RC PSYCH
ROYAL COLLEGE OF PSYCHIATRISTS

CR185

Alcohol and brain damage in adults

With reference to high-risk groups

RC GP Royal College of General Practitioners

Royal College of Physicians

COLLEGE REPORT

Alcohol and brain damage in adults

With reference to high-risk groups

College report CR185

The Royal College of Psychiatrists, the Royal College of Physicians (London),
the Royal College of General Practitioners and the Association of British Neurologists

May 2014

Approved by the Policy Committee of the Royal College of Psychiatrists: September 2013
Due for review: 2018

College Reports constitute College policy. They have been sanctioned by the College via the Policy Committee.

For full details of reports available and how to obtain them, contact the Book Sales Assistant at the Royal College of Psychiatrists, 21 Prescot Street, London E1 8BB (tel. 020 7235 2351; fax 020 7245 1231) or visit the College website at http://www.rcpsych.ac.uk/publications/collegereports.aspx

The Royal College of Psychiatrists is a charity registered in England and Wales (228636) and in Scotland (SC038369).

Contents

List of abbreviations

ACE-III, Addenbrooke's Cognitive Examination-III

ADHD, attention-deficit hyperactivity disorder

ARBD, alcohol-related brain damage

ARND, alcohol-related neurodevelopmental disorder

AUDIT, Alcohol Use Disorders Identification Test

AwIA, Adults with Incapacity (Scotland) Act 2000

BAP, British Association for Psychopharmacology

BMI, body mass index

CFT, children's friendship training

6-CIT, 6-item Cognitive Impairment Test

COX-2, cyclooxygenase 2

CPA, care programme approach

CT, computed tomography

DSM, *Diagnostic and Statistical Manual of Mental Disorders*

DTC, delayed treatment control

EMI, elderly mentally infirm

FAS, fetal alcohol syndrome

FASD, fetal alcohol spectrum disorder

FTE, full-time equivalent

GABA, gamma-aminobutyric acid

GP, general practitioner

ICD, *International Classification of Diseases*

IL, interleukin

i.m., intramuscular

iNOS, inducible nitric oxide synthase

IPP, imprisoned for public protection

i.v., intravenous

MAPPA, Multi-Agency Public Protection Arrangements

MCA, Mental Capacity Act 2005

MCP-1, monocyte chemoattractant protein-1

MMSE, Mini-Mental State Examination

MoCA©, Montreal Cognitive Assessment for Detection of Mild Cognitive Deficits

MRI, magnetic resonance imaging

MRS, magnetic resonance spectroscopy

NHS, National Health Service

NICE, National Institute for Health and Care Excellence

NMDA, *N*-methyl-*D*-aspartate

PFAS, partial fetal alcohol syndrome

Q-LES-Q-SF, Quality of Life Enjoyment and Satisfaction Questionnaire – Short Form

RCT, randomised controlled trial

REM, rapid eye movement

SAD-Q, Severity of Alcohol Dependency Questionnaire

SIGN, Scottish Intercollegiate Guidelines Network

TLR4, toll-like receptor 4

TNF-α, tumor necrosis factor alpha

Working group

Editor

- **Professor Kenneth Wilson** MD, MPhil, FRCPsych, Professor of Old Age Psychiatry and consultant specialising in alcohol-related brain damage, University of Liverpool, Stein Centre, St Catherine's Hospital

Co-editors

- **Professor Safi Afghan** MB, MCPS, MSc, MRCPsych, MBA consultant psychiatrist, Dudley and Walsall Mental Health Partnership NHS Trust, and Honorary Professor of Mental Health, University of Wolverhampton, Dorothy Pattison Hospital, Walsall
- **Dr Henrietta Bowden-Jones** MRCPsych, BA(Hons), DOccMed, MD (Imperial), Honorary Clinical Senior Lecturer, Faculty of Medicine, Department of Medicine, Imperial College London
- **Dr Rafey A. Faruqui** FRCPsych, FHEA, MA, DIC, MSc, Chair, Section of Neuropsychiatry, Royal College of Psychiatrists
- **Dr Adrian Feeney** MBBS, FRCPsych, BSc, LLM, consultant forensic psychiatrist, Ravenswood House and Winchester Prison CMHT, Southern Health NHS Foundation Trust
- **Dr Clare Gerada** MBE, MOM, FRCPsych, FRCP, FRCGP, Chair, Royal College of General Practitioners
- **Dr Nichola Kalk**, ST4 in general adult psychiatry, South London and Maudsley NHS Foundation Trust, and Honorary Clinical Fellow, Imperial College London
- **Professor Michael Kerr**, Professor of Learning Disability Psychiatry, Institute of Psychiatric Medicine and Clinical Neurosciences, Cardiff
- **Professor Michael Kopelman** PhD, FBPsS, FRCPsych, FMedSci, King's College London (Institute of Psychiatry), and South London and Maudsley NHS Foundation Trust
- **Professor Anne Lingford-Hughes**, Professor of Addiction Biology at Imperial College London and consultant psychiatrist at Central North West London NHS Foundation Trust
- **Dr Clarence Liu**, consultant neurologist, Department of Neurology, Barts Health NHS Trust, and Regional Neurological Rehabilitation Unit, Homerton University Hospital NHS Trust
- **Dr Jenny Svanberg**, consultant clinical psychologist, Forth Valley Substance Misuse Services, Stirling Community Hospital
- **Professor Alan J. Thompson** MD, FRCP, FRCPI, Garfield Weston Professor of Clinical Neurology and Neurorehabilitation, and Dean, Faculty of Brain Sciences, University College London
- **Dr Peter Trimble** MRCGP, MRCPsych, consultant psychiatrist, Belfast Health and Social Care Trust, and Honorary Lecturer, Queens University, Belfast
- **Dr Yulia Zyrianova** MSc, MRCPsych, MD, GDip, consultant child and adolescent psychiatrist, and member of the Executive Committee, Section of Neuropsychiatry, Royal College of Psychiatrsits

Contributors and reviewers

- **Dr Joy Bell**, ST5 senior general adult psychiatry and addictions trainee, Ulster Hospital, Dundonald, Northern Ireland
- **Dr Vanessa Craig** MB BCh, BAO, MRCPsych, ST4 in general adult psychiatry, Lagan Valley Hospital, Lisburn, Northern Ireland

- **Linda Johnstone**, lead nurse, Wirral Harm Reduction Unit (Alcohol and Drugs), St Catherine's Health Centre, Tranmere
- **Richard Morris**, Headway, information officer, Nottingham
- **Dr Chris Record** DPhil (Oxon), FRCP, consultant hepatologist and visiting fellow, Newcastle University.

Contacts for practice examples

Scotland

Fife

- Sally O'Brien, Nurse Team Leader, CAST Team, Torbain Ward, Whytemans Brae Hospital, Kirkcaldy KY1 2ND

Glasgow

- Dr Donna Mullen MBchB MRCPsych, Consultant Psychiatrist; Grant Brand, Team Leader, Alcohol Related Brain Damage Team, Glasgow Addiction Services, 86 Millbrae Road, Glasgow G42 9DM

England

Wirral

- Professor Kenneth Wilson, University of Liverpool, Stein Centre, St Catherine's Hospital, Derby Road, Birkenhead CH42 0LQ

Executive summary and recommendations

Alcohol-related brain damage (ARBD) is an umbrella term that accommodates the various psychoneurological/cognitive conditions that are associated with long-term alcohol misuse and related vitamin deficiencies. ARBD tends to affect people in their 40s and 50s, with females presenting a decade younger than males. At one extreme is the classical presentation of Wernicke–Korsakoff syndrome and at the 'milder' or less obvious extreme are the more frequent but subtle frontal lobe dysfunctions. We have employed the term ARBD because the *International Classification of Diseases* (ICD) and the *Diagnostic and Statistical Manual of Mental Disorders* (DSM) fail to provide satisfactory terms to cover all the manifestations and confuse the concept with dementia. This latter point is important as it is clearly evidenced that 75% of people with ARBD do improve with appropriate care. The term also provides a pragmatic solution to complexities of dual diagnosis in that 25% of people presenting with ARBD will have evidence of secondary microvascular stroke-related disorders and/or head trauma (Wilson *et al*, 2012). Consequently, such patients may have up to three simultaneous conditions resulting in cognitive damage.

Because of the diagnostic problems, patients not being aware that they have the condition, variability of presentation, poor levels of awareness in clinical settings and the stigma related to 'self-inflicted' alcohol-related disease, few data exist relating to the size of the problem. Routine clinical audits of case notes fail to address this as most cases are not diagnosed or recorded. The most robust evidence relates to fairly old post-mortem studies carried out on 40 000 community residents, which found that between 0.5 and 1.5% of the general adult population have changes in their brain as a consequence of alcohol misuse and most of these do not have a diagnosis recorded in clinical case notes during their lifetime (Cook *et al*, 1998).

This 'silent' problem is reflected in the absence of any national guidelines, standards of care or established pathways of care across most of the UK. Hence patients are unable to access appropriate service provision, fall into default circumstances (such as elderly mentally infirm (EMI) nursing homes, designed to cater for older, frail people with dementia) or receive no services at all. In these circumstances, the individual is likely to relapse into alcohol misuse, be readmitted into acute care for withdrawal and stabilisation of their physical condition and is subsequently discharged; and the cycle is repeated. This is particularly distressing as there is now clear evidence that appropriate services providing a rehabilitative model reduce all acute hospital bed-day usage by 85%, dramatically improve the quality of life of individuals and are able to maintain 75% of affected patients in non-institutional community settings. When receiving appropriate care, relapse into alcohol misuse runs at about 10% and there is a 10% mortality rate (Wilson *et al*, 2012). The financial implications for health service providers and commissioners are self-evident. There is less bed occupancy, improved health and social well-being and significant cost reduction across the rehabilitation period as the patient improves, with only 25% of patients requiring long-term institutional care (Wilson *et al*, 2012).

This report reviews the literature relating to the definition, epidemiology, information on the neurobiological changes associated with ARBD and implications for medical treatments, service organisation and provision, assessment, and psychosocial interventions. The expert panel has reviewed the evidence and derived recommendations for commissioners and service providers. We present specific recommendations in the context of four specialist settings: alcohol treatment services, prisons, acute hospitals and pregnancy/fetal

alcohol spectrum disorder (FASD). The report provides examples of service delivery models couched in the context of a team within a mental health trust, accessing clinicians across clinical teams, an ARBD team closely affiliated with the alcohol treatment services and a team embedded within an early onset dementia team. In the absence of significant research (except in a minority of areas), the evidence is derived from descriptive studies and clinical reviews. We believe that this guideline represents the best evidence available and it provides a source document for both commissioners and service providers in the assessment and management of this stigmatised and neglected group of patients.

Recommendations

Pharmacological management

Reducing toxicity of alcohol withdrawal

- For individuals who typically consume over 15 units of alcohol per day, and/or who score 20 or more on the Alcohol Use Disorders Identification Test (AUDIT; Babor *et al*, 1992), consider offering: an assessment for and delivery of a community-based assisted withdrawal or assessment and management in specialist alcohol services if there are safety concerns about a community-based assisted withdrawal.
- Chlordiazepoxide or diazepam are recommended for community detoxification.
- For in-patient detoxification in a general medical setting, benzodiazepine, carbamazepine or chlomethiazole are recommended.
- If Wernicke's encephalopathy is suspected or established, parenteral thiamine (i.m. or i.v.) of >500 mg should be given for 3–5 days (i.e. two pairs of ampoules Pabrinex® three times a day for 3 days), followed by one pair of ampoules once daily for a further 3–5 days depending on response.
- If patient is at high risk of Wernicke's encephalopathy (e.g. malnourished, unwell) prophylactic parenteral treatment should be given, using 250 mg thiamine (one pair of ampoules Pabrinex®) i.m. or i.v. once daily for 3–5 days or until no further improvement is seen.

Treating long-term Korsakoff's syndrome/ ARBD

- Ensure ongoing thiamine treatment.
- Maintain abstinence.
- For people with moderate or severe drinking, after withdrawal: acamprosate or oral naltrexone in combination with an individual psychological intervention focused specifically on alcohol misuse (cognitive–behavioural therapies, behavioural therapies or social network- and environment-based therapies).
- Disulfiram, in combination with a psychological intervention for individuals who have a goal of abstinence but for whom acamprosate and oral naltrexone are not suitable (or who prefer disulfiram and understand the relative risks of taking the drug).
- Baclofen can be considered as an alternative to the other drugs if required.
- For harmful drinkers[a] and people with mild alcohol dependence, offer a psychological intervention (such as cognitive–behavioural therapies, behavioural therapies or social network- and environment-based therapies) focused specifically on alcohol-related cognitions, behaviour, problems and social networks.

Psychosocial and cognitive rehabilitation

Commissioning care

- Clinical commissioning groups should commission established and clinically appropriate services to provide multidisciplinary, specialist care for the assessment and rehabilitation of patients with severe ARBD. The nature of service provision should capitalise on established strengths within the local health and social care provision. In the absence of established

a. Harmful use is 'A pattern of psychoactive substance use that is causing damage to health. The damage may be physical (as in the case of hepatitis from the self-administration of injected drugs) or mental (e.g. episodes of depressive disorder secondary to heavy consumption of alcohol). Harmful patterns of use are often criticized by others and frequently associated with adverse social consequences of various kinds. The fact that a pattern of use or a particular substance is disapproved of by another person or by the culture, or may have led to socially negative consequences such as arrest or marital arguments is not in itself evidence of harmful use.' (World Health Organization, 1992)

neuropsychiatric/psychological services or equivalent specialist services which should preferably provide such a service, consideration should be given to the embedding of 'specialisation' within the most appropriate established generic mental health service provision; enabling access to expertise, advice, multidisciplinary assessment (including Social Service support); and coordination or supervision of care pathways.

- Such specialisation should provide advice and support to other services who are managing people with mild to moderate ARBD, including community teams and alcohol services.
- As part of the assessment process, clinical commissioning groups should commission appropriate services for facilitating the early hospital discharge and short-term psychosocial assessment (up to 3 months). These facilities may have to manage clinically disturbed and mentally incapacitated patients.
- Arrangements should be in place to provide safe and active institutional rehabilitation for those patients who are not well enough to be rehabilitated into non-institutional settings after the initial 3-month period of assessment. However, it should be expected that the majority of patients (75%) will make some improvement over 3 years as a consequence of active rehabilitation.
- Funding for long-term institutional care for supporting people with permanent brain damage should be made available. A minority of cases (25%) may require permanent institutionalisation.
- A significant minority of patients will require ongoing social support in non-institutional settings after the 3-year period of therapeutic rehabilitation, so as to maintain their optimum level of independence in community settings.

General principles of psychosocial intervention

- Rehabilitation should be couched in the context of multidisciplinary support.
- Close liaison with alcohol treatment services is required.
- Every patient should have an active care plan with assigned key worker with expertise in the assessment and rehabilitation of working-age adults with cognitive deficits.
- The care plan should incorporate ongoing assessments of cognition – for example, the Addenbrooke's Cognitive Examination-III (ACE-III; Neuroscience Research Australia, 2013) or the Montreal Cognitive Assessment (MoCA©) for Detection of Mild Cognitive Deficits (Nasreddine *et al*, 2003) – behaviour and mental capacity, after withdrawal, after 3 months of abstinence and subsequently every 6 months until an optimum level of independence is achieved.
- The care plan should be couched in a collaborative arrangement with the patient and should be structured, goal oriented and monitored. It should facilitate and enhance the development of independence over a 3- to 4-year period, with ongoing review of care cost and planned reduction in support as indicated by the patient's improvement.
- Carers, institutional staff and families should be encouraged to participate in the rehabilitation under appropriate supervision of the specialist key worker.
- As the patient improves, transition between institutional and community care should be carefully managed and appropriately supported as part of the rehabilitative programme.

The legal framework: Mental Capacity Act 2005 (England and Wales), Adults with Incapacity (Scotland) Act 2000

- ARBD fulfils the legal criteria of mental disability.
- Patients may present with difficulties in decision-making in a wide variety of situations and should be facilitated in coming to their own decision.
- When assessing capacity in patients with ARBD:
  - Memory should be assessed.
  - Consideration should be given to the ability of the individual to recall any relevant discussion and decisions made during the interview. Notably, recall may be preserved and function well during the interview but may be significantly compromised some

minutes later. Consequently, it is frequently worth reviewing the interview and related decisions and testing recall of the issues and decisions made later in the day.

- Consideration must be given to the individual's ability to recollect previous events as many individuals will not have clear memories of their recent past. This may make it difficult for them to appreciate their current circumstances and the events that have contributed to their current situation.
- Corroborative histories may help in differentiating between confabulations and memories.
- Issues relating to decisions that need to be made may have to be broken down into steps, and the patient facilitated in working through their options.
- The patient may benefit from ongoing support and memory aids in helping to remember the decisions that they have made.
- Capacity is likely to fluctuate in ARBD and regular reassessments are recommended.

