1992 and 2018.

Samples sizes ranged from 10 patients (Sanvisens et al., 2017) to 881 (Draper et al., 2011), with a median of 42.5. Six studies referred to the Korsakoff syndrome patient group as patients with "Korsakoff syndrome," three studies referred to them as patients with "alcohol related dementia," two as patients with "alcohol-related brain damage" and one as patients with "alcohol amnesic disorder."

The studies were conducted in various settings. Thirty-three per cent of the studies were conducted in a hospital setting, 25% in a specialized Korsakoff setting and 17% in a nursing home. Other settings were a community service and an independent living facility (both 8%). One study was conducted in a combination of settings (Blansjaar et al., 1992).

The problems reported were related to somatic comorbid conditions, psychiatric comorbid conditions, behavioural symptoms and functional problems. Two studies reported on all four of these problems (Gerridzen et al., 2018; Wilson et al., 2012), three reported on somatic and psychiatric comorbid conditions (Draper et al., 2011; Gerridzen & Goossensen, 2014; Wijnia et al., 2012), two reported on behavioural symptoms and functional problems (Blansjaar et al., 1992; Horton, Duffy, & Martin, 2015), two reported only on behavioural symptoms (Ferran et al., 1996; Ganzevles et al., 1994), one reported on somatic and psychiatric comorbid conditions and behavioural symptoms (Schepers et al., 2000), one reported on somatic and psychiatric comorbid conditions and functional problems (Cheon et al., 2008) and one only on somatic comorbid conditions (Sanvisens et al., 2017).

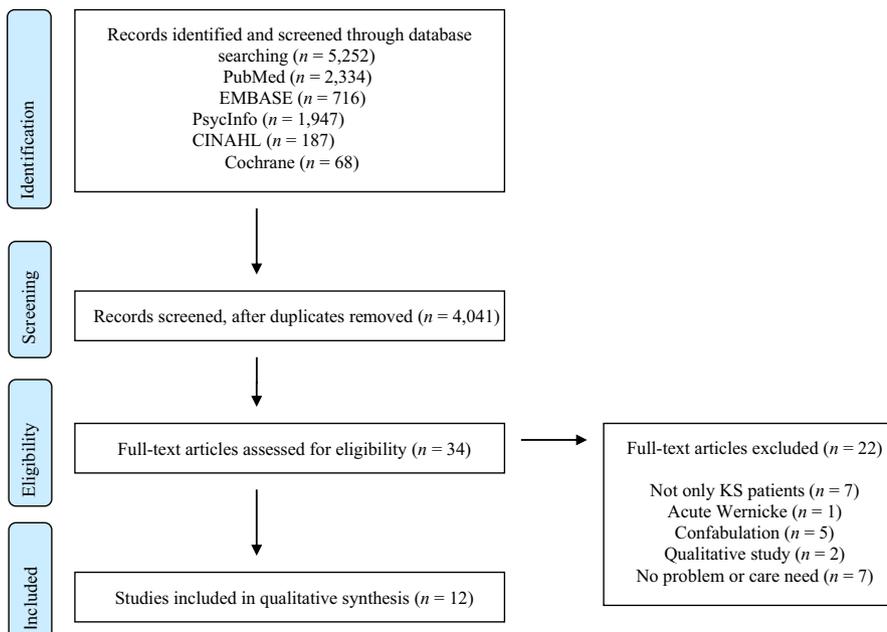


FIGURE 1 Flow chart of the literature search and selection phase including reasons for exclusion

3.2 | Methodological quality

Table 2 presents an overview of the quality scores indicated by the STROBE instrument. Based on these quality assessment scores, we may conclude that the quality of the included articles was moderate to high.

3.3 | Somatic comorbid conditions in Korsakoff syndrome

Table 3 presents an overview of the somatic comorbid conditions in patients with KS. Its presentation of data is in accordance with the ICD-10 categories (World Health Organization, 2004). To provide overall estimates of the occurrence of the somatic conditions in patients with KS, we pooled the individual conditions reported in four or more studies. These overall estimates showed that 31.3% of

the patients suffered from liver disease, 25.9% had cardiovascular disease, 25.6% COPD, 15.6% diabetes mellitus, 15.1% hypertension, 10% epilepsy, 8.0% had had a cerebrovascular accident, and 3.3% had a malignancy.

