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**Review**

Assessment, diagnosis, care and support for individuals with Korsakoff's syndrome in the Netherlands

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Résumé : Une proportion de patients atteints de troubles de l'usage d'alcool peut également présenter des troubles cognitifs. Ceux-ci peuvent aller de déficits très graves, comme c'est le cas chez les personnes atteintes du syndrome de Korsakoff (SK), à des troubles cognitifs légers à modérés liés à l'alcool. De plus, une abstinence prolongée peut également entraîner une récupération complète des déficits cognitifs apparents chez les patients non Korsakoff. Cet article passe en revue les parcours de diagnostic et de soins aux Pays-Bas pour les personnes atteintes de troubles cognitifs liés à l'alcool (suspectés), y compris le SK. Il existe des centres experts pour le SK qui peuvent effectuer un diagnostic multidisciplinaire en tenant compte des facteurs cognitifs, somatiques, psychiatriques, sociétaux et autres. De plus, pour les personnes atteintes de SK, un réseau national de centres experts Korsakoff est disponible qui peut fournir des soins 24 heures sur 24 adaptés aux déficits et aux besoins des patients atteints de SK. De plus, il existe des interventions ambulatoires destinées aux personnes atteintes de troubles cognitifs liés à l'alcool qui ne répondent pas aux critères du SK. Ce modèle peut servir d'exemple à d'autres pays pour la mise en place de soins spécialisés pour les personnes atteintes de SK dus à l'alcool et de troubles connexes, qui ne reçoivent pas toujours les soins et le traitement nécessaires compte tenu de leur combinaison souvent complexe de déficits.

Mots-clés : Syndrome de Korsakoff ; soins de longue durée ; troubles cognitifs liés à l'alcool ; neuropsychologie

Abstract: A proportion of patients with alcohol use disorder may also have cognitive impairments. These may range from very severe deficits, as is the case in individuals with Korsakoff's syndrome (KS), to mild-to-moderate alcohol-related cognitive impairments. Furthermore, prolonged abstinence may also result in full recovery of apparent cognitive deficits in non-Korsakoff patients. This paper reviews the diagnostic and care pathways in the Netherlands for individuals with (suspected) alcohol-related cognitive disorders, including KS. Centres of expertise for KS exist that can perform a multidisciplinary diagnostic work up, taking cognitive, somatic, psychiatric, societal and other factors into account. Also, for individuals with KS, a nation-wide network of specialized Korsakoff centres is available that can provide 24h care that is tailored to the deficits and needs of KS patients. Moreover, ambulatory interventions aimed at individuals with alcohol-related cognitive impairments who do not meet the KS criteria are available. This model may serve as an example for other countries for setting up specialized care for individuals with alcoholic KS and related disorders, who may not always receive the care and treatment that is required given their often complex combination of deficits.

Key-words : Korsakoff's syndrome; long-term care; alcohol-related cognitive disorders; neuropsychology



2. INTRODUCTION

Korsakoff's syndrome (KS) is a neuropsychiatric disorder resulting from vitamin B1 (thiamine) deficiency associated with malnutrition [1]. It is the chronic, irreversible state that may occur after a Wernicke's encephalopathy (WE), an acute neurological disorder with a sudden onset characterized by oculomotor abnormalities, cerebellar dysfunction and a confusional state [2], which is treated with thiamine supplementation. WE (and KS) often occurs in the context of excessive alcohol use, but non-alcoholic WE and KS have been reported in patients with gastrointestinal diseases, hyperemesis gravidarum, anorexia nervosa, severe infections or bariatric surgery [3]. In case of treatment delays (or no treatment at all), WE may result in permanent lesions in the diencephalon, notably the thalamus and mammillary bodies [4], underlying KS.