High-risk patient populations

Alcohol treatment services

- Specialisation in the recognition and management of people with mild to moderate ARBD is built up within each alcohol treatment service and implications for commissioning agencies should be considered.
- Alcohol treatment services and related pathways of care should cater for the significant minority of alcohol misusers who will present with ARBD.
- All new patients referred to alcohol treatment services have a cognitive assessment, which should be nested within an assessment of the psychological and social needs of the individual. Cognitive assessment may take the form of a number of structured examinations ranging from fairly brief, such as the 6-item Cognitive Impairment Test (6-CIT; Brooke & Bullock, 1999) or the Mini-Mental State Examination (MMSE), through to more sophisticated interviews using the ACE-III or MoCA©.
- Cognitive testing should be carried out as soon as the individual is entered into the treatment programme, and subsequently after 3 months of abstinence. If there is residual cognitive impairment, then 6-monthly cognitive assessments should be undertaken over a follow-up period of up to 3 years.
- Therapists should gain experience in mental capacity assessment as required by the Mental Capacity Act 2005 (MCA) (England and Wales) and Adults with Incapacity (Scotland) Act 2000 (AwIA).
- Patients with severe cognitive problems or those who are incapacitated to the degree that they are at risk should be referred for specialist ARBD assessment.
- When there is a likelihood of Wernicke's encephalopathy and related symptoms, in-patient referral and i.v. thiamine should be considered.
- All patients are assessed for risk of thiamine deficiency in the absence of Wernicke's encephalopathy-related symptoms and if there are significant risk factors then i.m. thiamine treatment is indicated, but the clinician should be aware of the allergic history of the patient (e.g. history of eczema, asthma, allergies to medications and previous treatments). Anaphylactic reactions are experienced in 1 per 5 million pairs of ampoules of Pabrinex® given i.m. (Taylor *et al*, 2012).
- All patients who have received parenteral thiamine should be continued on oral thiamine.
- Anyone receiving medically supported withdrawal should be prescribed oral thiamine even when no risk factors of Wernicke's encephalopathy are present.
- Close liaison between alcohol treatment services and local 'specialist' services, commissioned to cater for ARBD, is recommended.

Prison service

- Alcohol withdrawal may need to be conducted under care of the local hospital.
- Primary and secondary screening should incorporate alcohol screening instruments.
- Individuals identified as having alcohol-related problems should be signposted to appropriate support facilities.

- People with alcohol-related problems should be reassessed in terms of needs prior to release from prison and referred to appropriate external agencies including the Multi-Agency Public Protection Arrangements (MAPPA) panel.

Acute hospital-based settings

- A simple screening instrument (Wilson *et al*, 2012) should be used to identify at-risk patients in acute hospital settings. This should be supported by a primary diagnostic process which includes appropriate physical and radiological (scanning) investigations, a psychosocial review (including examination of frontal lobe function), and engaging carers or family where appropriate.
- Where indicated, the patient should be assessed in the context of the MCA or AwIA.
- The high turnover in acute medical and surgical wards requires a rapid response to referrals for assessment, to enable assessment while the patient is alcohol free as an in-patient and facilitate rapid removal of physically stabilised patients from acute wards as quickly as possible.
- Funding support should be designed to enable ready access to appropriate services and rapid discharge from acute medical wards.
- The first 3 months of abstinence are associated with considerable cognitive and behavioural improvement. During this period, the incapacitated patient should be protected from alcohol exposure and other risks until able to make and manage their own decisions.
- Ongoing assessment of capacity, clinical status, cognition and behaviour should be continued over the first 3 months with view to construction of an appropriate care plan, ARBD rehabilitation, referral to other agents (e.g. alcohol treatment services) or discharge as appropriate.

Pregnancy and FASD

- The dangers of alcohol consumption during pregnancy should be routinely explained to all who are either planning pregnancy or are expectant.
- Physicians should routinely ask about prenatal alcohol exposure as part of history taking in patients who appear to be displaying attention-deficit hyperactivity disorder (ADHD) symptomatology but who may have FASD.
- Treatment plans should be targeted towards families, emphasising early education.
- Interventions should be tailored to the needs of the individual: specific interventions of known efficacy include parent- or carer-assisted children's friendship training (O'Connor *et al*, 2006).
- Child and adolescent neuropsychiatric/neuropsychological teams should play a central role in the initial assessment and diagnosis of these conditions, and the development of specialisation and specialist centres should be considered so as to facilitate early diagnosis and intervention.

Lay summary

The term alcohol-related brain damage covers a wide variety of conditions that affect the brain and nervous system. Patients will present with acute confusion, often as a consequence of alcohol withdrawal. The confusion may be more permanent when associated with severe physical illness and malnutrition, as a consequence of vitamin B1 deficiency.

The more long-lasting confusional states will vary in severity and when more severe, may present as a condition called Korsakoff's syndrome, which is relatively rare in its true form. This is characterised by significant problems in both long- and short-term memory and is often associated with problems in balancing, changes in eye movements and the experience of false memories (confabulation) in which the patient will mix up past experiences with current circumstances and may 'remember' quite complicated events which have never happened. Other forms of ARBD are more common. The most common type relates to problems with the front part of the brain, responsible for bringing together memories and experiences from the past, sorting them and using them to help the individual to make judgements and decisions relating to their immediate circumstances as well as the future. In undertaking this exercise, the brain has to understand information, process it, weigh it up, assess it in the context of previous experiences and come to a decision. Further, control of social behaviour may be compromised and the condition may be associated with impulsivity. Necessarily, this part of the brain is very important in making decisions relating to planning, risk assessment, implications of behaviour, social responsibility and understanding other people's feelings.

Women who drink more than 28 standard drinks (a minimum of 28 units a week) and men who drink 35 standard drinks (a minimum of 35 units a week) for 5 years or longer are likely to experience some changes in their intellect, even though many will not be aware of it. However, carers, relatives and other people may notice this and it may jeopardise work, family relationships and domestic and financial issues. Usually the person's intellect will recover over a period of 3 months of complete alcohol abstinence. However, even when abstinent, a combination of long-term alcohol misuse-associated health problems and vitamin deficiency may well result in longer-standing intellectual problems, some of which may improve over a subsequent 2–3 years of abstinence. A small minority will be left with significant brain damage and will require long-term care in an institution (approximately 25% of people presenting with severe ARBD).

Lack of experience in the assessment of brain damage, the stigma associated with long-term alcohol misuse and the lack of understanding by health professionals mean that the condition is rarely identified by clinicians. Consequently, in the UK few services exist designed to cater for people with ARBD. Patients describe being 'passed from pillar to post' and not receiving appropriate care, and often being placed in nursing homes designed for older people. Such patients often experience multiple admissions into acute medical care, fail to benefit from alcohol treatment services and die prematurely. This is particularly tragic, as most individuals will improve with appropriate care. When referred to appropriate services, the use of acute hospital beds can be reduced by up to 85%, the quality of life of patients is greatly enhanced and many will continue to live relatively independent lives in non-institutional settings.

This report has been devised to provide information for service commissioners and providers in the assessment and management of people presenting with ARBD. The introduction (p. 12) provides an overview of the nature of ARBD and describes the three types of related intellectual deficit.

Defining and categorising the problem

Classification of ARBD remains a problem for commissioners and service providers. The main criteria by which mental illnesses are identified are the *International Classification of Diseases* published by the World Health Organization and the *Diagnostic and Statistical Manual of Mental Disorders*, the US equivalent. Both these diagnostic systems fail to provide a unified diagnostic category for ARBD. Consequently, patients with ARBD can be categorised variably, with no one diagnosis providing a suitable category. In particular, the concept of 'dementia' has been incorporated within some of the criteria and this has connotations of irreversible progression, which is not the case in ARBD when the patient retains abstinence. Hence, we have adopted the well-recognised term of alcohol-related brain damage to provide an 'umbrella' term for the wide variety of chronic psychoneurological diseases that are a consequence of direct and indirect alcohol misuse and vitamin deficiency. The term is flexible enough to accommodate the 25% of patients presenting with concomitant small vessel disease of the brain (minor strokes, often 'silent', but potentially affecting intellectual performance) and head trauma, in people with previously established ARBD; both common complications of long-term alcohol misuse.

The size of the problem

The number of people with ARBD is very difficult to estimate as many patients are not diagnosed, so a diagnosis is not recorded in medical records and consequently not identified in audits of notes and records. This is an important issue, as many commissioning agencies will want some 'evidence' of the size of the problem if they are to commission services. Any clinical audit is likely to generate a significant underrepresentation of numbers presenting with ARBD. The best evidence indicates that between 0.5 and 1.5% (0.5% in the UK) of the adult population will have changes in their brain as a consequence of excessive alcohol misuse (this information is taken from large post-mortem studies of people in a variety of countries). From a pragmatic perspective, the Wirral specialised services, catering for a population of about 300 000 people, receive approximately three referrals a month from acute hospital care. These patients represent the most severe forms of ARBD and have been admitted into acute care with profound confusion and disturbance. It is also likely that a significant number of people with recurrent admissions to accident and emergency as a direct or indirect consequence of alcohol misuse will have some evidence of ARBD. Likewise, people who are long-term alcohol misusers and attending alcohol treatment services are vulnerable to malnutrition and low vitamin intake and are likely to experience some brain changes of a temporary or permanent nature. Other populations that may be at high risk are prisoners.

Drug management

ARBD is associated with structural and chemical changes in the brain in areas that influence memory and the frontal lobes. These changes are consistent with the clinical findings and reflect the severity of the condition. Notably, as the intellect of patients improves through abstinence and appropriate care and treatment, so do the brain changes, as visualised by scans. This report focuses on the chemical changes that have been found in the laboratory and real-life situations and that contribute to our understanding and medical treatment of ARBD. The main focus of attention is glutamate, a naturally occurring chemical in the body that is responsible for conducting chemical messages between the relevant brain cells. It is evident that this chemical is adversely affected in alcohol misusers undergoing withdrawal. The immune and inflammatory systems of the body also offer an attractive area for further research. These chemical models provide a background by which we can understand the action of some of the drugs used in managing maintenance of alcohol abstinence and provide a springboard for further research.

The main importance of drug treatment lies in the management of detoxification of the patient presenting while in alcohol withdrawal. Well-evidenced

research indicates that alcohol withdrawal should be managed with the support of drugs, either in community or hospital settings. Drug management will reduce the likelihood of ARBD for the individual. Likewise, it is critical that vitamins are given so as to reduce the likelihood of ARBD. In particular, vitamin B1 is known to have protective properties and is often given intravenously during the acute phases of withdrawal. However, other vitamins should be considered as many such patients are malnourished and are particularly prone to damage as a consequence.

There are a variety of drugs that can be used to help individuals to maintain abstinence. Some of these may reduce craving and some may make the patient feel unwell and vomit if alcohol is taken after the drug. Most of these drugs are prescribed through the advice of specialist services and are usually given in the context of ongoing counselling and psychological support. It is very important to continue providing vitamin supplementation and it may have to be provided by injection (to help absorption and compliance) if the individual is at high risk of alcohol misuse relapse and brain damage.

Psychosocial management

Service delivery and organisational issues

The main problems facing patients with ARBD include significant stigma and the lack of knowledge concerning the condition in health and social care communities. This has been described by patient groups and researchers and both issues contribute to the lack of service provision and pathways of care. These problems are reflected in the absence of significant national guidance from either the Department of Health or the National Institute for Health and Care Excellence (NICE), or the Scottish Intercollegiate Guidelines Network (SIGN). Notably, there have been a number of documents commissioned by the Scottish Government which have made recommendations relevant to ARBD, including *A Fuller Life* (Cox *et al*, 2004), *Delivering for Mental Health* (Scottish Executive, 2006) and the Mental Welfare Commission (2010a) report. As a consequence of the lack of guidance, there is little motivation or understanding of the importance of developing local service provision. In the absence of recorded diagnosis, pathways of care and advocacy, services are usually non-existent or default and inappropriate at best.

Service models

A few examples of service provision have been documented and inform this report (see pp. 63–72). The evidence suggests that a specialised model provides the best long-term outcome for patients. In this context the term 'specialised' really means cultivating a resource and provision with experience in managing this group of patients. This resource may be a 'specialist' clinician (nurse, occupational therapist) based in a community mental health team, with access to other members of the team as required. This model has been described in the literature as a potential service model (MacRae & Cox, 2003) but no specific examples have been reported. An alternative model includes embedding a specialised team within another established service, such as a dementia team or affiliation with the local alcohol treatment service. Examples of these models exist. Yet another model is available (Fife, see pp. 63–66) in which a core team has been established with open access to expertise in other community teams as required. These three descriptions imply a degree of success in providing services in each locality. An alternative model describes the commissioning of neuropsychiatric services to provide a robust platform for the delivery of such a service (such an arrangement has been reported in London). Alternative, 'specialised' service provision may be found in the private sector, providing a range of 'in-house' services, including institutional care, residential, supported living and domestic support. Again, these are relatively rare and may not cater for geographical needs of the population or be linked to local mental health and alcohol treatment services.

Institutional care

Even though not essential for all patients with ARBD, the role of institutional care should also be considered. It is evident that small units offering personalised care planning and rehabilitation do play an important role. It is also important that the

default placement of individuals in age-inappropriate nursing homes is associated with increased disability and poor prognosis in most cases.

Institutional care in non-hospital settings can play a number of roles. It can provide safety and care for patients who are mentally incapacitated and unable to care for themselves either in the short or long-term. It provides a mechanism by which patients can be quickly discharged from acute medical care (once their physical state has been stabilised) and assessed over the first 3 months, during which a significant majority will improve. Specialised institutional care can provide a rehabilitation programme with a view to optimising self-care, autonomy and independence, and rehabilitating the patient into less dependent, non-institutionalised community placements. Two examples of this are evidenced within the document (see p. 38).

Institutional care does not necessarily have to be specialised provided there is appropriate funding to provide additional personalised care (when necessary) under the supervision of an experienced clinical team. Service examples exist in which the small, independent, private institutions, already working with adults of working age, have been trained through supervision from a specialised National Health Service (NHS) team (Wirral ARBD service). This approach has the advantage of having an innate flexibility and being potentially responsive to a changing 'market' environment. It also facilitates 'person specific' care plans through enabling a wider choice of institutional settings, rather than being confined to a 'one institution fits all' model. However, such a model does require an appropriately resourced team and funding packages (examples of this can be found in Glasgow, where training packages are offered to home care workers). Likewise, residential and home workers are supervised and trained with the support of specialist services in the Wirral.

Psychosocial treatments

These fall into two components. First, on a general note, cognitive rehabilitation should be subjected to a care plan, with support of a multidisciplinary team. The main drivers are to be collaborative, to progressively enhance independence and to optimise the environment so as to assist the individual and maintain abstinence. There are a variety of techniques designed to facilitate this approach. They principally draw on providing a structured plan with clear goals for the individual, facilitating a gradual improvement in autonomy and providing increased social support and networking. Engaging family and friends plays an important role in the care plan, as is the continued monitoring of mental capacity and alcohol education and management. In general, the rehabilitation of severe cases of ARBD can be described within five 'phases' or stages (see pp. 33–34 for further discussion). First is the acute physical stabilisation, followed by a period of fairly rapid improvement. These two phases are followed by a longer period of gradual improvement through rehabilitation, ending with an adjustment of the living environment to cater for residual cognitive damage, and a longer-term follow-up to prevent relapse and enhance socialisation. The role of charitable organisations is emphasised with recommendations for referral to Headway (www.headway.org.uk), or other relevant support services.

Mental Capacity Act 2005 and Adults with Incapacity (Scotland) Act 2000: implications

One of the most important issues to take into consideration is the fact that patients with ARBD have the potential of having a serious mental illness and should not be considered as experiencing 'just' alcohol dependency. The MCA and the AwIA make it quite clear that patients do not have mental capacity if through reason of mental disability they are unable to understand information relating to a decision about to be made, retain the information, use or weigh the information as part of a decision-making process and communicate their decision and act on it (AwIA). In undertaking a capacity assessment, it is important to be able to demonstrate mental disability. In non-experienced hands, this might be undertaken with well-proven instruments of which there are a number to choose from. It is in the context of this assessment that the

individual should be facilitated in the decision-making process.

ARBD may affect memory. In particular, the individual may not be able to remember conversations that have taken place within the past few minutes, with varying degrees of rapidity of memory loss. They may have difficulty in recalling memories from the past, so that they are unable to recall the effect that their actions have had on their physical, mental and social well-being and, consequently, they may not be able to evaluate and learn from their actions. They are often prone to experiencing false memories (confabulations) so as to try and make sense of their circumstances. Likewise, ARBD frequently affects the front part of the brain which is responsible for synthesising information, understanding abstract concepts such as risk assessment and the implications of decision-making and impulse control. Such patients are highly suggestible and often vulnerable to social abuse and neglect.

Special groups

Alcohol treatment services

It is anticipated that the NICE guidelines (National Institute for Health and Clinical Excellence, 2011) recommending that alcohol treatment services undertake a psychological, social and cognitive assessment of new patients presenting to services will enable the identification of a small group of patients with varying degrees of ARBD. This report draws on evidence relating to the intellectual problems likely to be experienced by these patients and recommends psychological and educational adaptations to alcohol treatment programmes. Patients attending alcohol treatment services should have an assessment within a week or two of referral so any implications for clinical management can be anticipated and catered for. However, it is likely that the majority of patients with intellectual impairment will recover over the first 3 months of abstinence. Ongoing assessment is indicated in those with residual damage and patients who are finding it difficult to engage and who may be mildly impaired. A minority of patients will experience prolonged intellectual impairment and may need more intensive, long-term follow-up. A small minority may display severe degrees of intellectual problems that impinge on mental capacity and present a significant risk of self-neglect, vulnerability or self-harm. Such patients warrant referral for advice, specialised assessment and management.

Prison services

It is well known that a lot of prisoners experience mental illness and it is anticipated that a significant minority of prisoners will have varying degrees of ARBD. A considerable proportion of these individuals will improve through abstinence. It is recommended that routinely employed alcohol misuse screening instruments are used to identify people at risk when admitted to prison. These individuals should be reassessed a second time after they have settled into prison routine. If they are found to show intellectual impairment prior to release, then they should be referred to appropriate external service.