3.4 | Psychiatric comorbid conditions in Korsakoff syndrome

Table 4 presents an overview of the psychiatric comorbid conditions in patients with KS. For this, we transposed the data from the included studies into the corresponding DSM-5 categories (American Psychiatric Association, 2013). The three most reported mental disorders were psychotic disorders, mood disorders and personality disorders; to calculate an overall estimate, they were pooled. Nearly a third of all patients (30.1%) had mood disorders, 14.3% had personality disorders, and 14.2% had psychotic disorders.

TABLE 2 Quality appraisal of the included studies ($n = 12$) (von Elm et al., 2014)

Reference #	#1	#2	#3	#4	#5	#6	#7	#8	#9	#10	#11	#12
Title and abstract												
1. Title/abstract	1	1	-	-	-	1	1	1	1	-	1	1
Introduction												
2. Background	1	1	1	1	1	1	1	1	1	1	1	1
3. Objectives	1	1	1	-	-	-	1	1	1	1	1	1
Methods												
4. Study design	1	1	-	-	-	1	1	1	1	-	-	-
5. Setting	1	-	1	1	1	1	1	-	1	1	1	1
6. Inclusion criteria	-	1	1	1	1	1	1	1	1	1	1	1
7. Variables	-	-	1	1	1	1	1	1	-	1	1	1
8. Data sources	-	1	1	-	-	1	1	1	-	1	1	-
9. Bias	-	-	-	-	-	-	-	-	-	-	-	-
10. Study size	1	1	1	1	1	1	1	1	1	1	1	-
11. Quantitative variables	1	-	-	-	-	1	1	-	1	1	-	-
12. Statistical methods	-	-	-	-	-	1	1	-	1	-	-	-
Results												
13. Participants	1	1	-	1	-	1	1	1	1	1	1	1
14. Descriptive data	1	-	-	1	1	1	1	1	1	1	1	1
15. Outcome data	1	1	1	1	1	1	1	1	1	1	1	1
16. Main results	1	1	1	1	1	1	1	1	1	-	1	1
17. Other analysis	1	-	1	1	-	1	-	1	-	-	1	1
Discussion												
18. Key results	1	1	1	1	1	1	1	1	1	1	1	1
19. Limitations	-	1	1	-	-	1	1	1	1	-	1	1
20. Interpretation	1	1	1	1	1	1	1	1	1	1	1	1
21. Generalizability	-	1	-	-	-	-	-	1	-	1	-	1
22. Funding	-	1	1	-	-	1	1	1	1	-	1	1
Total score out of 22	14	15	14	12	10	19	19	18	17	14	17	16

1 = fulfilled; - = not fulfilled, not reported or unclear.

TABLE 3 Somatic comorbid conditions in Patients with Korsakoff's syndrome

ICD-10	Reference	Diagnosis	N (%)	Range (%)	Average (%)	Overall total (n/N)			
Certain infectious and parasitic diseases	#3	Infectious diseases	119 (13.5%)						
	#3	Septicaemia	20 (2.3%)						
	#9	Cause of death: bacterial infection	1 (10%)						
Neoplasms	#3	Neoplasms	47 (5.3%)	5.3%–13.0%	9.20%	162/1856 (3.3%)			
	#6	Malignancy	72 (13.0%)						
	#7	Malignancy	33 (11.7%)						
	#9	Cause of death: cancer	1 (10%)						
	#11	Carcinoma	9 (7%)						
	#6	Malignancy of the oropharynx	22 (4.0%)						
	#6	Lung carcinoma	4 (1.0%)						
Diseases of the blood and blood-forming organs, and certain disorders involving the immune mechanism									
Endocrine, nutritional and metabolic diseases	#3	Endocrine, nutritional, metabolic and immune	353 (40.1%)						
	#10	Endocrine	8 (10.4%)						
	#2	Diabetes mellitus	5 (26%)	10%–26%	18%	172/1102 (15.6%)			
	#6	Diabetes mellitus	90 (16.2%)						
	#7	Diabetes mellitus	46 (16.4%)						
	#10	Diabetes mellitus	8 (10.4%)						
	#11	Diabetes mellitus	19 (15%)						
	#12	Diabetes mellitus	4 (10%)						
Mental and behavioural disorders									
Diseases of the nervous system	#3	Nervous system	385 (43.7%)						
	#7	Neurological diseases	78 (27.8%)						
	#10	Neurological disorders	13 (16.9%)						
	#3	Epilepsy	48 (5.4%)	5.2%–24%	14.60%	184/1836 (10%)			
	#6	Epilepsy	79 (14.2%)						
	#7	Epilepsy	43 (15.3%)						
	#10	Epilepsy	4 (5.2%)						
	#12	Convulsions	10 (24%)						
	#12	Unspecified encephalopathy	8 (20%)						
	#12	Peripheral neuropathy	8 (20%)						
	#12	Upper motor neurone signs	3 (7%)						
Diseases of the eye and adnexa									
Diseases of the ear and mastoid process									
Diseases of the circulatory system	#3	Circulatory system	361 (41.0%)						
	#6	Cardiovascular disease	137 (24.6%)	6.5%–38.8%	22.70%	270/1042 (25.9%)			
	#7	Cardiovascular diseases	109 (38.8%)						
	#10	Cardiovascular system	15 (6.5%)						