KS is characterized as an abnormal mental state in which memory and learning are affected out of all proportion to other cognitive functions in an otherwise alert and responsive patient [5,6]. KS is accompanied by deficits in orientation, confabulations (i.e. incorrect memories which have no relation to the ongoing reality [7]), lack of illness insight [8] and apathy or other neuropsychiatric disorders [9]. Impairments in other cognitive domains may occur in patients with alcoholic KS, including executive dysfunction and social-cognitive deficits, but are probably the result of the chronic alcohol misuse, and not part of the core criteria of KS [10]. In DSM-5-TR terminology, KS is classified as Alcohol-induced Major Neurocognitive Disorder, Amnesic/confabulatory Subtype [11], a label that is formally incorrect, as the neurocognitive impairment is not due to alcohol neurotoxicity, but resulting from thiamine depletion in the context of alcohol misuse (i.e. alcohol-related rather than alcohol-induced).

With respect to the epidemiology of alcoholic KS, only a few studies have been performed. Prevalence was estimated at 3-5 cases per 10,000 inhabitants in the Netherlands in the late 1980s [12]. The annual incidence was estimated at 0.5-0.65 per 10,000 inhabitants in Scotland in the 1990s [13], and a recent study in Finland reported an incidence of 3.7 (for men) and 1.2 (for women) per 100,000 person years [14]. The age of onset usually lies between 40 and 70 but younger and older cases have been reported as well. The consequences of KS are severe, both for the individual with the diagnosis, for their support system (e.g. partners, children), and society, as people with KS are often unable to live independently at home due to the combination of the amnesia, lack of insight and severe alcohol use (or high risk of relapse on case of abstinence), which may be further complicated by somatic and psychiatric comorbidity and problems with the social context. Even though the prevalence of KS is much lower than other mental disorders, such as dementia, schizophrenia, or mood disorders, the syndrome is complex due to the combination of disorders and pathologies (referred to as 'low volume, high complex patients'). As a result, even specialized institutes for alcohol addiction, severe cognitive disorders or mental healthcare may exclude KS patients for assessment, treatment and care. This may be because of the lack of expertise, or because patients do not meet the inclusion criteria for referrals of a given institute. For instance, a young-onset dementia clinic may not take a person with KS because it is not a neurodegenerative dementia and because a history of severe alcohol misuse is making such a patient 'unsuitable' for that clinic. Alternatively, an addiction care institute may not take a referral from a possible KS case because they may not have the expertise for performing an extensive neuropsychological assessment or neurological consultation, and regular treatment options in addiction care, such as cognitive behavioural therapy or motivational interview, are not suitable for patients with KS.



Figure 1 : Map of the 44 member institutes of the Korsakoff Knowledge Centre in the Netherlands and Belgium (Flanders).

The pink locations refer to the 12 regional expertise centres for long-term care and the two centres with a special expertise status for long-term care (Atlant in Beekbergen and Slingsedael in Rotterdam). The green location indicates the Centre of Excellence for Korsakoff and Alcohol-related Disorders at Vincent van Gogh Institute for Psychiatry that meets the criteria for top clinical tertiary mental health care, certified by the Foundation for Top Clinical Mental Health Care (TopGGZ).

To optimize care for patients with KS in the Netherlands, institutes specialized in KS have been established over the years, which have been formalized in a nation-wide network organization, the Korsakoff Knowledge Centre (KKC) (www.korsakovkenniscentrum.nl). The KKC is supported by the Dutch Ministry of Health to optimize care and promote innovation and applied research for this low-volume high-complex patient group. Activities of the KKC include: the development and organization of training- and education programs, providing support and coordination of research projects, creating and updating practical guidelines and running initiatives to increase awareness about KS among the general public and policy makers. Professionals from the participating institutions contribute to these ends and participate in workgroups. To date, the KKC has 44 member institutes in the Netherlands, and two in Belgium (Flanders)(see Figure 1 for an geographical overview). Fifteen of these institutes have an expertise status, meaning that have to meet certain expertise criteria on the topic of KS (and WE) and are either part of the mental health-care system (i.e. psychiatric institutes) or long-term care facilities (i.e. nursing homes). The other members mostly are long-term care facilities, without expertise status. In 2022, 1375 beds were available in the long-term care for patients with KS. The latest estimation of the KKC is that this number

fluctuates between 1375 and 1500. Below, we will outline the referral routes, diagnostic work-up, treatment options and long-term care for individuals with KS from the Dutch perspective.