Acute hospital services

The main problem facing assessment and intervention in the context of acute hospital provision is the high-level turnover and rapid discharges required and expected by both service providers and commissioning agencies. Consequently, any service provision must be responsive and rapid if it is to provide a valued service. It is also evident that many people with ARBD are not picked up by medical and surgical teams. As a consequence, it is recommended that a simple cognitive screening instrument or instrument designed to identify high-risk patients (Wilson *et al*, 2012) is used by ward staff or liaison teams and further assessment is provided quickly and efficiently. It is important that patients are discharged to appropriate settings as soon as the physicians/surgical teams have stabilised or managed their physical state. Commissioning arrangements should cater for this, in facilitating access to funds quickly for a further period of assessment in a non-acute hospital institutional setting or other community settings as determined by patient needs and discharge planning. It is important that the specialist team is involved in this discharge procedure so as to facilitate appropriate placement and follow-up. Where necessary, the patient's mental capacity should be assessed and the patient should be supported in working with the team and carers in provision of an

appropriate discharge plan. During the following 3 months it is important that the patient maintains abstinence so that appropriate assessments can inform longer-term care planning.

Pregnancy and fetal alcohol spectrum disorder (FASD)

FASD is thought to be relatively common and alcohol ingestion during pregnancy is acknowledged as being one of the most frequent causes of birth defects in the world. Notably, there is some evidence indicating that the quantity or frequency of alcohol ingestion during pregnancy is not directly associated with the syndrome, implying the importance of other factors such as genetics. Advanced maternal age, poor nutrition, low socioeconomic status, frequent binge drinking, psychiatric diagnosis and high gravidity and parity have also been found to be risk factors. As is the case with ARBD in adults, FASD is underdiagnosed and may present with a variety of problems. Physical problems are common but the condition may present in the absence of obvious physical complications. Varying degrees of intellectual, damage and developmental issues are usual. Notably, the condition is associated with attention-deficit disorders and other mental health problems in later life. What evidence there is indicates that early diagnosis and specialist psychotherapeutic intervention plays an important part in helping families and those affected. The need to educate expectant mothers and those planning pregnancy is emphasised.

Introduction

Patients with ARBD present with variable psychosocial problems. They are likely to be aged 40–60 and experience concomitant brain damage associated with head trauma (Tarter & Edwards, 1986; Jones, 1989; Weinstein & Martin, 1995) and cerebrovascular disease (Woodburn & Johnstone, 1999). They are usually physically active and prone to high levels of fire hazard, agitation, disinhibition, delusional experiences (Ferran *et al*, 1996) and aggression (Harvey *et al*, 1998) when compared with patients in the same age group with dementia syndrome.

ARBD may be characterised by more subtle and much less specific cognitive damage than the classical Wernicke–Korsakoff syndrome. Frequently, there is relatively little evidence of anterograde amnesia (Torvik *et al*, 1982; Harper *et al*, 1986; Bowden *et al*, 1995). A major feature of presentation is the frontal dysexecutive syndrome (Ihara *et al*, 2000) involving the prefrontal and temporal areas of the cortex and related circuits. In particular, primary functions of goal-setting, reasoning, memory, strategic planning, response inhibition and processing environmental feedback can be affected (Luria 1973; Goldman-Rakic, 1987; Cummings, 1995), with implications for impairment of social awareness (Ukerman & Daum, 2008) and increased risk behaviour (Bjork *et al*, 2008). These findings are consistent with studies of structural imagery. The onset may be gradual and it is probable that most cases are relatively mild (Lishman, 1998). Significant cognitive impairment is frequently identified within acute hospital settings or through critical situations within the community (Smith & Hillman, 1999; Elleswei, 2000). However, many cases will not come to the attention of healthcare professionals; consequently, the estimated impact on health and social care services is almost certainly underrepresented (Thomson *et al*, 2002). A patient presenting with uncomplicated, acute post-withdrawal confusion or encephalopathy is likely to experience varying degrees of recovery and their rehabilitation is characterised by five phases (see p. 9, Psychosocial treatments).

Acute physical care

There is likely to be a period of acute confusion associated with encephalopathy, withdrawal and unstable physical illness. The duration will be informed by concomitant physical illness and may stretch to days or weeks. During this period the patient is being withdrawn from alcohol, should be treated with thiamine as recommended by guidelines and treated medically/surgically as appropriate. As with other delirious states, patients may be aggressive, have significant and fluctuating cognitive profile and may manifest significant psychiatric and behavioural problems.

Stabilisation

Cognitive state is likely to improve in a few weeks (Cocchi & Chiavarini, 1997a,b). After 3–6 weeks of abstinence, recovery appears to level off, with the most significant gains being made during this period (Grant *et al*, 1986). It is apparent that cognitive functions will vary in rate of recovery (Sullivan *et al*, 2000). This period is reflected in Oslin's Alcohol Dementia Criteria (Oslin & Carey, 2003), which allow for a period of approximately 3 months, after which the patient should be assessed to evaluate more long-standing cognitive deficits. During this early stage patients are often incapacitated in terms of making decisions relating to alcohol ingestion, self-care and domestic arrangements. Fluctuating cognitive disorders such as disorientation, amnesia, confabulation and behavioural disturbance frequently present. These cause problems in placement and care. Most patients will remain on the acute medical ward for considerable periods of time as a consequence of their psychiatric presentation. Such patients frequently require one-to-one supervision and management should be considered in the context of the appropriate legal framework (e.g. MCA, AwIA).

Transient, time-limited damage

As the acute presentation resolves with stabilisation of the presenting physical state, longer-term cognitive, functional and behavioural problems become evident and may take 2–3 years to resolve. This period is characterised by time-limited cognitive impairments (Bates *et al*, 2002) which are prone to spontaneous recovery (in the context of an alcohol-free environment), during which there is notable improvement in cognitive function. Controlled follow-up studies of abstinent alcoholics, using both structural and functional magnetic resonance imaging (MRI) have demonstrated brain modification reflecting this improvement (Sullivan & Pfefferbaum, 2005; Bartels *et al*, 2007); however, patients with additional pathologies (such as concomitant vascular lesions) failed to show as much improvement. There is evidence that some of the improvement may be related to general improvement in health and nutrition. Bates *et al* (2002) identify uncertainty relating to varying rates of improvement in different cognitive domains. Generally, verbal recall deficits appear to resolve within a few weeks, whereas memory, abstraction and perceptual motor skills may take a year or more. Other frontal lobe functions may take longer. There is some laboratory evidence indicating that specific cognitive training may improve cognitive performance. However, Bates *et al* (2002) surmise that any cognitive training has a non-specific effect and can be enhanced through 'ecological' and patient-specific rehabilitation. There is also some descriptive evidence indicating that specifically commissioned services may improve long-term outcomes for these patients. From a social and functional outcome perspective, at least three studies report follow-up data.

Price *et al* (1988) followed up for 1 year 37 patients discharged into the community without 'specialised' support. Ten of these patients (27%) were known to be successfully placed, a further 20 (54.1%) were described as dysfunctional and the remaining 7 died. Two years earlier, Lennane (1986) followed up 104 patients for between 8 months and 2 years, all followed up by a specialised team; 53 of these patients were classified as successful placements, 11 (10.6%) had been readmitted into hospital and the remainder were lost to follow-up or presumed dead. Both these studies took place in Australia. In a more recent study, Wilson *et al* (2012) followed up 41 severely affected patients within a specialist service for an average of 25 months and demonstrated a 10% mortality and a 10% relapse rate; 32 patients were either being actively rehabilitated or settled into appropriate community settings.

Long-standing damage

There are no longer-term follow-up studies of patients presenting with ARBD. In terms of outcome defined by satisfactory placement in appropriate social settings, Cox *et al* (2004) derive information from Victor's work of 1971 (Victor *et al*, 1971) and suggest that 25% of patients with ARBD make a full recovery. A further 25% make a partial recovery, with another 25% making minor recovery, and the remainder show no improvement at all. It is evident that ARBD is associated with significant relapse and mortality rates but the majority of patients may benefit from long-term follow-up, ongoing management of alcohol issues, appropriate nutrition and psychosocial care planning.

Summary

There is no doubt that the evidence base relating to the longer-term management of ARBD is poor. There are very few high-quality randomised controlled trials (RCTs) and most of the literature is of a descriptive nature and based on anecdotal reports. However, the surveys that have been conducted indicate that a significant and relatively small group of patients with severe ARBD is being denied access to service provision through potential stigma, lack of professional leadership and awareness of both commissioning agencies and service providers. Even though there may be relatively few patients with severe ARBD, they are very heavy users of acute secondary care and what evidence there is suggests that relatively simple interventions can enhance independence and quality of life and reduce the need to access NHS beds.

Clinical definition and diagnosis of alcohol-related brain damage and related syndromes

Syndromal presentations

In discussing ARBD, there are syndromes which are principally of a neurological nature, characterised by physical signs and symptoms. Second, there are syndromes which may be termed neuropsychiatric, in that they are predominantly characterised by cognitive, affective or personality change. These neuropsychiatric syndromes may, in turn, be subdivided into the acute/subacute and the chronic types (Kopelman, 1991).

Within the ambit of neurological syndromes are included:

- acute/chronic dysarthria and/or ataxia
- seizures resulting from alcohol withdrawal, hypoglycaemia, cerebral damage (e.g. following head injury) and the precipitation of epilepsy
- peripheral neuropathy
- various degenerative syndromes, e.g. of the corpus callosum (Marchiafava–Bignami disease), central pontine myelinolysis, cerebellar atrophy and retrobulbar neuritis and/or optic atrophy.

These neurological syndromes are discussed elsewhere (David *et al*, 2009) and will not be considered further in this document.

The acute/subacute neuropsychiatric syndromes include:

- acute withdrawal syndromes and delirium tremens
- alcoholic hallucinosis
- alcoholic blackouts
- Wernicke's encephalopathy
- hepatic encephalopathy
- alcoholic pellagra encephalopathy.

Chronic neuropsychiatric syndromes include:

- a coarsening of personality, partly the consequence of frontal lobe dysfunction
- the alcoholic Korsakoff's syndrome
- cognitive deterioration associated with cortical atrophy, sometimes labelled 'alcoholic dementia' but, perhaps, better known as alcoholic brain damage.

These syndromes will be considered in turn.

Acute/subacute syndromes

Delirium tremens

In delirium tremens, there is commonly a prodromal syndrome characterised by anxiety, sleeplessness, tremor, tachycardia and increased perspiration with sweaty palms. This is followed by the delirium, consisting of disorientation, a fluctuating level of awareness, hallucinosis, misperceptions and a

sense of intense fear, and by the 'tremens' consisting of tremor, motor restlessness and autonomic overactivity. The hallucinations can be visual, in which case they often consist of small animals or insects; they can be tactile; and they can be auditory, in which case they are often threatening and persecutory. They are characterised by an intense reality and commonly produce a sense of terror in the individual. The autonomic overactivity involves increased psychomotor activity with tremulousness, agitation, intense perspiration and dehydration, and tachycardia with a weak pulse. The onset of the disorder usually occurs 2–4 days after alcohol withdrawal and is associated with the presence of infection or trauma in 50% of cases (Lundquist, 1961). The episode usually terminates in a prolonged sleep after 3 days or less. Mortality rates are said to be approximately 5%. Where mortality occurs, this usually results from cardiovascular collapse or concurrent infection. Treatment involves fluid and electrolyte replacement, sedation and high-potency vitamin replacement (Chick, 1989).

Alcoholic hallucinosis

This was first described by Wernicke in 1900. Kraepelin in 1913 differentiated alcoholic hallucinosis from delirium tremens in terms of:

- the absence of disorientation
- a predominance of auditory hallucinations
- a reduced amount of agitation and arousal
- a longer duration of the disorder.

In addition, it is appropriate to add:

- that the disorder is not obviously related to alcohol withdrawal, and
- that the delusions are commonly said to be secondary to hallucinations.

In this condition, auditory hallucinations are by far the most common, often of derogatory or sexual content, but quite frequently in the third person (Cutting, 1978). Secondary delusions are also commonly present. Some patients are misdiagnosed as having schizophrenia and are kept on antipsychotic medication for prolonged periods, but other patients may, in fact, develop a schizophrenic disorder (in the absence of further alcohol intake) at a later stage.

Alcoholic blackouts

Acute alcohol-related memory loss is said to occur in three forms, which probably reflect a continuum of severity (Goodwin *et al*, 1969). **State-dependent phenomena** have been reported in individuals claiming blackouts. In such instances, the person may hide money or drink when intoxicated, cannot find it when sober, but goes straight to it again after heavy drinking. **'Fragmentary' blackouts** have been reported in 64% of hospitalised alcoholics by Goodwin and colleagues. In this form of blackout, there is no clear demarcation of the onset or termination of the memory loss, and there are very commonly 'islets' of preserved memory within the amnesic gap. The amnesic gap tends to shrink through time, in a similar fashion to recovery from a head injury. Finally, **'en bloc' blackouts** have a very definite onset, and they end with the person waking up and/or coming round with a sense of 'lost time'. There are usually no islets of preserved memory, and the memories do not recover through time. The memory loss can occur for a period of a few minutes or hours, and occasionally it lasts for a few days, giving rise to a fugue-like state, in which the person may go wandering, sometimes travelling substantial distances and booking into hotels, before he or she 'comes round' unaware of what has been happening during the period of the blackout.

Blackouts appear to be most closely related to:

- an early onset of the drinking history
- high peak levels of alcohol
- a history of frequent head injuries.

Wernicke's encephalopathy

This syndrome, first described by Wernicke (1885), consists of ophthalmoplegia, nystagmus, ataxia and confusion. It is often, but not necessarily, accompanied by peripheral neuropathy. The full syndrome is seen relatively rarely, in part because the ophthalmoplegia responds well to treatment and recovers relatively rapidly, as does the confusion. Notably, only 16.5% of cases present with all criteria (Harper *et al*, 1986). Although they have closely overlapping neuropathology, Wernicke's encephalopathy does not necessarily terminate in Korsakoff's syndrome, and Korsakoff's syndrome does not necessarily follow Wernicke's encephalopathy.

Wernicke's encephalopathy can result from a variety of disorders other than alcohol misuse, all of which result in poor intake or absorption of thiamine, such as gastric carcinoma, other gastrointestinal carcinoma, hyperemesis of pregnancy, haemodialysis, anorexia nervosa and other malignancy (see Kril & Harper, 2012). The syndrome is a medical emergency and patients can die from accompanying features of beriberi, including high-output cardiac failure. Untreated, it leads to death in up to 20% of cases or to Korsakoff's syndrome in the 85% of survivors. Up to 25% of the Korsakoff group will require long-term institutionalisation. When Wernicke's encephalopathy is suspected, treatment with high-dose parenteral thiamine and other B vitamins should be given promptly to offset the risk of death or the development of Korsakoff's syndrome (see also Kopelman *et al*, 2009). Parenteral thiamine needs to be given at first contact with the patient and before i.v. glucose which can precipitate the condition.

It is evident that Wernicke's encephalopathy is a fairly rare syndrome when confined to its full, classical presentation. Consequently, the term Wernicke's encephalopathy has become more generic in its use. Caine *et al* (1997) used the following criteria to operationalise the identification of Wernicke's encephalopathy: dietary deficiencies, oculomotor abnormalities, cerebellar dysfunction, and either altered mental state or mild memory impairment. Notably, only two of these symptoms need to be present to establish an operational definition.

Hepatic encephalopathy

Hepatic encephalopathy is a form of delirium which can develop in patients with both acute and chronic liver disease. Rarely, in acute liver disease such as fulminant hepatic failure from viral hepatitis, the condition (type A hepatic encephalopathy) rapidly progresses to deep coma from the development of profound cerebral oedema, which over the course of a few days can progress to coning and death. Much more commonly, hepatic encephalopathy complicates chronic liver disease such as portal systemic bypass (type B hepatic encephalopathy) or cirrhosis (type C hepatic encephalopathy), usually in combination (Masson *et al*, 2008). In these cases the condition may be episodic, when typically delirium develops and resolves over a few days, or persistent, when abnormalities of behaviour or cognition can be present over months or years. When cognition alone is affected, the condition is classified as minimal and diagnosis is dependent on psychometric assessment (Mardini *et al*, 2008). In patients with hepatic encephalopathy it is the recognition of liver disease in association with an elevation in blood ammonia which is the key to diagnosis.

Patients with type B and C hepatic encephalopathy have evidence of mild cerebral oedema (Mardini *et al*, 2011), which may also contribute to the neurological abnormalities, although the precise pathogenesis is uncertain (Haussinger & Schliess, 2009). In addition to ammonia, the accumulation of several toxins has been considered, including aromatic amino acids, mercaptans, short-chain fatty acids and endogenous benzodiazepines. There is also an imbalance between the neuroinhibitory GABAergic and excitatory glutamatergic transmitter systems. In patients with chronic liver disease, hepatic encephalopathy is typically precipitated by clinical complications of liver disease such as variceal bleeding, systemic infections and diuretic-induced electrolyte disorders, and these in turn may be associated with the development of neuroinflammation. In overt hepatic encephalopathy there is fluctuating delirium accompanied by neurological signs, including a flapping tremor of the hands (asterixis) and (classically) constructional apraxia. Warning signs include a fixed, staring appearance and reduction of spontaneous movements, as well as hypersomnia. There may be a sweet-smelling odour on the breath. Although predominantly a neuroinhibitory condition, at times there may be abrupt mood swings, irritability or disinhibition (Lishman, 1998; Werring *et al*, 2009). Since 80% of liver cirrhosis is due to alcohol misuse, the differentiation of persistent and minimal hepatic encephalopathy from ARBD can be extremely difficult, as alcohol-related brain atrophy (Amodio *et al*, 2003) correlates with psychometric and electroencephalographic abnormalities. Reassuringly, however, liver transplantation is associated with a 6 s.d. improvement in psychometric performance (Mardini *et al*, 2008). The blood ammonia response to amino acid or urea challenge (Mardini & Record, 2013) and associated magnetic resonance changes (Mardini *et al*, 2011) may prove helpful when there is diagnositic difficulty.