(Continues)

TABLE 3 (Continued)

ICD-10	Reference	Diagnosis	N (%)	Range (%)	Average (%)	Overall total (n/N)
	#11	Vascular disease, including heart attack	9 (7%)			
	#7	Coronary heart disease	33 (11.7%)			
	#10	Myocardial infarction	4 (5.2%)			
	#2	Hypertension	4 (21%)	10%–21%	15.50%	135/897 (15.1%)
	#6	Hypertension	90 (16.2%)			
	#7	Hypertension	37 (13.2%)			
	#12	History of portal hypertension/oesophageal varices	4 (10%)			
	#3	Stroke	13 (1.5%)	1.5%–22%	11.80%	157/1964 (8.0%)
	#6	Cerebrovascular accident	79 (14.2%)			
	#7	Cerebrovascular accident	35 (12.5%)			
	#10	Cerebrovascular accident	6 (7.8%)			
	#11	Stroke/subdural haematoma	15 (11.5%)			
	#12	Cerebral ischaemic/infarcts	9 (22%)			
	#7	Peripheral artery disease	19 (6.8%)			
	#7	Cardiac arrhythmia	13 (4.6%)			
	#10	Decompensatio cordis	4 (5.2%)			
	#7	Chronic heart failure	9 (3.2%)			
	#12	Heart failure/ fibrillation	5 (12%)			
	#7	Valvular disease	4 (1.4%)			
	#12	Deep venous thrombosis	4 (10%)			
Diseases of the respiratory system	#3	Respiratory system	173 (19.6%)			
	#2	Respiratory diseases	3 (15%)			
	#3	Lower respiratory tract infection	59 (6.7%)			
	#9	Cause of death: respiratory tract infection	1 (10%)			
	#6	COPD	167 (30%)	5.2%–30%	17.60%	267/1042 (25.6%)
	#7	COPD	80 (28.5%)			
	#10	COPD	4 (5.2%)			
	#11	COPD/pneumonia	16 (12%)			
Diseases of the digestive system	#3	Digestive system	397 (45.1%)			
	#10	Digestive system	9 (11.7%)			
	#2	Hepatic diseases	8 (42%)	5%–42%	23.50%	362/1156 (31.3%)
	#3	Liver diseases	307 (34.8%)			
	#9	Cause of death: liver disease	1 (10%)			
	#10	Alcoholic liver diseases	4 (5.2%)			
	#11	Liver cirrhosis/alcoholic hepatitis	40 (31%)			
	#12	Hepatitis C positive	2 (5%)			
	#11	Pancreatitis	7 (5%)			
	#12	Pancreatic disease	2 (5%)			

(Continues)

TABLE 3 (Continued)