2. DIAGNOSTIC WORK-UP

Typically, there are three routes in which patients are being referred to specialized Korsakoff clinics (see Figure 1, top panel). First, patients who have been admitted to a hospital in an acute confusional state and who are then diagnosed as having Wernicke's encephalopathy. These cases often have been admitted via the emergency room to a ward for gastroenterology and hepatology or neurology. Hospital stays in the Netherlands are very short (on average 4.5 days in 2021, compared to 8.8 days in France [15]), making it necessary to find a referral institute as soon as possible so the patient can be discharged. Second, there are the patients who are receiving treatment in addiction care that may be referred to specialized Korsakoff centres. This usually happens when addiction professions report that the patient does not progress in the treatment and that this may be due to cognitive dysfunction, requiring the need for a more extensive diagnostic work-up to assess whether there are indeed cognitive impairments after abstinence. Third, patients with severe AUD living at home who have a small social network (if at all) and who are care avoiders, i.e. not receiving psychiatric care, support or addiction treatment. These patients usually come under the attention of the health-care system when the home situation starts to get out of hand (i.e. neighbours complaining about the person's behaviour) or when suddenly a reclusive person becomes confused, and neighbours or others close to the person start to express their worries. Here, the general practitioner is the person who refers the patient to the specialized Korsakoff institute for diagnosis and advice.

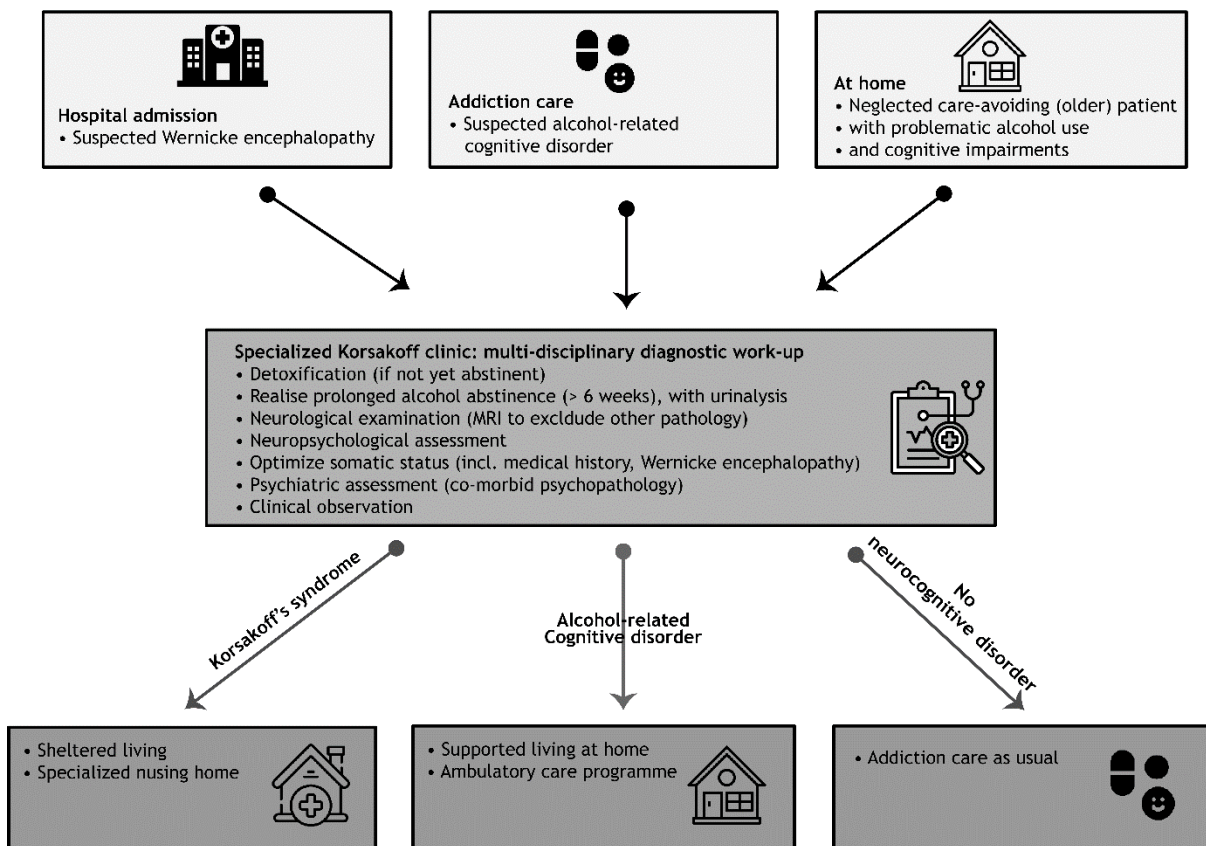


Figure 2 : Overview of the referral routes for an individual with (suspected) alcohol-related cognitive disorder