Alcoholic pellagra encephalopathy

An alcohol-induced pellagra encephalopathy, resulting from nicotinic acid depletion, has been reported, particularly in France where the combination of thiamine and pyridoxine rather than multivitamins was commonly given to alcoholics (Serdaru *et al*, 1988). Clinical features are a fluctuating confusional state involving global memory loss, visual hallucinations, restlessness alternating with apathy, and various physical signs (myoclonic jerks, hyper-reflexia, absent postural reflexes, a marked oppositional hypertonus and a rash on the back and chest). Clouding of consciousness can range from stupor to coma, and the confusional state is seen in all patients. Electroencephalography is always abnormal with bilateral slow-wave activity. Pathological features are neuronal chromatolysis (i.e. an enlargement of neurons with a reduction in size and eccentric placement of the nuclei), sometimes accompanied by degeneration of the corpus callosum and/or atrophy of the mammillary bodies and lesions in the thalamus. Occasionally, a syndrome resembling the Wernicke–Korsakoff syndrome may be manifest (Lishman, 1981).

Chronic syndromes

Coarsening of personality

The characteristic coarsening of personality, seen in chronic alcoholics, involves a loss of social, and sometimes sexual, inhibitions and a tendency to irritability, a facile jocularity, and abusiveness. This is not necessarily related to acute intoxication. The consequences of this include: family disruption (violence in the home and marital separation); an increased rate of accidents at home, work and on the road; and increased rates of absenteeism, redundancy, offending and vagrancy. Sexual impotence may also develop. Sometimes, the syndrome of 'morbid jealousy' may emerge. This personality change is commonly associated with frontal lobe atrophy, apparent on computed tomography (CT) or MRI brain scans and can be regarded as part of the dysexecutive syndrome – linking evidence of frontal lobe damage, following repeated cycles of intoxication and withdrawal in the context of chronic alcohol dependence.

The alcoholic Korsakoff's syndrome

Three comments should be made about the definition of the syndrome given in Box 1. First, no reference is made to 'short-term'/'long-term' memory, or to the extensiveness or pattern of the memory deficit. In fact, immediate recall of small quantities of information (so-called 'primary' or 'working' memory) is characteristically preserved, whereas the retrograde memory deficit may extend back many years or decades, as Korsakoff himself pointed out and as has been confirmed in modern experimental studies. Second, no reference is made to confabulation. 'Spontaneous confabulation', involving the fluent outpouring of erroneous material, is seen usually only in the (Wernicke) confusional state; and confabulation is by no means pathognomic of the chronic Korsakoff phase. Third, the emphasis is on the memory deficit being 'out of all proportion' to other cognitive impairments, although how this is defined remains controversial. It is also notable that the definition excludes executive dysfunction, which has been shown to be an early and chronic sign of ARBD (Ihara *et al*, 2000).

The classical neuropathology of what Victor *et al* (1971) termed 'Wernicke–Korsakoff syndrome' involves microhaemorrhages and endothelial proliferation (i.e. rupture and abnormal changes in the lining of blood vessels), together with focal areas of parenchymal necrosis, demyelination, gliosis and variable degrees of neuronal loss (i.e. degeneration of brain cells and tissue and nerve fibre linings with associated scarring). These abnormalities mainly occur in the so-called 'diencephalon', involving paraventricular and peri-aqueductal grey matter, the walls of the third ventricle, the floor of the fourth ventricle, and the cerebellum (i.e. deep midline and midbrain structures). Victor *et al* (1971) argued that the critical lesion site for the production

Box 1 Korsakoff's syndrome – definition

- **Korsakoff's syndrome can be defined 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, resulting from nutritional depletion, i.e. thiamine deficiency' (Kopelman, 2002; Kopelman *et al*, 2009).**

of memory deficit was the medial dorsal nucleus of the thalamus. However, three more recent studies have argued that atrophy of the mammillary bodies, together with concomitant lesions in the mammillothalamic tract and the anterior thalamus are the critical factors resulting in the memory disorder (Mair *et al*, 1979; Mayes *et al*, 1988; Harding *et al*, 2000). Sullivan & Pfefferbaum (2009), following a series of investigations, have beautifully illustrated signal alteration and/or atrophy in these key brain regions.

Long-term cognitive deterioration

As is clinically familiar, many patients manifest more widespread cognitive impairments of varying severity. This has been demonstrated and investigated in many studies. Aside from deficits in anterograde memory, there are commonly impairments in executive function, attention, speed of processing, visuospatial skills and performance IQ. Women are particularly vulnerable to cognitive impairments at a younger age and following a shorter drinking history (Acker, 1986).

These more widespread deficits are in part the consequence of the generalised cortical atrophy seen on CT and MRI brain scans, with particular involvement of the frontal lobes, which has been widely reported in alcoholics (Ron *et al*, 1982; Sullivan & Pfefferbaum, 2005), and which have also been well-described in neuropathological and histological studies (Harper, 2009).

Other pathologies also occur. This generalised cognitive decline was formerly described as a form of 'dementia', but it often arises from multiple underlying pathologies. Notably, there is an absence of the characteristic progressive neuropathology found in the established dementias of Alzheimer's disease and the frontotemporal dementias that can present in working-age adults. Characterisitic changes associated with ARBD include: recurrent head injury and haematomas, seizures, small-vessel disease, larger infarcts, hepatic toxicity, and concomitant smoking or other substance misuse, all of which are likely to be directly or indirectly of a secondary nature to the damage as a consequence of long-term alcohol misuse and associated vitamin deficiencies. Hence, the terms 'alcoholic brain damage' or 'alcohol-induced brain pathology' are preferable to 'alcoholic dementia'.

Impact on memory

As is well known, a distinction is usually drawn between so-called 'working memory', which holds and manipulates information for brief periods of time (a matter of seconds) and allocates resources, and secondary memory, in which information is stored on a permanent or semi-permanent basis. Secondary memory can, in turn, be subdivided into an episodic (or 'explicit') component, semantic memory and implicit memory. Episodic memory refers to incidents or events from a person's past (allowing the person 'to travel back mentally in time'), whereas semantic memory refers to knowledge of facts, concepts and language.

As described by Korsakoff (1889) himself, episodic memory is severely impaired in Korsakoff's syndrome, but other aspects of memory may be relatively preserved. Implicit memory includes classical conditioning, the procedural learning of perceptuomotor skills, and the facilitation of responses in the absence of episodic memory, known as 'priming'. Nicholas (2010) showed that these aspects of memory are preserved, or relatively preserved, in Korsakoff's syndrome, and a great deal of contemporary neuropsychological research has examined the dimensions of that preservation (Schacter, 1987; Migo *et al*, 2012). There is evidence that the contextual aspects of memory are particularly impaired in Korsakoff's syndrome (Pitel *et al*, 2008; Kessels & Kopelman, 2012), and that there is also an extensive retrograde amnesia, which can in some cases extend back 20–25 years before the onset of the Wernicke episode (Kopelman, 2008).

Although Korsakoff's syndrome is characterised by disproportionate impairment of memory relative to other cognitive functions, there is also evidence that impairments on executive tests are common in these patients, associated with frontal lobe pathology. Of particular importance is pathology in the orbitofrontal and ventromedial frontal cortices, as it is damage in these brain regions which is thought to be the basis of 'spontaneous' confabulation, where this occurs.

As discussed in a previous section ('Syndromal presentations', pp. 14–18), ARBD can give rise to a wide variety of more generalised cognitive

impairments, particularly involving executive function, attention, speed of processing, visuospatial skills and performance IQ, as well as memory.

Diagnosis and classification

Amnesic syndrome

ICD definition

The ICD-10 (World Health Organization, 1992) distinguishes between organic amnesic syndrome, not induced by alcohol or other psychoactive substances (F04), and amnesic syndrome, secondary to alcohol (F10.6) or other substances. This separation between neurological and alcohol-induced amnesic syndromes is in many ways unnecessary and unsatisfactory (Kopelman & Fleminger, 2002).

The amnesic syndrome secondary to alcohol or substance misuse is defined in ICD-10 as:

> 'a syndrome associated with chronic prominent impairment of recent memory; remote memory is sometimes impaired, while immediate recall is preserved. Disturbances of time sense and ordering of events are usually evident, as are difficulties in learning new material. Confabulation may be marked but is not invariably present. Other cognitive functions are usually well preserved and amnesic defects are out of proportion to other disturbances'.

The IDC-10 diagnostic guidelines specify that the

> 'amnesic syndrome induced by alcohol or other psychoactive substances […] should meet the general criteria for organic amnesic syndrome […] The primary requirements for this diagnosis are:
>
> (a) memory impairment as shown in impairment of recent memory (learning of new material); disturbances of time sense (rearrangements of chronological sequence, telescoping of repeated events into one, etc.);
>
> (b) absence of defect in immediate recall, impairment of consciousness, and of generalized cognitive impairment;
>
> (c) history or objective evidence of chronic (and particularly high-dose) use of alcohol or drugs.
>
> Personality changes, often with apparent apathy and loss of initiative, and a tendency towards self-neglect may also be present, but should not be regarded as necessary conditions for diagnosis.
>
> Although confabulation may be marked it should not be regarded as a necessary prerequisite for diagnosis.'

This definition lacks the grace, elegance and economy of that of Victor *et al* (1971):

> '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'.

A major problem is that ICD-10 does not allow easy classification of patients with disproportionate memory impairment relative to other cognitive function, secondary to alcohol but which falls short of an amnesic syndrome in severity. These are best categorised under 'mild cognitive disorder' (F06.7)

DSM definition

The classification in the DSM-IV (American Psychiatric Association, 1994) is much more satisfactory. 'Alcohol-induced persisting amnesic disorder' (291.1) is listed alongside 'amnesic disorder due to a general medical condition' (294.0), and diagnostic criteria for the former are given. These should include evidence of difficulty in learning new information and problems in recalling previously learned information. This memory impairment should be to such a degree that there is impairment and decline in occupational and social functioning. It is important to confirm that the memory impairment is not solely associated with a dementia, delirium or ongoing intoxication or withdrawal. There should also be evidence that the memory impairment is related to persisting effects of alcohol misuse as demonstrated by physical examination, the history or laboratory tests.

DSM-5 (American Psychiatric Association, 2013) incorporates amnestic syndrome under 'Substance/medication-induced major or mild neurocognitive disorder'. It differentiates between alcohol-related major neurocogntive disorder, non-amnestic-confabulatory type and amnestic confabulatory type. The plans for ICD-11 remain to be revealed.

Alcohol-induced dementia

In ICD-10, this is simply classified under alcohol-induced dementia (F10.73), for which the general criteria for dementia (F00–F03) must be

met. However, these earlier criteria reflect the characteristics of Alzheimer's dementia, rather than the patterns typically seen in alcohol-induced cognitive impairment. This is unsatisfactory.

DSM-5 has adopted the term 'neurocogntive disorder' as opposed to dementia. This diagnostic section is subdivided into 'delirium' (which includes substance intoxication and substance withdrawal delirium), and the major and mild cognitive disorders. These are subcategorised by cause, including the major progressive brain conditions such as Alzheimer's disease, traumatic brain injury, infections and substance/medication-induced major or mild neurocogntive disorder. The criteria for substance misuse neurocognitive disorder are:

1 The criteria are met for major or mild neurocogntive disorder.
2 The neurocognitve impairments do not occur exclusively during the course of a delirium and persist beyond the usual duration of intoxication and acute withdrawal.
3 The involved substance or medication and duration and extent of use are capable of producing neurocognitve impairment.
4 The temporal course of the neurocogntive deficits is consistent with the timing of the substance or medication use or abstinence (e.g. the deficits remain stable or improve after a period of abstinence).
5 The neurocogntive disorder is not attributable to another medical condition or is not better explained by another mental disorder.

Notably, it is important to specify whether the condition is persistent or not; persistence is defined as 'neurocogntive impairment continuing to be significant after an extended period of abstinence'.

The explanatory notes relating to diagnoses emphasise the likelihood of slow recovery after initiation of abstinence. In amnesic-confabulatory neurocogntive impairment (Korsakoff's) there is an emphasis on confabulation and it is frequently linked to Wernicke's encephalopathy (thiamine encephalopathy).

Clinical diagnosis of ARBD

One of the disadvantages of using the term dementia in relation to these conditions is that it implies a progressive or unremitting deterioration, which is not the case with ARBD when patients abstain from continuing alcohol misuse. This is an important distinction with potential implications for the commissioning of services (Smith & Atkinson, 1995). More recently, the term 'alcohol-related brain damage' (Lishman, 1998) has been adopted by Jacques & Stevenson (2000). ARBD is a clinical syndrome characterised by two seminal features: prolonged cognitive impairment and a causative link to excessive alcohol ingestion and thiamine deficiency. It covers a wide range of alcohol-related cognitive and neurological syndromes, including Wernicke's encephalopathy, Korsakoff's syndrome, alcohol dementia, cerebellar atrophy and frontal lobe dysfunction involving elements of both cortical and subcortical dysfunction (Schmidt *et al*, 2005).

From a practical, clinical perspective there are a number of issues which need consideration when defining the concept and providing guidance relating to the diagnostic process.

1 Patients presenting with ARBD will present with cognitive dysfunction which may include characteristics of Wernicke's encephalopathy/ Korsakoff's psychoses complex, but which may also include a more diverse cognitive presentation, of which frontal lobe signs and symptoms are the most common presentation. These symptoms may present either:
   - through an acute confusional state which may have manifestations of Wernicke's encephalopathy
   - in the context of long-term chronic presentation with variable cognitive dysfunction including frontal lobe dysfunction.
2 ARBD may resolve completely within the first 2–3 months of abstinence or there may be longer-term damage, usually related to concurrent thiamine deficiency or other complications.
3 Longer-term cognitive dysfunction associated with alcohol excess and thiamine deficiency can be classed into two domains:
   - non-permanent cognitive dysfunction that may take up to 2–3 years to resolve
   - residual permanent cognitive dysfunction.
4 A significant proportion of patients (25%) will present with evidence of cerebrovascular

disease and history of brain trauma (Wilson *et al*, 2012). The long-term effects of these concomitant disorders can only be resolved after a number of years during which more transient damage will improve. The adaptation of Oslin's criteria (Oslin & Carey, 2003) provides a pragmatic approach for identifying patients 'at risk' of ARBD and includes the possibility of co-occurence of vascular disease or trauma secondary to the onset of the condition.

Criteria for the clinical diagnosis of probable long-term ARBD include evidence of cognitive impairment (as demonstrated by clinical examination or use of appropriate instruments) and significant alcohol use as defined by the minimum average of 35 units for women and 50 units for men per week (modified from Oslin's criteria that employ 'standard alcoholic drinks'), for a period of more than 5 years. The period of significant alcohol use must occur within 3 years of clinical onset of the cognitive deficits.

The diagnosis of ARBD is supported by the presence of:

- alcohol-related hepatic, pancreatic, gastrointestinal, cardiovascular or renal disease, or other end-organ damage
- ataxia or peripheral polyneuropathy (not attributable to other non-alcohol-related causes)
- beyond 60 days of abstinence the cognitive deficit stabilises or improves
- after 60 days of abstinence, any neurological imaging, evidence of ventricular or sulcal dilatation improves
- neuroimaging evidence of cerebellar atrophy, especially of the vermis.

The following clinical presentation indicate that there may be complicating conditions such as vascular or traumatic lesions:

- the presence of language impairment, especially dysnomia or anomia
- the presence of focal neurological signs or symptoms (except ataxia or peripheral sensory polyneuropathy)
- neuroimaging evidence of cortical or subcortical infarction, subdural haematoma or other focal brain pathology
- elevated Hachinski Ischemia Scale score (Hachinski *et al*, 1975).

Thomson *et al* (2009) have listed a number of clinical indicators of a high risk of thiamine deficiency (Table 1).

Table 1 Clinical indicators of thiamine deficiency[a]

Clinical history	Early signs-symptoms	Later signs/symptoms
Weight loss in past year Reduced body mass index (BMI) General clinical impression of patient's nutritional status High dietary carbohydrate intake Recurrent episodes of vomiting in past month Co-occurrence of other nutritionally related conditions (polyneuropathy, amblyopia, pellagra, anaemia)	Loss of appetite Nausea/vomiting Fatigue, weakness, apathy Giddiness, diplopia Insomnia, anxiety, difficulty in concentration Memory loss	Classic triad: occulomotor abnormalities, cerebellar dysfunction (ataxia), and confusion and confabulations Quiet global confusion with disorientation in time/place

a. Patients may present with different combinations of symptoms and signs. Source: Thomson *et al* (2009).

Epidemiology of alcohol-related brain damage and related syndromes

Prevalence in community settings

Post-mortem studies-derived data

In meta-analyses of 39 704 post-mortems of people living in community settings from 11 centres in America and Europe, approximately 1.5% of brains showed lesions of Wernicke–Korsakoff syndrome in and near the mamillary bodies or cerebellar atrophy (Cook *et al*, 1998). Harper and colleagues (1998) undertook a comparative study of post-mortems drawing on samples from Australia as well. The lowest prevalence was found in France (0.4%), which has the highest per capita consumption of alcohol of the countries included in the study. The highest prevalence was found in Australia (2.8%), with a UK prevalence of 0.5%. Notably, the prevalence of these lesions is considerably higher in populations of people with alcohol dependence. Torvik *et al* (1982) found a prevalence of 12.5% of Wernicke–Korsakoff syndrome changes in 561 people with alcohol dependence and 26.8% showed cerebellar atrophy. Combining these findings and those of Victor *et al* (1989), it is estimated that 35% of those with alcohol dependence will exhibit post-mortem evidence of ARBD (Wernicke–Korsakoff syndrome/cerebellar atrophy). It has been noted that these lesions are associated with sudden death (Harper 1986). In 1998, Harper *et al* undertook a study of brains of deceased people (aged over 15 years) derived from 2212 sequential autopsies performed between 1996 and 1997 in Australia. Twenty-five cases of Wernicke–Korsakoff syndrome were identified (prevalence 1.1%), mostly among the 5.9% of the 2212 people who had a history suggestive of alcohol misuse. Only four cases (16%) had been diagnosed during life. The authors suggest that the decreased prevalence reflects the national policy of enhancement of bread wheat with thiamine.