ICD-10	Reference	Diagnosis	N (%)	Range (%)	Average (%)	Overall total (n/N)
	#11	Peptic ulcers/oesophageal stenosis	5 (4%)			
	#12	Duodenitis/gastritis/ulcers	5 (12%)			
Diseases of the skin and subcutaneous tissue	#3	Skin and subcutaneous tissue	99 (11.2%)			
Diseases of the musculoskeletal system and connective tissue	#12	History of significant fractures/dislocations	6 (15%)			
Diseases of the genitourinary system	#3	Genitourinary system	155 (17.6%)			
	#3	Urinary tract infection	62 (7.0%)			
	#12	Chronic urinary incontinence/renal disease	4 (10%)			
Pregnancy, childbirth and the puerperium						
Certain conditions originating in the perinatal period						
Congenital malformations, deformations and chromosomal abnormalities						
Symptoms, signs, and abnormal clinical and laboratory findings not classified elsewhere	#3	Symptoms, signs and ill-defined conditions	409 (46.4%)			
	#12	Polydipsia	1 (2%)			
	#12	Cerebella signs	4 (10%)			
Injury, poisoning and certain other consequences of external causes	#3	Injuries	168 (19.1%)			
	#3	Fractures	49 (5.6%)			
	#3	Head injury	53 (6.0%)			
	#7	Traumatic brain injury	21 (7.5%)			
	#12	Subdurals or significant head trauma or anoxic brain damage	6 (15%)			
External causes of morbidity and mortality						
Factors influencing health status and contact with health services						

3.5 | Behavioural symptoms in Korsakoff syndrome

Table 5 presents an overview of the behavioural symptoms in patients with KS, which were assessed using various assessment forms. The most measured—in six out of eight studies—were anxiety and aggressive/agitated behaviour, followed by depressive symptoms (five out of eight studies). Aggressive behaviour was reported to be prevalent in 20% (Wilson et al., 2012) up to 54% (Ferran et al., 1996) of patients with KS. Restlessness and agitation were prevalent in 10.4% of patients (Schepers et al., 2000). On the basis of the (self-report) Depression, Anxiety and Stress Scale (DASS), Horton et al. (2015) reported mild anxiety and depressive symptoms; on the basis of the Profile of Mood States (POMS), they also measured slightly elevated levels of (self-reported) anxiety and

depressive symptoms. Apathy, a well-known behavioural symptom in patients with KS, was indexed in three out of the eight studies. On the proxy-rated Neuropsychiatric Inventory–Questionnaire (NPI-Q), both Cheon et al. (2008) and Gerridzen et al. (2018) found a mild score on apathy/indifference. On the basis of the POMS, participants with KS in the study of Horton et al. (2015) were found to have less vitality and energy than the general population.

3.6 | Functional problems in Korsakoff syndrome

Table 6 shows that care needs for patients with KS were apparent mainly in the domains of social functioning, activities of daily living (ADL) and instrumental activities of daily living.

TABLE 4 Psychiatric comorbid conditions in Patients with Korsakoff's syndrome

DSM-V	Source	Disease	N (%)	Range (%)	Average (%)	Overall total (n/N)
Neurodevelopmental disorders						
Schizophrenia spectrum and other psychotic disorders	#3	Psychotic disorder	91 (10.3%)	7%–22.1%	14.6%	262/1,846 (14.2%)
	#6	Psychotic disorders	100 (18.0%)			
	#7	Psychotic disorder	62 (22.1%)			
	#11	Psychosis/hallucinosi	9 (7%)			
Bipolar and related disorders	#12	Bipolar affective disorder	1 (2%)			
Depressive disorders	#6	Mood disorders	177 (31.8%)	18%–41%	29.5%	303/1,006 (30.1%)
	#7	Mood disorder	86 (30.6%)			
	#11	Depression	23 (18%)			
	#12	Depression	17 (41%)			
Anxiety disorders	#6	Anxiety disorders	35 (6.3%)			
	#7	Anxiety disorder	26 (9.3%)			
Obsessive-compulsive and related disorders	#7	Obsessive-compulsive disorder	33 (11.7%)			
	#7	Hoarding	14 (5.0%)			
	#12	Hoarding	1 (2%)			
Trauma- and stressor-related disorders	#12	Post-traumatic stress disorder	1 (2%)			
Dissociative disorders						
Somatic symptom and related disorders	#6	Somatoform	11 (2.0%)			
Feeding and eating disorders	#6	Eating disorders	11 (2.0%)			
Elimination disorders						
Sleep-Wake disorders						
Sexual dysfunctions						
Gender dysphoria						
Disruptive, impulse-control and conduct disorders	#6	Suicide attempts	52 (9.4%)			
	#10	Behavioural disorders	19 (24.7%)			
Substance use and addictive disorders	#6	Other substance use disorders	39 (7.0%)			
	#12	Heroin dependency (on methadone)	1 (2%)			
Neurocognitive disorders	#6	Mental retardation	37 (6.7%)			
	#10	Mental disorders	21 (27.3%)			
Personality disorders	#6	Personality disorders	84 (15.1%)	12.1%–16%	14.1%	138/965 (14.3%)
	#7	Personality disorder	34 (12.1%)			
	#11	Personality disorder	20 (16%)			
Other disorders						