Upon receiving such a referral, consulting specialists from a Korsakoff clinic can visit the patient (preferably in the presence of a family member and/or care professional who knows the patient well) in the hospital, home environment or addiction centre to assess whether the patient can be transferred for a more extensive diagnostic work up, which then also requires realizing prolonged abstinence (if this has not already been established). Exclusion criteria for admission to a Korsakoff clinic include a too high somatic care burden (requiring hospital or rehabilitation care), the expectancy that the patient will die within a few months (e.g., due to another severe illness, such as final-stage cancer), or very severe behavioural disturbances (such as aggressive behaviour towards care professionals and other patients). When there is polysubstance use, detoxification in an addiction centre is advised. Having a history of AUD or evidence for recent severe alcohol misuse, and suspicion of cognitive problems due to the alcohol use and malnutrition (and not other causes, such as psychiatric disorders) usually are inclusion criteria. A documented WE in the context of another medical disease may not necessarily be an exclusion criterion. Most of the Korsakoff clinics who take patients directly from the patient's home environment, a hospital or addiction care facility are part of the mental-health care system in the Netherlands, with reimbursements going via the health-care insurance. This is usually an inpatient trajectory, with patients residing in the Korsakoff clinic for a period of 3-6 months. Patients can enter the trajectory on a voluntary basis, but a judicial authorization procedure may be required as part of the Compulsory Mental Healthcare Act to realize compulsory admission (if this is the only way of eliminating serious harm). Next, safe detoxification from alcohol is conducted in the Korsakoff clinic, and prolonged abstinence is verified via urinalysis. Cognitive screening may already take place in the hospital or at admission to the Korsakoff clinic, with the Montreal Cognitive Assessment (MoCA) as the recommended and validated instrument [16]. Somatic comorbidity is assessed and monitored during the stay in the institute, where the patient is living in sheltered units (with a shared living room and kitchen and individual bed rooms). Here, the patient is expected to engage in activities of daily living and social activities. Nursing staff observe the patient's daily functioning and neuropsychiatric symptoms, assisted by validated informant-based instruments such as the NOSCA [17], NVCL-R [18], BRIEF-A [19] and AMI [20]. After at least 6 weeks of verified alcohol abstinence [21], an extensive neuropsychological assessment is performed. Since individuals with an intellectual disability or lower intellectual functioning are overrepresented in addiction care [22], intelligence testing is part of the neuropsychological assessment. In addition, all major neurocognitive domains need to be assessed using validated neuropsychological tests, including learning and memory, orientation, attention and executive functioning, social cognition, information processing speed, and visuoconstruction. The neuropsychological assessment may include screening of perception and language, if problems are suspected in these domains. Performance validity testing is also recommended, making sure to adapt the tests' cut-off score to improve the specificity in individuals with severe cognitive impairment [23,24]. Neuropsychologists thus play a key role in the Korsakoff clinics. Furthermore, observation scales can be completed by informants, such as children, partner, or close friends who have known the patient for a long time. Self-report measures on mood and psychopathology may be administered in the patients themselves, provided that the response format is not too demanding for individuals with severe cognitive impairments. Examples include the Geriatric Depression Scale (GDS-15 [25]).