Community healthcare data

Much of the information comes from Scottish data. In 2002, Chiang estimated a prevalence of ARBD at 7 per 10 000 in the Argyle and Clyde area (MacRae & Cox, 2003). MacRae & Cox (2003) quote an unsourced figure of 341 cases in greater Glasgow (population approximately 1 199 629). The same authors report a prevalence of 14.4 per 10 000 in Inverclyde.

Prevalence derived from secondary care records

Hospital admission-derived data

A prospective study of hospital records, followed up by diagnostic certification of working-age adults presenting with cognitive impairment was undertaken by Harvey *et al* in 1998 in London (two areas). They found an overall prevalence of cognitive damage of 67.2 per 100 000 population aged 30–64 years. Of these, 12.5% were diagnosed with ARBD (suggesting a prevalence of approximately 6 per 100 000 in this age range).

Ferran *et al* (1996) found a prevalence of 7% attending a specialist memory clinic catering for working-age adults presenting with non-traumatic cognitive damage. In Australia, Wood *et al* (1986) found that 0.07% of the total admissions, 1.7% of patients admitted with alcoholism, and 13% of patients admitted with alcoholic psychoses exhibited Wernicke–Korsakoff syndrome as defined by having opthalmoplegia as well as cognitive disturbance. Approximately a decade later, Ma & Truswell (1995) noted a decrease in patients diagnosed with Wernicke–Korsakoff syndrome presenting to hospital settings in Sydney. In a comprehensive review of the literature conducted in 1995, Smith & Atkinson estimated that alcohol is a contributing factor in between 21 and 24% of all people of working age presenting with dementia.

UK example – the Wirral ARBD service

From a pragmatic perspective, the Wirral specialist service for ARBD (Wilson *et al*, 2012) has provided services for secondary hospital referrals for approximately 4 years. It is a tertiary service taking patient referrals from acute general hospital in-patient units (a total population of 333 809 registered with general practice surgeries of which 211 968 people are aged between 16 and 64 and 114 452 people are aged between 40 and 64). The service carries approximately 40 patients with confirmed, severe ARBD including Wernicke–Korsakoff syndrome and related syndromes at any one time and receives an average of three referrals a month. This is almost certainly an under-representation of the prevalence of ARBD and does not cater for people that do not warrant acute medical hospital in-patient care.

Underdiagnosis and estimation of prevalence

The prevalence data are varied. One of the more consistent findings from the literature is that ARBD is substantially underdiagnosed. This is a consequence of a number of issues.

As illustrated, most of the epidemiological studies draw on data generated from health records, including primary care (MacRae & Cox, 2003), secondary care (Ma & Truswell, 1995; Harvey *et al*, 1998) or post-mortem studies in which hospital records are referred to, to assert drinking history (Torvik *et al*, 1982; Harper *et al*, 1998). An implicit assumption in adopting healthcare records for assessment of prevalence is that all people with Wernicke–Korsakoff syndrome are formally diagnosed or have alcohol histories reported in their case notes. It is evident that only a small minority of cases are assigned such a diagnosis by healthcare professionals (Thomson *et al*, 2002; Agabio, 2004). Establishment of diagnosis is confounded by patients being unlikely to present to services (Thomson *et al*, 2002), general ignorance concerning the cognitive effects of excessive alcohol ingestion, the related lack of expertise (Anderson *et al*, 1999; Hillman *et al*, 2001), high levels of stigmatisation (Cox *et al*, 2004) and the variable presentation of the syndrome (Jacques & Stevenson, 2000). These issues are reflected in the exclusion of cognitive damage as a mental illness in the NHS National Treatment Agency for Substance Misuse review of the effectiveness of treatment for alcohol problems (Raistrick, 2000).

Many surveys concentrate on Wernicke–Korsakoff syndrome. This is a relatively rare manifestation of ARBD, especially when diagnostic criteria are confined to the classical presentation (Harper *et al*, 1989; Cook *et al*, 1998; National Institute for Health and Clinical Excellence, 2010). This issue is manifest in the findings of neuropathological studies in which cerebellar disorders are also found (Torvik *et al*, 1982). Neuropsychological investigations draw attention to the importance of frontal lobe damage experienced by heavy drinkers in the absence of amnesiac syndrome (Ihara *et al*, 2000; Chanraud *et al*, 2007), again indicating that the broader definition of ARBD is substantially under-represented by current prevalence studies.

Prevalence trends in the UK

The fairly sparse evidence indicates that the prevalence of Wernicke–Korsakoff syndrome is related to the prevalence of alcohol dependency and national alcohol consumption indices. The

prevalence is greater in areas of high levels of socio-economic deprivation and alcohol-related disease (MacRae & Cox, 2003). Ramayya & Jauhar (1997) demonstrated that there was an annual increase in diagnoses of people with Wernicke–Korsakoff syndrome being admitted to secondary care between the years 1990 and 1995 in Scotland. These observations are supported by a number of other researchers (Kok, 1991; McCreadie *et al*, 1991; Smith & Hillman, 1999). Jacques & Stevenson (2000) suggest that the increase in prevalence may reflect increased alcohol misuse, improving diagnostic expertise and the use of thiamine as a therapeutic agent.

The highest prevalence of ARBD is found between the ages of 50 and 60 (MacRae & Cox, 2003). However, national trends in alcohol consumption also indicate that younger people are being exposed to more alcohol earlier in life, with potential health implications (BMA Board of Science, 2008; Scottish Government, 2009). Women's alcohol consumption is on the increase (BMA Board of Science, 2008). Chiang (2002, in MacRae & Cox, 2003) found that a sixth of patients with ARBD were women. Women tend to have a shorter drinking history and present 10–20 years younger than men (Cutting, 1978). These trends may have implications for future service provision in terms of earlier presentation of ARBD and an increased prevalence in women. Notably, as long as 7 years ago, Acquired Brain Injury Services (ARBIAS), an Australian organisation which emphasises the early detection of ARBD, reported that over half of its patients are between the ages of 35 and 54, and their 2008–2009 report characterises a woman presenting with severe ARBD at the age of 33 years (Acquired Brain Injury Services, 2009, 2011).

Summary

As most community studies have relied on accessing medical notes through primary and secondary care, and as ARBD is usually underdiagnosed, many of these data will represent a significant underestimation of prevalence. Consequently, the post-mortem studies based on samples of the general population are probably the best representation of prevalence, indicating a prevalence of alcohol-related changes in the brain at approximately 0.5% of the general adult population in the UK. The prevalence may rise to as much as 30% in heavy and long-term drinking populations. When restricted to a stringent diagnosis of Wernicke's encephalopathy/Korsakoff's psychoses the prevalence is much reduced – approximately 1 per 1000, with approximately 2% of people who misuse alcohol developing the syndrome (Harper *et al*, 1995). Most cases of acute ARBD present through acute hospital settings but prevalence figures and problems with diagnosis indicate that a significant majority are not brought to clinicians' attention.

Neurobiological basis of Wernicke–Korsakoff syndrome and alcohol-related brain damage

Key targets: GABA and glutamate

Adaptations occur in two key neurotransmitter systems as a consequence of chronic excessive drinking, the inhibitory gamma-aminobutyric acid (GABA)-benzodiazepine and excitatory glutamatergic systems (Tsai & Coyle, 1998; Krystal *et al*, 2003; Ron & Wang, 2009). Alcohol acutely boosts GABA-benzodiazepine receptor function and antagonises *N*-methyl-*D*-aspartate (NMDA) glutamatergic function. Acute exposure to large amounts of alcohol in animal models is associated with increased NMDA receptors and impaired long-term potentiation (a process key in learning and memory) in rats (see White *et al*, 2000). This process is therefore thought to underlie alcohol blackouts or amnesia seen, for example, with an alcoholic binge or excessive drinking; a good clinical history should be taken to assess their presence (Ward *et al*, 2009a).

Tolerance to chronic alcohol consumption is associated with reduced GABA-benzodiazepine sensitivity and increased NMDA glutamatergic activity (see Tsai & Coyle, 1998; Krystal *et al*, 2003; Ron & Wang, 2009). In the presence of alcohol boosting GABAergic and blocking NMDA-glutamatergic activity, balance in the system is maintained. However, in the absence of alcohol, the hyperglutamatergic and hypoGABAergic states result in many of the symptoms and signs of alcohol withdrawal. Such a process is often a challenging time for the individual with symptoms such as tremor, anxiety and insomnia as well as more serious complications such as seizures and delirium tremens.

In support of these alterations in GABA and glutamate are a number of neuroimaging studies. In abstinent alcohol-dependent individuals, reduced levels of GABA-benzodiazepine receptors and function have been reported using ^{123}I-iomazenil single photon emission tomography and positron emission tomography, particularly in the frontal lobe (Lingford-Hughes *et al*, 1998, 2005). A later study, however, reported increased cortical benzodiazepine receptor levels after 1 but not 4 weeks of abstinence, particularly in non-smokers (Staley *et al*, 2005). The same group using magnetic resonance spectroscopy (MRS) reported that GABA levels reduced in a non-smoking alcohol-dependent sample over the first month, whereas in smokers GABA levels were lower and change was more variable, i.e. increased, reduced or limited (Mason *et al*, 2006).

Concerning glutamate, an early MRS study measuring Glx (glutamate + glutamine) did not show any differences in abstinent alcohol-dependent individuals compared with controls after 1 week or 1 month of sobriety (Mason *et al*, 2006). However, participants had to complete their detoxification without medication, whereas another more recent study showed a positive association between glutamate cerebrospinal fluid levels and severity of

alcohol dependence (Umhau *et al*, 2010). Therefore it is likely that the patients in Mason *et al* 's (2006) study may not have been very dependent on alcohol. An elegant translational MRS study reported increased glutamate levels in the anterior cingulate cortex in alcohol-dependent patients and rats in acute early withdrawal (Hermann *et al*, 2012). The glutamate levels normalised during the next 2 weeks, the patients having received benzodiazepines for their detoxification from alcohol.

Preclinical models support a role for 'anti-glutamatergic' approaches in reducing toxicity associated with increased glutamatergic activity in alcohol withdrawal. Acamprosate has been shown to reduce neuronal death and mortality rates, and therefore appears to be neuroprotective (Mann *et al*, 2008; Ron & Wang, 2009). Consistent with reducing glutamatergic tone, acamprosate alone before and during alcohol withdrawal in humans has been shown to reduce arousal measured with magnetoencephalography and improved sleep (Boeijinga *et al*, 2004; Staner *et al*, 2006). An MRS study showed that acamprosate reduced glutamate/creatine in anterior cingulate of alcohol-dependent individuals undergoing medically assisted withdrawal with diazepam over 25 days compared with placebo (Umhau *et al*, 2010). Based on this evidence, many clinicians now give acamprosate in addition to their usual benzodiazepine medication during detoxification.

Alternative strategies available to the clinician to reduce this hyperglutamatergic state during withdrawal include using anticonvulsants. An RCT comparing placebo, diazepam, memantine (NMDA antagonist), topiramate (alpha-amino-3-hydroxyl-5-methyl-4-isoxazolepropionate (AMPA)/kainite receptor inhibitor) and lamotrigine (glutamate release inhibitor) reported all the medications were equally superior to placebo (Krupitsky *et al*, 2007). Notably, an RCT reported that in patients who had more than two previous detoxifications, carbamazepine resulted in better outcomes regarding future alcohol consumption than in those who had received lorazepam for alcohol detoxification (Malcolm *et al*, 2000). It should be noted that this is using anticonvulsants alone and not in addition to a benzodiazepine (which are effective anticonvulsants) (see Lingford-Hughes *et al*, 2012). There is a possibility that repeated detoxifications are likely to increase the risk of complications, implying that detoxification should not be undertaken in isolation without due preparation for supporting abstinence. Future studies and RCTs need to address whether using more 'anti-glutamatergic' pharmacotherapeutic strategies would result in less neurotoxicity and associated improved cognitive performance or at least reduced rate of decline.

Deficiencies in thiamine and other vitamins: treating Wernicke's encephalopathy

Alcohol dependence exacerbates thiamine deficiency by impairing uptake, storage and utilisation of thiamine (Thomson, 2000). *In vitro* and *in vivo* animal models both support an additive effect of alcohol exposure and thiamine deficiency (He *et al*, 2007; Ke *et al*, 2009). Animal models able to dissociate the effect of thiamine and alcohol show that chronic excessive alcohol intake without thiamine deficiency results in cell loss in the hippocampus and cortex and impairment in working and episodic memory (Vetreno *et al*, 2011).

Replacing thiamine is key in anyone with alcohol problems, particularly in those whose diet is poor, to prevent acute Wernicke's encephalopathy or more enduring Korsakoff's syndrome. A high index of suspicion must be maintained for these disorders because it is not uncommon that they are missed – they are hard to distinguish from other forms of ARBD (Sechi & Serra, 2007). Neuroimaging findings suggest that volumetric white matter changes in alcoholics without a history of Wernicke–Korsakoff syndrome occur in the same areas and may represent a milder form of those seen in Wernicke–Korsakoff syndrome (Sullivan & Pfefferbaum, 2009). Expression of thiamine-dependent enzymes is decreased in the cerebellum and frontal cortex of alcoholics with no history of Wernicke–Korsakoff syndrome (Alexander-Kaufman & Cordwell, 2007; Alexander-Kaufman *et al*, 2007).

It is particularly important to replenish using parenteral preparations, since oral formulations are unlikely to be sufficient due to poor absorption in alcoholism (Thomson *et al*, 2002; National Institute for Health and Clinical Excellence, 2010; Lingford-Hughes *et al*, 2012). Whereas replenishing thiamine is generally thought of in the context of alcohol withdrawal, thiamine deficiency can present at any time associated with reduced intake, for example when a person is eating too little or in association with physical illness which may be a cause of increased thiamine demand.

If there is any concern that Wernicke's encephalopathy is present or a person is at risk, then parenteral thiamine should be given. The British Association for Psychopharmacology (BAP) recommendations are given in Box 2. Intravenous thiamine should be administered in an in-patient setting, under medical supervision as there is a risk of acute anaphylaxis. However, i.m. thiamine has an anaphylactic incidence rate of 1 per 5 million pairs of ampoules (Taylor *et al*, 2012) and may be given by staff trained in the management of acute anaphylaxis and administration of i.m. adrenalin.

There is less evidence regarding supplementation in healthy uncomplicated alcohol-dependent/heavy drinkers (i.e. those at low risk) but BAP recommends that oral thiamine >300 mg per day should be given during detoxification. However, this is contrary to the recommendations of NICE (National Institute for Health and Clinical Excellence, 2010) which find little supporting evidence for the use of thiamine in low-risk groups.

Box 2 Patients at risk of Wernicke's encephalopathy: British Association for Psychopharmacology recommendations

- **'If patient is at high risk of Wernicke's encephalopathy (e.g. malnourished, unwell) prophylactic parenteral treatment should be given, using 250 mg thiamine (one pair of ampoules Pabrinex®) i.m. or i.v. once daily for 3–5 days or until no further improvement is seen and if Wernicke's encephalopathy is suspected or established, parenteral thiamine (i.m. or i.v.) of >500 mg should be given for 3–5 days (i.e. two pairs of ampoules Pabrinex® three times a day for 3 days), followed by one pair of ampoules once daily for a further 3–5 days depending on response'.**

Source: Lingford-Hughes *et al* (2004).

Immune function in the central nervous system: a possible therapeutic target

A novel therapeutic target in the treatment of acute and chronic neurodegeneration is 'neuroinflammation', which is believed to be important in exacerbating degeneration in a range of acute and chronic neural insults (for a review, see Lucas *et al*, 2006). Neuroinflammation refers to an immune response by resident immune cells in the nervous system – microglia – with or without peripheral immune cell invasion.

Preclinical studies

The bulk of the evidence for a role of neuroinflammation in ARBD comes from preclinical studies. Activated microglia have been demonstrated in a mouse model of alcohol dependence (Syapin & Alkana, 1988), and have been shown to be present 14 days after the last alcohol dose in a rat alcohol-dependence model sufficient to produce physical dependence and mild cognitive deficits (Obernier *et al*, 2002). Similarly, increased brain pro-inflammatory cytokines interleukin 1 (IL-1) and tumor necrosis factor alpha (TNF-α) in response to chronic high alcohol administration have been demonstrated, persisting for several days while peripheral cytokines were no longer detectable (Qin *et al*, 2008).

There is evidence for the induction of neuroinflammation via both direct and indirect mechanisms. Alcohol has been reported to stimulate toll-like receptor 4 (TLR4) – a receptor that recognises protein sequences associated with pathogens – directly in astrocytes and microglia *in vitro* (Fernandez-Lizarbe *et al*, 2009), leading to expression of the transcription factor TNF-α and expression of enzymes which regulate the production of prostaglandins and nitric oxide, cyclooxygenase

2 (COX-2) and inducible nitric oxide synthetase (iNOS) (Vallés *et al*, 2004). Inflammatory microglial activation and increase in inflammatory cytokines, nitric oxide and prostaglandins in the brain induced in a rodent model of alcohol dependence were reduced to control levels when TLR4 was eliminated by knock-out (Alfonso-Loeches *et al*, 2010), as were associated cognitive deficits (Pascual *et al*, 2007). Peripheral inflammation because of increased gut bacteria translocation has been suggested as an indirect mechanism of neuroinflammation, as peripheral cytokines are known to affect microglial phenotype (Wang & Hazell, 2010). The hyperglutamatergic state during withdrawal has also been suggested to be a neuroinflammatory stimulus related to microglial activation (Ward *et al*, 2009b). However, recent research suggests that microglia are partly activated rather than fully activated during withdrawal – a non-inflammatory phenotype (Marshall *et al*, 2013). Last, preclinical models of thiamine depletion show early microglial activation with blood–brain barrier disruption (Todd & Butterworth, 1999) in equivalent areas to those affected in human populations (Wang & Hazell, 2010).