Role functioning was impaired in 90% of the patients (Blansjaar et al., 1992). Assessment with the Groningen Social Disabilities Schedule (GSDS) showed that basic role functioning (such as self-care and family-role functioning) was less impaired than functioning in more complex roles such as the occupational role and the role as citizen. Gerridzen et al. (2018) reported that over half of their patients had low-to-moderate engagement in social activities (54.4%). Minor issues in basic ADL were found in a majority of patients (Cheon et al., 2008)—from 74.4% (Gerridzen et al., 2018) to 82% (Wilson et

al., 2012)—meaning that they required prompting in basic self-care activities and had difficulty in more complex self-care skills (Wilson et al., 2012). The range of patients in whom basic ADL was impaired lay between 18% (Wilson et al., 2012) and 25.6% (Gerridzen et al., 2018). Korsakoff patients thus required supervision and constant prompting in everyday activities and self-care. Patients were significantly impaired in the instrumental activities of daily living (Cheon et al., 2008; Gerridzen et al., 2018; Horton et al., 2015), ordinary housework being impaired in 76.2% and managing finances in 96.1%

TABLE 5 Behavioural symptoms in Patients with Korsakoff's syndrome

Category	Reference	Assessment	Scale/Outcome	N (%)	Mean
Anxiety	#1	BPRS	Anxiety		1.4
	#2	NPI	Anxiety		1.05
	#7	NPI	Anxiety	70 (24.9%)	0.6
	#4	ICD-10	Anxiety	3 (27%)	
	#8	POMS	Tension-anxiety		51.75
	#8	HADS	Anxiety		6.8
	#8	DASS	Anxiety		8.1
	#10	ICD-10	Nervousness/anxiety	4 (5.2%)	
Agitation/Aggression	#2	NPI	Agitation/aggression		0.68
	#7	NPI	Agitation/aggression	165 (58.7%)	1.2
	#4		Aggression	6 (54%)	
	#4	SIMS	Agitation	3 (27%)	
	#8	POMS	Anger hostility		46.25
	#10	ICD-10	Restlessness/agitation	8 (10.4%)	
	#12	Medical Chart	Aggression	8 (20%)	
Depression	#1	BPRS	Depression		1.8
	#2	NPI	Depression/dysphoria		2.58
	#7	NPI	Depression/dysphoria	122 (43.4%)	0.9
	#4	ICD-10	Depression	4 (36%)	
	#8	POMS	Depression-dejection		52.15
	#8	HADS	Depression		4.9
	#8	DASS	Depression		11.35
	Sleep behaviour	#2	NPI	Sleep/night-time behaviour	
#7		NPI	Night-time behaviour disturbance	86 (30.6%)	0.5
#4		SIMS	Insomnia	2 (18%)	
#8		POMS	Fatigue-inertia		48.90
Apathy	#2	NPI	Apathy/indifference		3.42
	#7	NPI	Apathy/indifference	139 (49.5%)	0.9
	#8	POMS	Vigour activity		43.00
Disinhibition	#2	NPI	Disinhibition		0.79
	#7	NPI	Disinhibition	148 (52.7%)	1.0
	#4	SIMS	Disinhibition	4 (36%)	
Delusions	#2	NPI	Delusions		0.58
	#7	NPI	Delusions	90 (32.0%)	0.7
	#4	SIMS	Delusions	3 (27%)	
Irritability	#2	NPI	Irritability/liability		1.00
	#7	NPI	Irritability/liability	192 (68.3%)	1.4
Hallucinations	#2	NPI	Hallucinations		0.21
	#7	NPI	Hallucinations	25 (8.9%)	0.2
Confusion	#8	POMS	Confusion-bewilderment		56.90
	#4	SIMS	Wandering	3 (27%)	
Mania	#7	NPI	Euphoria/elation	70 (24.9%)	0.4
	#4	ICD-10	Mania	3 (27%)	

(Continues)

TABLE 5 (Continued)