A consultant neurologist performs a neurological examination, with a specific focus on cerebellar dysfunction and oculomotor disturbances. Psychiatric consultation may be required in the case of comorbid psychopathology that may complicate the interpretation of the diagnostic information, such as delirium or psychotic symptoms. Magnetic resonance imaging (MRI of the brain) can be performed to exclude other pathology (e.g. cerebrovascular lesions, traumatic brain injury) and to take into account

potential neurodegenerative pathology (i.e. cortical and medial temporal lobe atrophy). Atrophy of the mammillary bodies may be visible on MRI, but cannot be considered a reliable biomarker for making the diagnosis of WE. Extensive review of the medical and psychiatric history is crucial, as well as current and history of substance abuse (for which structured instruments such as the MATE are helpful [26]). Taking into account all available evidence and test results, a diagnosis is made using the DSM-5-TR classification system (which is required in Dutch mental-health care for reimbursement) and the criteria for KS outlined in Kopelman [27]. Operational diagnostic criteria for KS include: 1) an episodic memory impairment (according to established criteria [28]) that is evident on all memory tests and disproportionate compared to deficits in other cognitive domains that may be present (such as executive dysfunction or social-cognitive deficits), 2) relatively spared fluid intelligence compared to crystallized intelligence, in accordance with the premorbid level of functioning [29] (e.g. in the case of intellectual disability), 3) supported by deficits in orientation (time and place) and 4) confabulations (either provoked or spontaneous). Evidence of a recent WE is helpful, but not a necessity (as often such information is lacking in the case of care-avoiding individuals), but a relatively sudden onset of the cognitive dysfunction and a history of malnutrition is part of the diagnostic criteria. Assessment of thiamine levels is usually not helpful for the diagnosis of WE, as clinical guidelines require immediate thiamine supplementation, resulting in normal thiamine levels even when the patient meets all diagnostic criteria of a WE. Slowly progressive cognitive decline over months or years does not meet the criteria for KS, but may be indicative for a neurodegenerative disease such as Alzheimer's disease [30]. In addition, chronic, excessive alcohol may result in various degrees of cognitive impairment, ranging from mild cognitive impairments to major neurocognitive disorder. KS is an example of the latter, however, this category also includes patients with cognitive disorders without KS. Prolonged alcohol abstinence may improve cognitive functioning, but cognitive deficits as part of KS are irreversible and will not revert [31] back to a normal, premorbid level of functioning. In the case of transient cognitive impairments (e.g. initial poor performance on memory tests that dissolve after prolonged abstinence), a diagnosis of KS should not be made. In case of other comorbid conditions or pathology that may affect cognitive functioning (such as a history of stroke, traumatic brain injury, or epilepsy) a strict diagnosis of KS is often not possible (in this case, a classification of dementia or major neurocognitive disorder with a multifactorial aetiology can be made).

3. AFTER THE KORSAKOFF DIAGNOSIS

Individuals diagnosed with KS require specific care. Their severe memory deficits, in combination with lack of illness insight, apathy, and other neuropsychiatric and cognitive symptoms, make every-day functioning challenging. Furthermore, the alcohol use disorder which is present in most patients with KS requires explicit attention to prevent relapse. Moreover, the diencephalic brain damage in KS patients is irreversible, making the cognitive symptoms chronic in nature. Here we discuss evidence on cognitive rehabilitation in KS and the relevance of Dutch specialized long-term care facilities.

Long-term care facilities

Since little or no improvements in cognitive function are to be expected in individuals with KS in the chronic phase, support and care should be aimed at reaching and maintaining an optimal level of functioning in daily life, given the cognitive impairments and consequent limitations and participation problems [32]. Due to the severity of the cognitive deficits, the neuropsychiatric symptoms, and the history of alcohol use disorder (with the risk of relapse and the socioeconomic challenges that come with AUD), offering optimal support in the patient's home environment is not possible in most cases, as this would be too extensive (including e.g., support in maintaining a day-night balance, activating someone to go to daytime activities, dispensing medication, support with staying abstinent from alcohol). Often, social support is limited or absent altogether, as many patients live alone and have a complicated relationship with (ex-)partners, siblings or children.