Preclinical studies have also offered the prospect of intervention. Pre-treatment with indomethacin, a non-steroidal anti-inflammatory drug, decreased neuronal death, iNOS and COX-2 in a binge model of alcohol dependence and was associated with some recovery of memory impairment (Pascual *et al*, 2007). Minocycline, a medication that suppresses microglial activation, prevents it in Wernicke–Korsakoff syndrome and is associated with a delay in development of neurological signs of the syndrome (Wang & Hazell, 2010).

Clinical studies

Although increased numbers of microglia in the brains of alcohol-dependent patients post-mortem have been described, they have not been found to exhibit an inflammatory phenotype relative to controls (He & Crews, 2008). Given the highly plastic phenotype of microglia this could represent past proliferative bursts. In the same study, expression of monocyte chemoattractant protein-1 (MCP-1), a chemokine, was also increased. Gliosis – clusters of activated microglia and astrocytes – has been described in the thalamus and around the third ventricle in post-mortem specimens from patients with Wernicke–Korsakoff syndrome (Kril & Harper, 2012). Microglial activation has been demonstrated *in vivo* in alcohol-dependent patients with hepatic encephalopathy (Cagnin *et al*, 2006) and in Wernicke's encephalopathy (Tsukahara *et al*, 2005), but it has not thus far been reported in uncomplicated alcohol-dependent patients.

Increased pro-inflammatory and anti-inflammatory cytokines early in abstinence have been described (Gonzàlez-Quintela *et al*, 2000), as has increased pro-inflammatory cytokine production by dendritic cells from alcohol-dependent participants. Peripheral cytokines are known to communicate with the central nervous system via vagal afferents, periventricular macrophages and dedicated transporter systems (Laso *et al*, 2007). Following peripheral lipopolysaccharide challenge, IL-6 has been shown to correlate with microglial activation (Hannestad *et al*, 2012). Clinical studies in dementia suggest that higher peripheral pro-inflammatory cytokine concentrations are associated with a poorer cognitive outcome (Holmes *et al*, 2009). Peripheral pro-inflammatory cytokines have been found to correlate with craving and depressive symptoms in alcohol-dependent patients (Leclercq *et al*, 2012), but their relationship to cognition is as yet unexamined.

Therapeutic approaches

Existing alcohol pharmacotherapy has effects on the immune system, though the relevance of this to efficacy is unknown. Diazepam was explored prior to highly active antiretroviral therapy as a treatment for HIV encephalopathy as it inhibits microglial release of pro-inflammatory cytokines *in vitro*, although at higher concentrations than used clinically (Lokensgard *et al*, 1998). Opioid antagonists naltrexone and naloxone have been shown to decrease microglial activation via inhibition of TLR4 in the context of chronic pain, though again at high concentrations (Hutchinson *et al*, 2008). The peripheral blood monocytes of abstinent alcoholics undergoing group therapy showed different cytokine expression to that of healthy controls – raised IL-4

but decreased TNF-α and IL-1. Those treated with disulfiram, naltrexone and gammahydroxybutyrate showed no difference in cytokine profile (Franchi *et al*, 2010). It is unclear whether the differences reflected differences in abstinence rather than direct pharmacological effect. Last, anti-TNF-α normalised REM sleep in abstinent alcohol-dependent patients (Irwin *et al*, 2009), further pointing to a relationship between immune mechanisms and neuropsychiatric complications of alcoholism.

Summary

Undoubtedly, inflammatory processes are involved in ARBD and the hope is that by characterising these, a therapeutic target will be evident. Currently, preclinical models suggest that non-steroid anti-inflammatory drugs reduce inflammatory processes, and elsewhere minocycline is being tried in several other neuropsychiatric disorders for its therapeutic potential.

Clinical management

Pharmacological management

Reducing toxicity of alcohol withdrawal

Managing withdrawal

As described, alcohol detoxification/withdrawal is associated with a hyperglutamatergic and hypoGABAergic state which underpins increased risk of seizures and neuronal death. Both of these processes are likely to have an adverse impact on cognitive function. To reduce risk of such withdrawal-related harms, medically assisted withdrawal should be offered as per NICE guidance (National Institute for Health and Clinical Excellence, 2011):

> 'For service users who typically drink over 15 units of alcohol per day, and/or who score 20 or more on the AUDIT, consider offering:
>
> an assessment for and delivery of a community-based assisted withdrawal, or
>
> assessment and management in specialist alcohol services if there are safety concerns about a community-based assisted withdrawal' (p. 10).

Regarding medication, although a reducing regimen of a benzodiazepine (chlordiazepoxide or diazepam) is recommended for community detoxification (National Institute for Health and Clinical Excellence, 2011), for in-patients in a general medical setting, benzodiazepine, carbamazepine or chlomethiazole was suggested (National Institute for Health and Clinical Excellence, 2010). BAP guidelines describe the evidence for a range of medications that have been studied in alcohol withdrawal and suggest that if symptoms are present, medication should be given (Lingford-Hughes *et al*, 2012). Currently, there is limited evidence to suggest which medication is best for an individual patient, therefore the clinician should prescribe whichever medication they are confident in using. Many patients requiring treatment for alcohol withdrawal have alcohol-induced liver damage of varying severity and such patients require urgent review by specialist hepatologists. Such patients have increased sensitivity to sedative drugs which can precipitate coma. Chlormethiazole in particular should not be used.

Indications for thiamine treatment

Parenteral thiamine The majority of patients presenting with ARBD (either in an acute setting or more subtly in community settings) are likely to experience cognitive recovery over the first 2–3 months of abstinence. However, as already described, thiamine deficiency is one of the main factors recognised as being important in determining the severity and longevity of ARBD in patients presenting with alcohol misuse. The use of thiamine in both acute and long-term management to prevent permanent brain damage should be considered.

If there is any concern that long-term or permanent damage such as in Wernicke's encephalopathy or other features of thiamine-related disorders are present or person is at risk, then parenteral thiamine (Pabrinex®) should be given. As already mentioned (see Table 1, p. 21), several signs/symptoms should alert the clinician to the need for i.v. thiamine (Caine *et al*, 1997). BAP recommendations are given in Box 2, p. 27.

In the situations outlined in Table 1, i.m. thiamine may be considered as there is considerable likelihood that oral thiamine will be relatively ineffective. If there is high risk of Wernicke's encephalopathy (e.g. patient is malnourished, unwell), see BAP recommendations (Box 2, p. 27). Oral thiamine cannot be relied on in this situation (Thomson *et al*, 2009).

It is evident from these observations that in acute cases, presenting with one or more acute

symptoms, i.v. thiamine should be considered. Intramuscular thiamine should be considered in less acute cases in which there is a risk of developing thiamine deficiency ARBD. Such patients may have evidence of milder cognitive impairment, have long histories of substantial alcohol misuse (of at least 5 years), and have clinical and historical evidence of malnutrition and co-occurrence of other physical illnesses and symptoms.

Oral thiamine There is less evidence regarding supplementation in healthy, uncomplicated, alcohol-dependent/heavy drinkers (i.e. those at low risk) but BAP recommends oral thiamine >300 mg/d during detoxification.

Oral thiamine should be offered to harmful or dependent drinkers if they are malnourished or at risk of malnourishment; if they have decompensated liver disease; if they are in acute or medically assisted withdrawal; or before and during a planned medically assisted alcohol withdrawal. Oral thiamine prophyalxis should follow parenteral thiamine treatment (National Institute for Health and Clinical Excellence, 2010).

Recommendations

1. For individuals who typically drink over 15 units of alcohol per day, and/or who score 20 or more on the AUDIT, consider offering an assessment for and delivery of a community-based assisted withdrawal, or assessment and management in specialist alcohol services if there are safety concerns about a community-based assisted withdrawal.
2. Chlordiazepoxide or diazepam are recommended for community detoxification.
3. For in-patient detoxification in a general medical setting, benzodiazepine, carbamazepine or chlomethiazole are recommended.
4. If Wernicke's encephalopathy is either evident or suspected then the recommended treatment guidelines should be followed (Box 2, p. 27).

Long-term pharmacological management

There have been a few studies of pharmacotherapy in Korsakoff's syndrome, but all are small and none show particular promise. They include clonidine plus fluvoxamine, fluvoxamine alone, reboxetine, rivastigmine or donezepil (Lingford-Hughes *et al*, 2012). Therefore ensuring thiamine and other vitamins are appropriately replenished and maintaining abstinence are key.

Maintaining abstinence

It is very clear that continued drinking is associated with cognitive decline and therefore maintaining abstinence is key to allowing the brain and cognitive performance to recover. NICE reviewed the evidence regarding which pharmacological and psychological approaches are most effective (National Institute for Health and Clinical Excellence, 2011). Briefly:

> 'For harmful drinkers and people with mild alcohol dependence, offer a psychological intervention (such as cognitive behavioural therapies, behavioural therapies or social network and environment-based therapies) focused specifically on alcohol-related cognitions, behaviour, problems and social networks' (p. 9);
>
> 'After a successful withdrawal for people with moderate and severe alcohol dependence, consider offering acamprosate or oral naltrexone in combination with an individual psychological intervention (cognitive behavioural therapies, behavioural therapies or social network and environment-based therapies) focused specifically on alcohol misuse' (p. 10);
>
> 'After a successful withdrawal for people with moderate and severe alcohol dependence, consider offering disulfiram in combination with a psychological intervention to service users who:
>
> have a goal of abstinence but for whom acamprosate and oral naltrexone are not suitable, or
>
> prefer disulfiram and understand the relative risks of taking the drug' (p. 25).

The BAP guidelines (Lingford-Hughes *et al*, 2012) describe the evidence base for a wide range of medications including baclofen, topiramate and pregabalin. In addition to recommending acamprosate, naltrexone or disulfiram, they recommend that baclofen should be considered.

It must also be remembered that many patients with alcohol problems have a coexisting psychiatric disorder which will need to be managed; this is also covered in NICE and BAP guidelines (Lingford-Hughes *et al*, 2012).

Management of ARBD in alcohol services is presented in Fig. 1, p. 49.

Summary

Long-term pharmacological management of the maintenance of abstinence should be couched in the context of a psychotherapeutic and supportive relationship. The choice of drug treatment is informed by the patient's presentation, previous experience and current drinking status.

Recommendations

1 Ensure ongoing thiamine treatment.

2 Maintain abstinence.

3 For people with moderate or severe drinking, after withdrawal – acamprosate or oral naltrexone in combination with an individual psychological intervention (cognitive–behavioural therapies, behavioural therapies or social network- and environment-based therapies) focused specifically on alcohol misuse.

4 Disulfiram in combination with a psychological intervention for patients who have a goal of abstinence but for whom acamprosate and oral naltrexone are not suitable (or who prefer disulfiram and understand the relative risks involved).

5 Baclofen can be considered as an alternative to the other drugs if required.

6 For harmful drinkers and people with mild alcohol dependence, offer a psychological intervention (cognitive–behavioural therapies, behavioural therapies or social network- and environment-based therapies) focused specifically on alcohol-related cognitions, behaviour, problems and social networks.

Psychosocial and cognitive rehabilitation of severe alcohol-related brain damage

Generic principles of psychosocial rehabilitation for severe or longer-lasting ARBD

The majority of patients presenting to alcohol treatment services will significantly improve in cognitive performance within 3 months of abstinence. Some patients will continue to have more permanent cognitive problems and may warrant a more structured rehabilitation programme. North *et al* (2010) identify some of the key principles associated with the psychosocial rehabilitation of people with ARBD. The authors draw attention to the prioritisation of abstinence, a rehabilitative approach to activities of daily living and active family engagement in the context of multidisciplinary management. Wilson *et al* (2012) build on this in describing a model of intervention catering for patients presenting with severe levels of cognitive impairment, referred from acute hospital settings. The model adopts five therapeutic stages.

The **first stage** refers to the physical stabilisation and withdrawal from alcohol (usually conducted in acute hospital settings as all these patients have severe cognitive impairment). In the **second stage**, the patient is managed in a settled and protective environment (in institutional or domestic settings; Baddeley *et al*, 2002). Principles of care include introduction of care planning and a multidisciplinary team (MacRae & Cox, 2003) in the context of psychosocial and mental capacity assessments. A number of specific cognitive assessments are available for facilitating standardised cognitive assessment, allowing for the monitoring of change across time. Such assessments should incorporate assessment of frontal lobe functionality and, notably, the MMSE does not include these items. Readily available instruments that are free to access include the ACE-111 (Neuroscience Research Australia, 2013) and the MoCA© (Nasreddine *et al*, 2003). These instruments do not require formal training. Alternative instruments that are not as likely to identify people with frontal disturbance include more simple instruments such as the 6-CIT.

Specific environmental and therapeutic interventions include:

- abstinence (Malloy *et al*, 1990)
- good nutrition (Malloy *et al*, 1990)
- mood stabilisation (Malloy *et al*, 1990)
- regularisation of sleep pattern (Malloy *et al*, 1990)
- calm, stable environment (Kopelman *et al*, 2009)
- introduction of psychosocial support (MacRae & Cox, 2003; North *et al*, 2010; Wilson *et al*, 2012)

Box 3 Principles of treating depression gathered from the literature

- **A holistic approach to rehabilitation (Prigatano *et al*, 1996)**
- **Access to neuropsychiatric assessment and rehabilitation (MacRae & Cox, 2003). The main purpose of rehabilitation is to enhance the individual's sense of internal control (Ylvisaker & Feeney, 1998). This involves the introduction of a programme of functional rehabilitation (defined as achieving positive psychosocial adaptations by means of collaborative interventions provided in real-world settings) (Ylvisaker & Feeney, 1998). This is facilitated through a milieu-based approach to rehabilitation of the individual (Heinssen, 1996) in which increasing independence in relevant life skills (Giles, 1994) should be purposefully encouraged in real-life settings (Ylvisaker & Feeney, 1998).**
- **The environment, whether institutional or domestic, should be facilitative – one in which adaptations can be made to accommodate and optimise the changing cognitive profile of the individual (Heinssen, 1996; Bates *et al*, 2002).**
- **Long-term follow-up and ongoing social support may be required for those with significant, long-standing cognitive damage (Wilson *et al*, 2012).**

- early engagement of family and other interested parties already involved with the patient (Ylvisaker & Feeney, 1998; Jacques & Anderson, 2002)
- early engagement of specialist alcohol treatment services (MacRae & Cox, 2003)
- introduction of memory and orientation cues (Baddeley *et al*, 2002)
- structured personal hygiene routines (Jacques & Anderson, 2002).

This stage usually lasts 2–3 months, during which there is usually significant cognitive improvement. Cognitive testing should be carried out during stage two, but especially at about 3 months, to assist in determining the need for entering stage three.

The **third stage** is active psychosocial rehabilitation, in which development of activities of daily living is encouraged within the context of a multidisciplinary team management and close working relationships with carers and families, supported by alcohol management (prioritising abstinence). Intervention is principally based on a behavioural model, incorporating diary-keeping, activity-scheduling, graded tasking, and problem-solving and memory-cuing (Acquired Brain Injury Services, 2011; Wilson *et al*, 2012), and draws on descriptive research conducted in patients with acquired brain injury and patients with ARBD (Bates *et al*, 2002; MacRae & Cox, 2003). Notably, comorbid depression has been found to be of relatively high prevalence (Wilson *et al*, 2012). One study has demonstrated the efficacy of cognitive–behavioural treatment for depression in people with established ARBD (Morrison & Pestell, 2010). Principles of treatment of depression in ARBD include those listed in Box 3.

This third stage may last up to 3 years, until an optimal level of cognitive improvement has been achieved. It is recommended that cognitive testing and assessment is continuous but formalised every 6 months. Assessments should also include aspects of activities of daily living and psychiatric review as emergent psychiatric disorders, in particular depression, are frequent.

When further cognitive/behavioural improvement is not anticipated, there should be a seamless transition to the **fourth stage** in which the patient is established in an environment which facilitates as much independence as possible.

The **last (fifth) stage** is derived from national recommendations for the care of people with chronic alcohol misuse (Department of Health & National Treatment Agency for Substance Misuse, 2006) in that the patient should be encouraged to engage in structured activities and weekly routines, promoting long-term independence and minimising the likelihood of relapse. Building both informal and formal social networks should also be promoted as a means of reducing the likelihood of relapse (Department of Health & National Treatment Agency for Substance Misuse, 2006), facilitating ongoing care and support as the patient improves and facilitating the generalisation of newly acquired behaviour and skills into new environments (Ylvisaker & Feeney, 1998).

The five-stage model is characterised by relatively assertive follow-up in both institutional and domestic settings but is associated with only 10% alcohol misuse relapse, a 10% mortality rate and reduction of use of acute hospital beds by 85%. The majority of the 41 patients on which the model was developed remain in community-based, non-institutional settings (Wilson *et al*, 2012). A clinical manual

specifically relating to this model of intervention can be found at www.arbd.nhs.uk.