Category	Reference	Assessment	Scale/Outcome	N (%)	Mean
Eating abnormalities	#7	NPI	Appetite/eating abnormalities	93 (32.6%)	0.6
Aberrant motor behaviour	#7	NPI	Aberrant motor behaviour	63 (22.4%)	0.5
Disorientation	#1	BPRS	Disorientation	22 (50%)	
Grandiosity	#1	BPRS	Grandiosity	21 (47%)	
Recklessness	#4	SIMS	Recklessness	2 (18%)	
Alcohol misuse	#4	SIMS	Alcohol misuse	10.5 (97%)	
Fire hazard	#4	SIMS	Fire hazard	6 (55%)	
Poor mobility	#4	SIMS	Poor mobility	5 (40%)	
Incontinence	#4	SIMS	Incontinence	2 (16%)	
Stress	#8	DASS	Stress		10.80
Planning	#5	GOK	Planning		4.68
Affection	#5	GOK	Affection/emotion		4.79
Social behaviour	#5	GOK	Social behaviour		4.95
Perception	#5	GOK	Perception		5.62
Memory	#5	GOK	Memory		5.65
ADL	#5	GOK	ADL		5.76
Dementia	#5	GOK	Dementia		6.95

(Gerridzen et al., 2018). When performing tasks such as preparing a meal or doing housework task, patients were more clumsy, required more physical effort and were less efficient than those in the general population (Horton et al., 2015).

4 | DISCUSSION

4.1 | Summary of evidence

This literature review was intended to develop an overview not only of comorbid somatic, psychiatric, behavioural and functional problems in patients with KS, but also of the care needs related to them. We found that KS patients had a wide variety of comorbid problems in all four domains. With regard to comorbid somatic conditions, pooled frequency analysis showed that the most prevalent illnesses were liver diseases, cardiovascular diseases, COPD, diabetes mellitus and hypertension. The most frequent psychiatric comorbidities were mood disorders, personality disorders and psychotic disorders (Draper et al., 2011; Gerridzen & Goossensen, 2014; Gerridzen et al., 2018; Wijnia et al., 2012). Behavioural problems were also very common, particularly anxiety, aggressive/agitated and depressive symptoms (Schepers et al., 2000). Functional problems were reported in social functioning, activities of daily living and instrumental activities of daily living. Together, these results indicate that comorbid somatic, psychiatric, behavioural and functional problems are common in patients with KS. They therefore represent challenges to the planning of effective integrated and nursing care.

The co-occurrence and complexity of Korsakoff patients' comorbid somatic, psychiatric, behavioural and functional problems are compounded by their burdensome contextual influences and lack of self-awareness. A proper response to Korsakoff patients care needs thus requires high-quality integrated care, a discipline that blends the expertise of mental health and general care (National Institute of Mental Health, 2017). Integrated care focuses not only on the early recognition of comorbid somatic, psychiatric, behavioural and functional problems, but also on the effective treatment of these problems and the care needs associated with them. Given their intensive contact with patients in everyday life and care, nurses and nurse assistants should play an important role in the delivery of integrated care to patients with KS—particularly with respect to the (early) recognition of comorbid somatic and psychiatric conditions, meeting their physical and emotional needs and promoting their social functioning and quality of life (Passalacqua & Harwood, 2012).

In view of the detrimental consequences of chronic alcoholism and self-neglect, it is not surprising to see that such devastating comorbidities in KS lead to long-term institutionalization (Alderdice, McGuinness, & Brown, 1994; Gale et al., 2014; Lemke & Schaefer, 2010; Schepers et al., 2000). There was no account given in the included articles whether the comorbid conditions were pre- or post-existing to the diagnosis of KS, but as pre-existing pathology comorbid with alcoholism is already severe, patients with KS are likely to experience even more somatic and psychiatric conditions than patients with alcohol dependence. These findings are corroborated and extended by our finding that all levels of functioning in KS are not only severely compromised, but also parts