In the Netherlands, specialized long-term care facilities have been established over the years, which provide 24-hour care for individuals with KS. Long-term care in the Netherlands is funded by public money rather



than health-care insurance. KS long-term care facilities are usually units in larger nursing homes (that may also offer care for dementia patients), in which small groups of KS patients live together, and perform everyday-activities together, such as preparing and cooking meals, engage in social activities (watching tv, playing games) and participate in (sometimes paid) therapeutical work activities in the facility (such as gardening, taking care of animals in a petting zoo, or performing entry-level jobs). Most of these KS nursing homes are 'dry', in that the use of alcohol is not allowed (note that this policy is increasingly under debate in some institutes), but patients have a large degree of freedom inside and outside the institute (they are, for instance, allowed to visit the nearby village, go for walks etc.). Family and friends may visit. These institutes provide a balance between group activities and privacy, since all residents have their own room (with a private or shared bathroom) that they can decorate themselves, whereas the kitchen and living room are shared. As noted above, expertise and best practices are shared among institutes, as specialized nursing homes and mental health care institutes (with a multidisciplinary team, including psychologists and nurses) are united in the KKC centre of expertise, which also provides schooling and training for care professionals working in long-term care.

Cognitive rehabilitation

Although there are a few case reports suggesting that cognitive rehabilitation in individuals with KS may be helpful [33], its effectiveness is limited. That is, brain training with a restorative aim (e.g. repeated practice of attention or memory tasks) is not effective, since at best it results in task-specific improvements that do not generalize to everyday functioning. In turn, compensatory strategy training relies on cognitive functions (e.g. memory, executive function) that are impaired in individuals with KS [34]. Compensatory should be based on the use of preserved abilities to compensate for altered abilities. A rehabilitation method that relies on preserved abilities (i.e., implicit memory) is errorless learning [35]. Here, patients with KS are taught specific information or skills in a step-by-step approach, minimizing the occurrence of errors as much as possible to prevent implicit consolidation of erroneous responses that interfere with later recall. Several studies showed that errorless learning is beneficial for skill learning in KS patients, also reducing behavioural problems and improving quality of life [36-39]. Another rehabilitation approach that has found to be promising in KS is relying on external strategies, which includes the use of electronic calendars, and wearables such as smart watches [40], pagers [35] and cameras [41] to support memory function. However, it must be stressed that large-scale randomized controlled studies on the effectiveness and efficacy of cognitive rehabilitation in KS patients are lacking [33,42,43].

The therapeutic milieu

The long-term care facilities specialized in KS care in the Netherlands can acquire a regional expertise status if they meet a number of criteria (e.g., availability of multidisciplinary care, demonstratable collaborations with health care partners in the region, the institute must engage in research activities). There are currently 12 regional expertise centres in the Netherlands. Centres can also acquire a special expertise status (N = 2), for which they need to meet more criteria on top of the regional criteria (e.g., 40 places for patients with KS, have a last resort function (for patients that cannot be placed elsewhere), have a national consultation function, and actively engage in scientific research in collaboration with a university.

Most long-term care facilities specialized in Korsakoff care have units with different "residential milieus", often including more active (with more [group]activities and greater focus on the patients' autonomy and self-efficacy) and calmer residential units (with the focus on balancing activities and recreation). Although patients residing in long-term care facilities do not formally undergo treatment in the strict sense (i.e. 'curative' interventions aimed to improve KS and its related cognitive dysfunction), interventions are being offered as part of routine care. For instance, an empathy-based directive approach and errorless learning are very much part of the therapeutic milieu of all KKC institutes, helping to optimize functioning and promote patient autonomy, quality of life and self-management. The empathy-based directive approach [44] entails an approach that is individually-tailored, aimed at personal connection and the patient's own



background, while at the same time adopting a directive approach (i.e., providing immediate and clear feedback on patterns of behaviour in specific situations). Professional caregivers support activities of daily living using errorless learning principles, that is, structured and pre-determined practice, rather than a trial-and-error approach. Specific interventions aimed at neuropsychiatric symptoms and behavioural problems may be offered, which are usually adapted protocols from the dementia field. For instance, a specific intervention focusing on apathy [45] is currently being evaluated for the use in KS patients. Also, protocols exist that empower professionals to deal with challenging behaviour such as apathy and aggression. The KKC network offers specific in-company trainings for care professionals on all these approaches.