Care of older people with ARBD

It is well recognised that older people with ARBD are less likely to recover from cognitive deficits during abstinence compared with younger people (Pfefferbaum *et al*, 1997). As a consequence, the 'Wintringham project' in Melbourne (www.agedcare.org.au/what-we-do/housing-retirement-living/innovative-housing-solutions/wintringham) has initiated a specialised model of residential care which prioritises the dignity and respect for older people with ARBD; residents are not required to be abstinent but staff facilitate a variety of treatment options. Commentary relating to the role of abstinence is difficult in the absence of further detail concerning the clinical and psychiatric conditions (including capacity to make decisions) of individual patients. This model of care continues to be challenged by the balance between autonomy and acceptable levels of protection, the balance between individualised care and the need to adopt a community-based lifestyle, and the balance between abstinence and managed harm reduction and minimisation, especially in long-term older residents with severe impairments (Rota-Bartelink & Lipman, 2007).

Specific cognitive interventions

The evidence relating to specific cognitive interventions in the rehabilitation of ARBD is not robust. Svanberg & Evans (2013) have undertaken a comprehensive review of the literature published after 1990. In comparing patients with Korsakoff's syndrome and healthy controls, VanDamme & d'Ydewalle (2008) found that giving more time, greater explanation and encouraging patients with Korsakoff's syndrome to explain increased their performance in making associations between learned pairs of words. Mimura *et al* (2005) found that performing actions as represented in verbalised 'action phrases' enhanced the recall of the phrase. There is some indication that 'errorless learning' (Kessels *et al*, 2007) (as opposed to learning information by trial and error in which a person receives feedback about the mistakes made) may enhance recall. In errorless learning the individual is asked to repeat information immediately after it has been presented and does not rely on the longer-term memory functions. This is consistent with Baddeley & Wilson's (1994) finding that not being allowed to guess improves recall over time. Morgan *et al* (1990) used memory cuing, both through staff and electronic diary prompting, to successfully enhance attendance at meetings and therapeutic programmes; this is supported by Baddeley *et al* (2002) drawing attention to the importance of memory cuing in clinical practice. Cuing with fragments of words or letters helps recall (Heinrichs *et al*, 1992). Verbal prompting (Morgan *et al*, 1990), facilitating learning through re-enforcement, incorporating specific and person-appropriate outcomes are also useful in aiding recall (Hochalter & Joseph, 2001). Bardenhagen *et al* (2007) is the only study reported in Svanberg & Evans's review that explores reasoning and planning, and emphasises the importance in providing structured rules to facilitate problem-solving difficulties encountered in patients with Korsakoff's syndrome. Fals-Stewart & Lucente (1994) suggest that the effect of cognitive rehabilitation can be enhanced by tailoring the intervention to the specific needs of each patient. More specifically, practice has been shown to improve visuospatial skills (Forsberg & Goldman, 1985). Notably, training (Goldman & Goldman, 1988) and practice (Stringer & Goldman Rakic, 1987) in cognitive tasks generalises to other cognitive domains (Forsberg & Goldman, 1987). Roehrich & Goldman (1993) have demonstrated the efficacy of bibliotherapy in terms of cognitive rehabilitation.

It is self-evident that ongoing cognitive assessments and identified problems should inform the design of the treatment of the individual, with therapeutic engagement and programmes adjusted as required (Box 4). This will include enhanced follow-up and contact with patients and arrangement of appropriate social support.

Recommendations

1. Rehabilitation should be couched in the context of multidisciplinary support.
2. Close liaison with alcohol treatment services is required.

Box 4 Examples of individual psychosocial adaptations derived from literature

- Regular review of cognitive status and capabilities
- Increasing the amount of time and patient engagement in understanding and remembering explanations
- Techniques in cuing and prompting recall and actions
- Performing and role playing in an attempt to help learn new information
- Aiding recall through providing relevant rewards
- Encouraging the learning of new information by the individual repeating information as soon as it is presented, and avoiding guessing of answers or material
- Providing 'rules' and guidance in helping people to problem solve:
  identify the problem
  collect information about the problem
  generate solutions
  select and implement the solution
  evaluate the results
- Providing the individual with written material
- Targeted, enhanced contact and follow-up, as more frequent contact with and positive support of individuals with cognitive damage are associated with better outcomes
- Educational programmes and skill retraining may have to be delayed for the first few weeks so as to benefit from cognitive recovery
- Educational programmes, including visual presentations may have to be simplified, with each session being shorter and with more repetition

3 Every patient should have an active care plan with an assigned key worker who has expertise in the assessment and rehabilitation of working-age adults with cognitive deficits.
   - The care plan should incorporate ongoing assessments of cognition (e.g. the ACE-III or the MoCA©), behaviour and mental capacity – after withdrawal, after 3 months of abstinence and subsequently every 6 months until an optimum level of independence is achieved.
   - The care plan should be couched in a collaborative arrangement with the patient and should be structured, goal oriented and monitored.
   - The care plan should facilitate and enhance the development of independence over a 3- to 4-year period, with ongoing review of care cost and planned reduction in support as indicated by the patient's improvement.

4 Carers, institutional staff and families should be encouraged to participate in the rehabilitation under appropriate supervision of the specialist key worker.

5 As the patient improves, transition between institutional and community care should be carefully managed and appropriately supported as part of the rehabilitative programme.

Barriers to care

Clinical issues

As most people with ARBD have been alienated from their families and friends and are socially isolated (Jacques & Stevenson, 2000), they have few natural advocates. Such patients are not usually identified or brought to the attention of clinical services until significantly impaired, with presentation frequently associated with dramatic changes in behaviour (Acquired Brain Injury Services, 2009). Most reviewers draw attention to widespread clinical ignorance relating to the diagnoses of ARBD (MacRae & Cox, 2003). As ARBD may frequently present with frontal lobe dysfunction (Schmidt *et al*, 2005), commonly used assessment instruments such as the MMSE are unlikely to identify early cases (MacRae & Cox, 2003). These problems are compounded by the frequent lack of insight experienced by patients with ARBD. Memory impairment is problematic in terms of the patient being unable to retain information regarding appointments, participating in alcohol treatment programmes and being able to provide biographical and alcohol histories to clinical staff. Such difficulties may lead to patients being deemed 'poorly motivated' if the impairments are not recognised, excluding them from many traditional alcohol treatment services.

The more easily identified memory problems are usually compounded by frontal lobe damage (Luria, 1973; Goldman-Rakic, 1987; Cummings, 1995) including difficulties in reasoning, synthesising information, appreciating implications of decisions and understanding the condition and implications of subsequent exposure to alcohol.

National guidance

Service providers and commissioners are supported with very little national guidance in the provision of services for people with ARBD. This is evidenced in seminal documentation by the Department of Health, NICE and professional bodies. In 2006, the Department of Health published *Models of Care for Alcohol Misusers* (Department of Health & National Treatment Agency for Substance Misuse, 2006). This is a detailed document which contains assessment and treatment advice. Notably, it refers to the need for 'comprehensive assessment' including cognitive and occupational therapy assessment of individuals. However, apart from this, the document fails to address the issues of ARBD with its potential effect on insight, screening, treatment and prognosis. Subsequently, the Department of Health guidance *Local Routes: Guidance for Developing Alcohol Treatment Pathways* (2009) fails to mention cognitive damage and associated implications other than suggesting a 'comprehensive assessment'.

Current NICE guidelines (National Institute for Health and Clinical Excellence, 2010) concerning the treatment of alcohol use disorders and physical complications are confined to the acute treatment of Wernicke's encephalopathy. The guideline does not address the longer-term issues of ARBD.

In documents addressing alcohol-related problems in terms of service provision (Royal College of Physicians, 2009; Moriarty *et al*, 2010) and patient information for people with alcohol-related problems (Royal College of Physicians, 2003), no mention was made of ARBD. In a review published in the *British Journal of Psychiatry*, Gupta & Warner (2008) draw attention to the increasing prevalence of neurocognitive damage related to excessive alcohol ingestion. A subsequent editorial addressing the same topic highlights the difficulties confronting patients with ARBD in the context of the current configuration of service provision (Wilson, 2011). In 2010, the British Society of Gastroenterology recommended the formation of joint medical psychiatric alcohol care teams to manage patients in the acute hospital setting and the establishment of a hospital-led, multi-agency Assertive Outreach Alcohol Service, but the long-term care of ARBD was not considered. The only document that offers some guidance in the psychosocial management of ARBD is a report published by the Royal College of Physicians (2001). It emphasises the potential of a specialised neuropsychiatry service to assess and provide specialist care for patients with ARBD under the age of 65. Notably, the issues have been in part addressed in a number of Scottish governmental documents including *A Fuller Life* (Cox *et al*, 2004), *Delivering for Mental Health* (Scottish Executive, 2006) and the Mental Welfare Commission (2010b) report.

Organisational issues

The paucity of national and professional guidance is reflected in problems associated with service commissioning and provision. The needs of carers working with people with ARBD have been addressed in a publication from the Dementia Services Development Centre (McCabe, 2006), but rarely does a single mental health specialty take responsibility for this patient group (Lennane, 1986; Price *et al*, 1988). The lack of expertise and related services is reflected in the findings of a Care Services Improvement Partnership and Alzheimer's Society commissioned study of patients with ARBD in England and Wales (Boughy, 2007). The research highlights a lack of diagnostic expertise, general ignorance within psychiatric, medical and nursing staff, no evident pathways of care and being 'passed from pillar to post', stigma and lack of resources. The lack of commissioned services, the failure of trusts to generate local pathways of care and the lack of clear professional guidance have direct implications for acute hospital trusts, as failure to provide appropriate care planning results in prolonged in-patient stays. Popoola *et al* (2008) reviewed 44 patients with ARBD admitted into acute hospital care over a 6-month period and found the average length of stay in the hospital was 84.0 +/- 72.3 days and mean lost bed days was 15.9 +/- 36.6. These circumstances reflect much

of the current situation in the UK and are associated with increased likelihood of early readmission and increased mortality (Price *et al*, 1988). As a consequence, those patients who are recognised within the healthcare system are often placed in inappropriate institutions, including nursing homes designed for older people.

Commissioning care

The evidence indicates that specific commissioning of services will reduce acute hospital bed usage (Price *et al*, 1988; Wilson *et al*, 2012). It is important that access to funding is readily available to reduce the time that a patient is held on acute medical/surgical wards. In the majority of cases (75%) patients will improve to some extent (Wilson *et al*, 2012). Consequently, there is a strong likelihood that the care packages will reduce in complexity and intensity over the rehabilitative period of 2–3 years. This may be reflected in a reduction of funding for each care package across time.

Service configurations

The main thrust of commissioning should be to augment existing service provision, so as to provide an integrated and coordinated response to diagnosis, assessment and rehabilitation (MacRae & Cox, 2003). For the ease of discussion, ARBD service models can be divided into three categories.

1. Single-service model

First, the evidence suggests that specialist assessments should be carried out through mutidisciplinary teams with specialist knowledge of rehabilitation (MacRae & Cox, 2003). In the first model, a single service is commissioned to deliver the totality of care and rehabilitation. These service providers usually have access to a range of provision, including institutional care (nursing/residential), less dependent environments including supported living and outreach support into domiciliary settings. Such organisations have significant experience with working-age adults with various degrees and types of cognitive impairment. Within an NHS setting, neuropsychiatric services offer a useful and easily adaptable service model for managing ARBD (Royal College of Physicians, 2001) and will often have close links with social service provision and networks of experienced institutions and support systems. However, there are relatively few comprehensive neuropsychiatric services within the UK, and of these, only a minority are commissioned to cater for people with ARBD.

In the absence of a comprehensive coverage, private organisations have the opportunity to fill in the gaps. Examples of such organisations can be found in Glasgow (e.g. Loretto (www.lorettoha.co.uk/Care/What+We+Do/), providing a rehabilitative service for people with ARBD based on person-centred care and also services for people with mental health problems, intellectual disabilities and homeless people). Carenza Care (Boughy, 2007) in Wales also provides specialised ARBD services through small residential, supported living and outreach services. Many other service providers will exist, with varying degrees of specialisation. When developing these services it is important for commissioners to specifically promote the active rehabilitation of patients rather than just social and long-term care. The advantages of such organisations are that they may respond to gaps in the healthcare market. However, they are often 'out-of-area' and expertise and cost will vary. Another problem may lie in the relative lack of integration with NHS social and healthcare provision.

2. ARBD services within mental health trusts

The Fife, Wirral and Glasgow examples (pp. 63–72) are specifically commissioned ARBD services that are delivered by NHS provider organisations. These services generally undertake assessment and rehabilitation of patients with ARBD, but also provide advice and interface with other NHS clinical services. In one case, expertise has been built up within an early onset dementia service (Wirral, see pp. 66–68). This is not ideal, as it may be difficult to develop an active cognitive rehabilitation model within a service that is primarily designed to provide management for long-term terminal diseases (MacRae & Cox, 2003). However, advantages include access to a wide network of institutions and service providers with experience with working-age adults with cognitive dysfunction. In this model, individual care rehabilitative care packages are negotiated on a patient-by-patient basis. This is time consuming, but does enable the development

of personalised care packages, open to change as the patient improves. By being couched within a bigger team, access to additional clinical expertise is facilitated and there can be close integration with other NHS services, accessing private care and facilities as required. An alternative configuration has been established in Fife (Scotland) (see pp. 63–66). This is another integrated model in which expertise is embedded within the context of a greater mental health trust with ready access to clinicians in other community teams in support of the management of patients with ARBD. Again, this model offers a focus for building expertise but enables access to a wider multidisciplinary skill base, catering for the variable needs of the patient population. The last example is a well-established service in Glasgow (see pp. 68–72) which works in close affiliation with the local alcohol treatment team. In all three cases services have been established in relatively high-prevalence areas, catering for a relatively large patient population (MacRae & Cox, 2003).

3. Specialist services embedded in generic teams

In less prevalent areas, 'specialisation' or 'specialists' may be embedded within generic teams. Such specialists may adopt similar roles to care coordinators of patients with ARBD referred to the team, coordinating the local pathways and building up expertise (MacRae & Cox, 2003). We are not aware of any examples of this model.

What evidence there is indicates that a degree of specialisation is warranted in terms of reducing hospital usage and improving quality of life of people with severe ARBD. The configuration of commissioned services will be informed by current design of established service provision. Consideration should be given to the degree of integration of a commissioned service with other mental health provision (as many of these patients will have concomitant mental health problems) and alcohol treatment services. It is also evident that as alcohol treatment services are now recommended to screen new patients for cognitive damage (National Institute for Health and Clinical Excellence, 2011), commissioners should explore the implications of providing appropriate modification of alcohol treatment programmes in existing services and establish appropriate pathways of care for more severe cases.

The role of institutions

A significant proportion of patients discharged from acute hospital care are likely to be experiencing mental incapacity and behavioural disturbance making them unsafe to be discharged into non-institutional settings. Institutional facilities should be available to enable discharge from acute medical/surgical wards as soon as the physical condition of the patient has been stabilised. Subsequent rehabilitation should aim at optimising the independence of the patient. Treating individuals with ARBD as dementia cases because of difficulty in finding accommodation or lack of service provision will result in further deterioration (MacRae & Cox, 2003). Outcome studies of patients who misuse drugs or alcohol and have cognitive dysfunction in long-term specialist residential settings have demonstrated better outcomes than when those patients were placed in generic institutions (DeLeon & Jainhill, 1981; DeLeon 1984; Fals-Stewart, 1992). These findings are supported by Ganzelves *et al* (1994) who discovered that patients with ARBD referred to specialised institutions showed better preservation and improvement in social functioning and enhanced speed of information processing than when in non-specialised homes. Furthermore, Blansjaar *et al* (1992) followed up patients in specialist nursing homes and in specialist sheltered accommodation and reported that those in sheltered accommodation made considerably better sociobehavioural improvement than those in a nursing home environment. It is evident that the absence of local specialist institutions can be mitigated through the development of enhanced care packages tied into a structured rehabilitative programme supervised by a regional specialist team, operating within targeted non-specialised institutions (Wilson *et al*, 2012). This approach has both advantages and disadvantages – it is time intensive and requires regular and frequent follow-up and supervision by the specialist team, and individual care packages have to be negotiated for each patient. However, the model provides flexibility in development of service provision, enabling patients to be placed in situations which optimise their management, whether nursing, residential or

supported living. It also caters for changes in the healthcare 'market' in which many of these establishments are provided by private organisations and may come and go with market pressures. Such an approach may be adopted in the absence of any specialised institution and is not dependent on pre-established provision in the early stages of service development. When referring to private facilities, whether institutional or otherwise, it is important to maintain ongoing care planning and support through an experienced team until the optimum level of cognitive recovery and independence is achieved.

The role of charitable organisations

Patients with ARBD should be routinely referred to their local Headway carer support group (www.headway.org.uk) and a comprehensive assessment by a specialised team. People should also be signposted to the Headway UK free helpline on 0808 800 2244. Other relevant organisations to consider for referral include the Stroke Association (www.stroke.org.uk) and Alzheimer's Society (www.alzheimers.org.uk). It is worth noting that Headway is facilitating the development of specialist ARBD services within the Approved Provider Scheme, to specialise in the active rehabilitation of younger people affected by forms of ARBD. Although these services have not yet received accreditation, further information and updates concerning approved units is available on the Headway website (www.headway.org.uk/approved-care-providers.aspx).

Summary

In the absence of services it is recommended that services are commissioned and designed to cater for the local population needs, capitalising on the strengths of already established services (Box 5). Where there are already functioning, comprehensive neuropsychiatric services with expertise in managing people with acquired brain damage, they are an obvious platform through which care can be provided. In the absence of NHS-based neuropsychiatric service provision, and where there are well-founded and experienced private units specialising in the rehabilitation of people with ARBD, such services may offer a viable option.