TABLE 6 Functional problems in Patients with Korsakoff's syndrome

Category	Reference	Assessment	Scale/Outcome	N (%)	Mean
Social dysfunction	#1	GSDS	Disabled role functioning	40 (90%)	
			Functioning in complex roles is compromised.		
	#7	RISE	Mean score (range 0–6)	4.1	
			low engagement (0–2)		56 (19.9%)
		moderate engagement (3–4)	97 (34.5%)		
		high engagement (5–6)	128 (45.6%)		
Activities of daily living	#2	S-ADL	Minor issues in basic ADL	209 (74.4%)	3.37
			Independent or supervision		
	#7	ADLH	Impaired	72 (25.6%)	
			Do not have any significant problems in self-care	2 (12%)	
			Experience minor problems, with evidence of some disorganization and decline from premorbid levels of functioning	4 (24%)	
			Require prompting in basic self-care and have difficulty in more complex skills	8 (47%)	
		Require supervision and constant prompting in everyday activities and self-care	3 (18%)		
Instrumental activities of daily living	#2	S-IADL		64 (22.8%)	21.74
			Independent, set-up only, supervision		
	#7	IADL ordinary housework	Impaired	214 (76.2%)	
			Independent, set-up only, supervision	4 (1.4%)	
	#7	IADL managing finances	Impaired	270 (96.1%)	
			Mean score (competence cut-off 2, risk zone 1.7–2.3)		
#8	AMPS	Motor ability	1.74		
		Mean score (competence cut-off 1, risk zone 0.7–1.3)			
		Process ability	1.03		

of a complex interplay. These findings also imply that prevention through alcohol policy and education and nutritional support in primary care is needed for people at risk drinking and/or with an alcohol dependence.

With regard to behavioural symptoms, our findings are in line with a recent study which reported that the most prevalent behavioural symptoms were depressive symptoms (2%–50%, median 27%) and agitation and aggression (10%–54%, median 27%) (Gerridzen et al., 2017). A primary objective in the daily care of patients with KS is to manage their behaviour. The high prevalence of aggression in Korsakoff patients has also been reported in a criminal forensic setting: Ekstrom, Kristiansson, and Bjorksten (2017) found that, due to personality disorders and related aggressive behaviours, patients with alcohol-related brain damage (ARBD) were overrepresented in prisons. Due to their high level of aggression but their low general activity levels, specific attention should be paid to managing patients with KS' social interactions and group processes, to supervising and constant prompting in their everyday activities and

self-care and to activating them to undertake action and take initiatives (Ganzevles et al., 1994).

In this study, we deal separately with our findings on comorbid somatic and psychiatric conditions, our findings on behavioural and functional problems and our findings on the care needs associated with them. In practice, however, these problems occur simultaneously, leading to complex interactions. Several of the included articles reported two or more health problems, suggesting a complex interplay between psychiatric and somatic issues (Cheon et al., 2008; Draper et al., 2011; Gerridzen & Goossensen, 2014; Gerridzen et al., 2018; Schepers et al., 2000; Wijnia et al., 2012; Wilson et al., 2012). Unfortunately, we know of no studies that elaborate on the specific nature of these complex interactions. We can only conclude that they are likely to lead to adverse disease outcomes, lower quality of life and reduced life expectancy (Sanvisens et al., 2017; Schepers et al., 2000).

A central concern in nurses' recognition of care needs and health problems in Korsakoff patients is their impaired self-awareness of their illness. Deficits in self-awareness have been reported at various

levels of the dysexecutive syndrome (cognitive, behavioural and emotional) (Steinmetz, TheisenFlies, & Federspiel, 2016). Relative to the general population and other patient groups, patients with KS show a deviant presentation of symptoms, perceived problems and care needs. It is also relevant to note that, in their daily care routine, KS patients demonstrate a strong social desirability, which complicates care professionals' interaction with KS patients regarding their symptomatology (Egger, Wester, De Mey, & Derksen, 2002). The severity of their cognitive problems was highlighted in a recent study that found large discrepancies between professionals' scores and the scores given by patients in a self-reported quality-of-life assessment (Steinmetz et al., 2016). The authors gave three possible explanations for these discrepancies: a lack of self-awareness on the part of the patients, a high degree of social desirability in the patients' reports and the fact that the patients' interpretation of the questions was state dependent rather than trait dependent, and had thus led to their higher quality-of-life scores. As such impaired self-awareness delays the diagnosis of health problems, it also delays the start of effective treatment. One example is the diagnosis of cancer at a late, and sometimes untreatable, stage (Sanvisens et al., 2017).