Activities in long-term care

In addition to these approaches, all KKC nursing homes promote an active and healthy lifestyle. Activities are being offered that promote the patients' self-efficacy. These can include entry-level jobs for which patients receive payment, or other meaningful activities, such as taking care of animals or repairing bicycles. Engaging in social activities, sports and games is also promoted. That is, many KS patients in long-term care report to feel lonely and to miss intimate relationships [46]. Actively engaging friends and family (who often have a complicated relationship with the patient), for instance by providing psychoeducation or inviting them to social events in the institute, is therefore important. There are many healthcare disciplines (e.g. elderly care physician, dietician, occupational therapist, music therapist, nurses, psychologist, physical therapist, social work, speech therapist, spiritual care, vocational worker) that need or can be involved in the general care for patients with KS, depending on the patients' needs. Somatic co-morbidity is monitored by elderly care physicians, a medical specialty aimed at the problems and needs for nursing home residents. Psychologists with a background in gerontology and/or neuropsychology are usually involved in mediative interventions, that is, to support the caregiver team and to empower them on dealing with cognitive dysfunction, challenging behaviour and psychiatric co-morbid disorders. A physiotherapy program may also be offered, as these may further improve the patient's functional status [47,48] and music therapy is also part of the care program [48].

4. CARE FOR NON-KORSAKOFF PATIENTS

Not all patients receive a KS diagnosis after the diagnostic work up. That is, prolonged abstinence may improve cognitive symptoms to a normal level. Since there are no cognitive impairments in these patients, there are no contraindications for regular addiction care or psychotherapy. As a result, these patients are referred back to for instance the addiction care facility to maintain abstinence or to mental-health care for treatment of the psychopathology (such as trauma therapy or treatment for depression).

There is also the group of patients in whom cognitive impairments are still present after sobriety, but who do not meet the KS criteria. For instance, the problems can be less severe, or do not affect learning and memory. For these patients, 24-hour care is usually not required and they can be referred back to their home environment. However, the presence of cognitive impairments (even if they are not severe) may be a risk factor for relapse, and a challenge for regular addiction care. For patients with mild to moderate alcohol-related cognitive disorders, a tailored relapse prevention program is required, for instance, in smaller groups, by employing external aids to support knowledge transfer and by adaptations in the environment [47]. Recently, we developed a 12-session cognitive-behavioural therapy-based addiction intervention for relapse prevention that is promising, in that it is feasible, increases alcohol abstinence self-efficacy, and reduces craving [49]. For this group, ambulatory support is also facilitated, in which specialists from a Korsakoff centre act as case-managers who visit the patient in their home environment on a regular basis, with the aim to maintain abstinence, optimize functional independence and improve social and societal participation [49].

5. CONCLUSION

Patients who are suspected of having alcohol-related cognitive impairments require special care. The diagnostic work-up should not only assess cognitive impairments related to the alcohol use disorder, but must also take into account psychiatric and somatic comorbid disorders, duration of abstinence, possible effects of misuse of other substances, and possible other aetiologies (e.g. cerebrovascular disease, Alzheimer's disease) [51]. This can be achieved by a multidisciplinary team of specialists, including clinical neuropsychologists, neurologists, psychiatrists and specialized nurses. Subsequent treatment and care are very much dictated by the diagnosis made (see Figure 1 bottom panels). For patients who receive the KS diagnosis, 24-hour care in specialized nursing homes or sheltered living facilities is often required. Patients who have alcohol-related cognitive disorders, but who not meet the criteria for KS may receive an outpatient treatment program. Those who after thorough assessment do not have any cognitive impairments (or whose impairments fully recovered after prolonged abstinence) may be referred back to regular addiction care for relapse prevention or to mental-health care facilities for psychotherapy. Although KS as a syndrome is not among the most prevalent mental disorders, the combination of disorders (at a cognitive, neuropsychiatric, somatic, functional and social level) requires special expertise. In the Netherlands, this is carried out by having a nation-wide Korsakoff platform, which acts as a network of regional mental-health care and long-term care institutes specialized in the assessment and treatment of KS patients. Through this network, high-quality diagnoses can be made, and patients can be cared for in a manner that is tailored towards their complex combination of disorders with the aim to improve autonomy, self-efficacy, participation and – ultimately – quality of life. This model has been referred to as an example for other countries in which individuals with alcohol-related cognitive disorders may not always receive the attention and care they require [52].

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