A significant role in the manifestation of somatic, psychiatric, behavioural and functional problems and their care needs is also played by the setting in which patients with KS live. Nursing home patients with KS are less cooperative than those in an alcohol clinic or sheltered Korsakoff accommodation—a possible reflection of their dissatisfaction with their living environment (Blansjaar et al., 1992). Nursing home patients also had worse social functioning, complained about feeling imprisoned and had more often complaints of comorbid conditions, all of which contributed to their functional decay (Blansjaar et al., 1992). Unlike more regular inpatients of nursing homes, patients with KS were often found not to feel at home in a nursing home (Oudman & Zwart, 2012). Ganzevles et al. (1994) also suggested that the occurrence of behavioural problems was largely determined by living and working conditions.

The above strongly implies that care for patients with KS needs to be delivered by multidisciplinary teams consisting of physicians, nurses, nursing assistants, psychologists, physical therapists, occupational therapists, dieticians, social workers and speech therapists (Arts et al., 2017; Kopelman et al., 2009; I. Smith & Hillman, 1999), all of whom should have access to accurate multidimensional assessment and diagnostics tools. One such multidimensional diagnostic guideline was developed by Pruijssers, Meijel, Maaskant, Keeman, and Achterberg (2016) for people with intellectual disabilities and comorbid problem behaviours. By helping professionals to effectively assess and analyse the interacting problems and care needs, such a guideline can support the development of a comprehensive and personalized treatment and care plan for Korsakoff patients (Prujssers et al., 2016).

4.2 | Limitations

This is the first review to focus on health problems and care needs in patients with KS in all the relevant domains of functioning:

physical, psychological, behavioural and functional. Its strength lies in the comprehensive, broad search strategy, which ensured that no relevant articles related to our research question were overlooked.

Although the articles we included did not always specify the number of diseases per patient, the reported prevalence of diseases in one research in a given population allowed us to conclude that some of the patients in the research population must have had more than one somatic and/or psychiatric disease. But these studies did not enable us to conclude whether these diseases were related to each other, and, if so, how. A similar problem is that little literature is available on related care needs in patients with KS. With regard to future research, we recommend a greater focus on the complex interplay of health problems that occur in the various domains of functioning, and the consequences of this for diagnostics and the proper planning of treatment and care.

We acknowledge that many articles included in this systematic review were originally published in Dutch. The majority of articles published on care needs are from the Netherlands based on their care system delivering long-term care to this specific population. In many other countries, such care facilities have not been developed (see Kopelman et al., 2009 for details).

Of importance, we included all studies on care needs from inception, and most of the published studies are of relatively old age. This suggests that with the significant changes in care provision for KS patients, new strategies to deal with the complex nursing problems are required.

4.3 | Implications for mental health nurses

The findings from this systematic review imply that the deployment of content specialist mental health nurses is of major importance to deliver effective (often highly complex) care for patients with KS, given the highly prevalent occurrence of comorbid somatic, psychiatric and psycho-social care needs. Mental health nurses play an essential role in the (early) recognition of comorbid somatic and psychiatric conditions, and initiating adequate treatment and care for these conditions and related care needs. In this way, mental health nurses can contribute effectively to optimal health, functioning and quality of life in these patients.

The central position of mental health nurses in the process of care and treatment also provides opportunities to contribute to adequate coordination and continuity of integrated care planning for Korsakoff patients. To date, these options are only used to a limited extent. Typically, psychologists and psychiatrists hold the most prominent positions in these care processes, with suboptimal use of the knowledge, skills and practical opportunities of mental health nurses to promote good organization and quality of care.

Essential for mental health nurses is state-of-the-art knowledge and skills on somatic and psychiatric disorders in this patient group, including related care needs. For this purpose, the development and implementation of training programs for mental health nurses working with patients with KS is required.

5 | CONCLUSIONS

With regard to the physical health and behavioural, psychological and functional problems of patients with KS, this review highlights the presence of a wide variety of comorbid conditions. Our first recommendation is developing multidimensional diagnostics for patients with KS, which is the basis of integrated care planning. Second, given the complexity of problems and care needs, we also propose integrated care within a multidisciplinary context in which, given their central position in the care process for this patient group, nurses and nurse assistants have a prominent role. Third, to ensure that problems and care needs are assessed comprehensively, we recommend the testing and implementing of multidimensional diagnostic guidelines in daily care. Finally, to ensure that those in the nursing profession acquire the competencies they require to play a full role in the diagnostic process and follow-up integrated care planning, we recommend the development of the appropriate training and coaching modules.

CONFLICT OF INTEREST

None.

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