Box 5 Service commissioning principles

Commissioning of services for alcohol-related brain damage should focus on:

- **the development of a single point of referral**
- **the building of expertise in diagnosis and management and development of a care pathway**
- **integrated social and psychiatric care**
- **assertive follow-up and management**
- **the adoption of patient-centred approach to rehabilitation**
- **ready access for specialist services to wider mental health expertise**
- **provision of in-patient access and access to longer-stay institutions.**

Notably, this configuration of service provision will rely on close working relationships with local generic mental health and alcohol services. In the absence of pre-established services of this nature, commissioners should consider the commissioning of specialisation within general mental health/alcohol service provision. This model of small specialist teams, integrated within other services and drawing on more generic multidisciplinary experiences of mental health, dementia services and alcohol treatment provision may well suit geographical areas in which there is a high prevalence rate (MacRae & Cox, 2003). In areas of low prevalence, pathways of care and related key workers should be identified within local services to facilitate rehabilitation, relapse prevention and unplanned readmission into acute care. Irrespective of the model, specialised services should support alcohol treatment services that have been adapted to cater for those with alcohol dependence with mild to moderate ARBD attending the service with a view to reducing their alcohol intake.

In severe ARBD, institutional care is likely to be required during the first stages of the rehabilitation (first 3 months), particularly in patients presenting with severe degrees of incapacity and confusion. After the first 3 months a significant proportion of patients will benefit from further institutional rehabilitation until well enough to be discharged into a more independent environment. Many of these individuals will need ongoing social support after the active rehabilitation programme has achieved its optimum effect. Approximately a quarter of patients will remain in long-term

institutional settings. The expertise and size of the institute are important and what limited evidence there is indicates that EMI nursing homes are not recommended; smaller units are important and significant support by the specialist team is recommended if the institution has little or no experience of managing the rehabilitation of people with ARBD. Last, it is recommended that a centralised data monitoring system provides the most robust mechanism in terms of monitoring prevalence and trends (MacRae & Cox, 2003).

Recommendations

1 Clinical commissioning groups should commission established and clinically appropriate services to provide multidisciplinary specialist care for the assessment and rehabilitation of patients with severe ARBD. The nature of service provision should capitalise on established strengths within the local health and social care provision. In the absence of established neuropsychiatric/psychological or equivalent specialist provision (which should preferably provide such services), consideration should be given to the embedding of specialisation within the most appropriate established generic mental health service provision; enabling access to expertise, advice, multidisciplinary assessment (including Social Service support) and coordination or supervision of care pathways. Such specialisation should provide advice and support to other services who are managing patients with mild to moderate ARBD, including community teams and alcohol services.

2 As part of the assessment process, clinical commissioning groups should commission appropriate services for facilitating the early hospital discharge, short-term psychosocial assessment (up to 3 months). These facilities may have to manage clinically disturbed and mentally incapacitated patients.

3 Arrangements should be put in place to provide safe and active institutional rehabilitation for those patients who are not well enough to be rehabilitated into non-institutional settings after the initial 3-month period of assessment. However, it should be expected that the majority of patients (75%) will make some improvement over 3 years, as a consequence of active rehabilitation.

4 Funding for long-term institutional care for supporting people with permanent brain damage should be made available. A minority of cases (25%) may require permanent institutionalisation.

5 A significant minority of patients will require ongoing social support in non-institutional settings after the 3-year period of therapeutic rehabilitation, to maintain their optimum level of independence in community settings.

Legal framework

NICE guidelines recommend that all new cases referred to alcohol treatment services should have an assessment of cognitive function (National Institute for Health and Clinical Excellence, 2011). As a significant minority of heavy drinkers are known to have ARBD (Cook *et al*, 1998), it is likely that a comprehensive assessment will identify a subgroup of patients who exhibit cognitive problems. The implications of these are important. First, cognitive impairment may have an impact on the individual's awareness and understanding of their current circumstances. Second, it may have implications in terms of adherence to and understanding of interventions.

It is important that the therapeutic approach to the management of people with cognitive damage accommodates these issues and that the needs of the individual are considered in the context of the appropriate legal framework if necessary.

Mental Capacity Act 2005 and Adults with Incapacity (Scotland) Act 2000

Both acts provide the framework to facilitate an assessment of the individual's capacity to make decisions. They enshrine five principles (with the additional principle of acting on decisions in the AwIA):

1. **A presumption of capacity** – every adult has the right to make his or her own decisions and must be assumed to have capacity to do so unless it is proved otherwise.
2. **Individuals being supported to make their own decisions** – a person must be given all practicable help before anyone treats them as not being able to make their own decisions.
3. **Unwise decisions** – just because an individual makes what might be seen as an unwise decision, they should not be treated as lacking capacity to make that decision.
4. **Best interests** – an act done or decision made under the act for or on behalf of a person who lacks capacity must be done in their best interests.
5. **Least restrictive option** – anything done for or on behalf of a person who lacks capacity should be the least restrictive of their basic rights and freedoms.

Mental capacity is the ability to make a decision. This includes the ability to make a decision that affects daily life – such as when to get up, what to wear or whether to go to the doctor when feeling ill – as well as more serious or significant decisions. The MCA explains mental incapacity thus (see also Box 6):

> 'For the purposes of this Act, a person lacks capacity in relation to a matter if at the material time he is unable to make a decision for himself in relation to the matter because of an impairment of, or a disturbance in the functioning of, the mind or brain.'

The MCA provides examples of impairment of the mind or brain which include the long-term effects of brain damage and the symptoms of alcohol or drug misuse.

When assessing whether a person is able to make a decision, the MCA states that there are four components that need to be assessed:

Box 6 Mental incapacity as defined by the Mental Capacity Act 2005

A person lacks mental capacity if:

1. **He is unable by reason of mental disability to make a decision for himself on the matter in question, or**
2. **He is unable to communicate his decision on the matter because he is unconscious or for any other reason.**

'A person is unable to make a decision for himself if he is unable –

(a) to understand the information relevant to the decision,

(b) to retain that information,

(c) to use or weigh that information as part of the process of making the decision, or

(d) to communicate his decision (whether by talking, using sign language or any other means).'

The AwIA also includes 'acting on the decision'.

The MCA provides details and examples, illustrating the importance of trying to support the individual in making their own decision regarding the topic under discussion. It includes the need to provide the individual with information pertaining to:

- the nature of the decision
- the reason why the decision is needed, and
- the likely effects of deciding one way or another, or making no decision at all.

Issues in relationship to alcohol-related cognitive impairment

The concept of denial, motivation and engagement

The concept of denial as an ego defence mechanism is described by Freud as far back as 1937. When anxiety becomes too overwhelming, it is then the place of the ego to employ defence mechanisms to protect the individual. Feelings of guilt, embarrassment and shame often accompany the feeling of anxiety. It is a cardinal feature in terms of the psychopathology of addiction and plays an important role in the 12-step programme (Alcoholics Anonymous) in the management of addiction, in which abandonment of denial is seminal to undertaking the first, fourth, fifth, eighth and tenth steps. Denial may take many forms and there is some indication that denial of an addiction to alcohol to a second party may be associated with the individual having a conscious awareness of their problem (Dyson, 2007). As most people with alcohol dependence will exhibit varying degrees of denial, it is important to differentiate between this natural defence mechanism and the inability of the individual to understand, retain and weigh up information and communicate their decision (Rinn *et al*, 2002). Lack of engagement in alcohol treatment programmes may be a consequence of undiagnosed cognitive damage and service adaptations may have to be made to cater for this particularly vulnerable group of patients.

The long-term effects of alcohol on cognition (ARBD)

Alcohol, thiamine deficiency and related ischaemic changes and trauma may affect the function of the brain in many ways, sometimes obviously, but more frequently in a more subtle fashion. In particular, frontal lobe function is a common presentation (Ihara *et al*, 2000). It may be mild in its presentation, with very little effect on capacity and the conduct of daily life. In particular, assimilating information, weighing up information, understanding concepts (such as alcohol dependency) and being aware of the consequences of decisions should be explored in the context of a structured examination of cognitive function.

Memory problems are another common presentation of ARBD. People with ARBD may experience problems in both short-term (anterograde) and long-term (retrograde, episodic) memory. These problems can be confounded by the experience of false memories (confabulations). Thus, when examining capacity issues the person may make decisions within the interview context but half an hour later may have no recall of the decision that they have made. They may benefit from ongoing psychological support to help them to retain information so as to make consistent decisions over time.

Autobiographical memories are likely to be patchy, resulting in significant periods of memory loss for which the individual will have little memory or none. Problems with memory may stretch back as far as 25 years into the individual's past. Retrograde amnesia is characterised by a temporal gradient in which more distant memories are clearer and amnesia becomes more profound closer to the acute presentation. In establishing whether an individual has capacity to make decisions relating to future alcohol-related behaviour or other aspects

of their life, it is important to assess their recollection of past experiences (including the length and nature of their alcohol misuse and related problems and implications) that might influence their understanding of their current situation.

Summary

In the first instance it is important to establish the degree of cognitive dysfunction and a diagnosis of ARBD. Second, it is important to differentiate between anxiety-derived denial and cognitive difficulty in processing information. This can be aided by clear clinical evidence of cognitive disability. Last, it is necessary to explore the individual's capacity to make specific relevant decisions, and to be aware of the potential impact of processing problems and memory issues often experienced by people with ARBD. In many cases, capacity assessment may be undertaken in consultation with other team members with experience in this field.

Recommendations

1 ARBD fulfils the legal criteria of mental disability.

2 Patients may present with difficulties in decision-making in a wide variety of situations and should be facilitated in coming to their own decision.

3 When assessing capacity in patients with ARBD:

- Memory should be assessed.
- Consideration should be given to the ability of the individual to recall any relevant discussion and decisions made during the interview. Notably, recall may be preserved and function well during the interview but may be significantly compromised some minutes later. Consequently, it is frequently worth reviewing the interview and related decisions, and testing recall of the issues and decisions made, later in the day.
- Consideration must be given to the individual's ability to recollect previous events as many will not have clear memories of their recent past. This may make it difficult for them to appreciate their current circumstances and the events that have contributed to their current situation.
- Corroborative histories may help in differentiating between confabulations and memories.
- Issues relating to decisions that need to be made may have to be broken down into steps, and the patient facilitated in working through their options.
- The patient may benefit from ongoing support and memory aids in helping to remember the decisions they have made.
- Capacity is likely to fluctuate in ARBD, hence regular reassessments are recommended.

High-risk populations: patients presenting to alcohol treatment services

Many patients presenting to alcohol services will be at risk of thiamine deficiency and a considerable proportion may experience some degree of cognitive dysfunction (Bates *et al*, 2002). Untreated thiamine deficiency is associated with long-term cognitive and neurological damage and treatment may involve parenteral thiamine and prophylaxis. The cognitive deficits are likely to have a direct impact on prognosis in terms of response to alcohol treatment programmes (Bates *et al*, 2006). It is likely that most alcohol treatment services do not cater for the cognitive damage experienced by a significant proportion of patients. What evidence there is suggests that appropriate cognitive testing and assessing risk of thiamine deficiency should be the norm in the assessment of such patients. Therapeutic programmes can be appropriately adjusted to meet individual needs (Meek *et al*, 1989; Glass, 1991). It is important to note that provided alcohol abstinence is achieved and nutrition stabilised with appropriate thiamine and vitamin supplementation, cognitive performance is likely to improve in most cases.

Background

Cognitive effects due to acute intoxication

In the first instance, people presenting to an alcohol service for detoxification and withdrawal are likely to experience some cognitive change as a direct result of alcohol in their blood. The effects of alcohol on cognitive performance are well recognised and include changes in attention and concentration, difficulty in terms of memory and judgement, associated with varying levels of consciousness. As the person recovers from acute intoxication, cognitive performance is likely to recover, too.

Medium-term cognitive effects

A significant minority of patients with a history of more long-standing alcohol misuse are likely to experience medium-term cognitive change, which may take up to 3 months to recover. Provided such patients maintain abstinence, a significant proportion will recover completely.

Longer-term effects (usually related to thiamine deficiency)

A minority of patients presenting with cognitive dysfunction, even if abstinent for 3 months, will continue to experience longer-standing cognitive deficits. These are usually a consequence of the direct effect of excessive, long-standing alcohol exposure and multiple withdrawals and/or malnutrition and thiamine deficiency. As up to 25% of these patients have evidence of small strokes and head trauma (Wilson *et al*, 2012), further investigations may be required, including scans and investigations to exclude other causes of cognitive dysfunction. Existing evidence indicates that these individuals may improve to varying degrees over the following 3 years in the context of alcohol

abstinence. They will need modification of their care packages and ongoing nutritional support and thiamine supplementation.

Permanent effects (usually thiamine deficiency related)

A minority of patients will have permanent brain damage. They may present with classical Korsakoff's syndrome but are more likely to present with less well-defined problems associated with frontal lobe dysfunction. It is important to note that all these longer-term conditions may be associated with concomitant cerebrovascular disease and/or head trauma. Concurrent mental illness is also frequent.

Implications for assessment

NICE guidelines (National Institute for Health and Clinical Excellence, 2011) recommend that all patients referred to alcohol treatment services should have a cognitive assessment. It is self-evident that individuals presenting to alcohol services (for withdrawal) may have raised alcohol blood levels and as a consequence there may be a direct effect of alcohol on cognitive performance. Longer-term cognitive dysfunction can only be assessed after 2 months of abstinence (Oslin & Carey, 2003). In the absence of more specific guidelines, practical options should be considered.

A cognitive examination (e.g. MoCA© or ACE-III) should be considered early in the withdrawal process. Patients at risk of developing thiamine deficiency-related brain damage should be identified (Oslin & Carey, 2003; Thomson *et al*, 2009) and those at risk should be prescribed parenteral thiamine (these instruments include items designed to test frontal lobe disorders, frequently encountered in people with ARBD, as other, shorter instruments (e.g. 6-CIT may not be as sensitive in picking up frontal lobe dysfunction).

After withdrawal, prior to formal engagement in alcohol education and related treatment, a further examination should be undertaken with a view to:

- establishing the level of insight and mental capacity the person has with regard to managing the planned programme
- informing the timing of the programme/intervention, bearing in mind that cognitive performance is likely to improve in the context of 3 months' abstinence, good nutrition and appropriate psychosocial support
- adjusting interventions and degree of engagement required to suit the individual's personal needs, informed through awareness of cognitive problems.

In some cases, the degree of cognitive damage (as identified through cognitive examination) may be so severe that any attempt to engage is compromised; the patient is unable to make relevant, informed decisions and may be a danger to himself or others as a consequence of the confusion. In these cases, the patient should be considered as having a significant mental disability and the best interest of the patient should be considered in terms of the MCA or the AwIA; appropriate referral should be made for further neurocognitive assessment and management. Figure 1 portrays a rudimentary pathway of care that may be developed or adjusted to meet the local needs of individuals presenting to alcohol treatment services with cognitive damage.

Likewise, all patients should have a review of their nutritional status and the risk of thiamine deficiency assessed:

- when there is one or more signs of Wernicke's encephalopathy, the patient should be managed under medical supervision with i.v. thiamine as an in-patient
- when there is a significant risk of thiamine deficiency but no evidence of Wernicke's encephalopathy, the patient should be treated with i.m. thiamine but the clinician should be aware of the allergic history of the patient (see p. 4).

Implications for alcohol treatment programmes

There appears to be an association between amount and duration of alcohol consumption and degree of cognitive dysfunction at presentation to alcohol treatment services (DeFranco *et al*, 1985; Giancola *et al*, 1996; Ling *et al*, 2010). There may also be a correlation between the number of withdrawal episodes and cognitive impairment (Wagner

Glenn *et al*, 1988; Duka *et al*, 2010). Most studies that have examined cognitive dysfunction in people attending alcohol treatment services have usually compared recently detoxified alcohol-dependent patients with non-dependent controls. The commonly affected intellectual domains are given in Box 7.

A comprehensive cognitive assessment and knowledge of the individual needs of the patient should inform adaptation of routinely delivered alcohol treatment programmes (Fals-Stewart & Lucente, 1994). Research findings indicate that some of the possible adaptations include those listed in Box 8.

Summary

A considerable proportion of patients presenting to alcohol treatment services will have varying levels of cognitive impairment, either as a direct consequence of alcohol intoxication or as a consequence of long-standing alcohol misuse and thiamine deficiency. The majority are likely to recover over the first 2–3 months of abstinence. However, a small minority may be left with longer-standing cognitive damage. Two important and related issues should be considered in the assessment. First, ongoing cognitive and mental capacity assessments and adjustment of therapeutic engagement and programmes should be made to cater for the individuals with mild to moderate cognitive deficits. This may include enhanced follow-up and contact with patients who are difficult to engage because of their cognitive dysfunction. Second, when a patient is undergoing medically controlled withdrawal, oral thiamine should be prescribed. When thiamine deficiency is suspected or the patient is considered to be at high risk of Wernicke's encephalopathy, i.m. thiamine supplementation should be given by staff trained in the management of anaphylaxis. Intravenous thiamine should be used when Wernicke's encephalopathy or related symptoms are present. Intravenous therapy should be undertaken in an in-patient setting under medical supervision. Every patient receiving parenteral thiamine should be continued on oral thiamine.

Recommendations

1 Specialisation in the recognition and management of people with mild to moderate ARBD is built up within each alcohol treatment service and implications for commissioning agencies should be considered.

2 Alcohol treatment services and related pathways of care should cater for the significant minority of alcohol misusers who will present with ARBD.

Box 7 Intellectual domains commonly affected by excessive and prolonged alcohol consumption: evidence in literature

- **The ability to concentrate (DeFranco *et al*, 1985)**
- **Difficulties in learning new information (anterograde amnesia) (Alterman *et al*, 1989; Mann *et al*, 1999; Zinn *et al*, 2004; Schmidt *et al*, 2005)**
- **Problems in reasoning (Beatty *et al*, 1996; Mann *et al*, 1999; Zinn *et al*, 2004) and problem-solving difficulties (Beatty *et al*, 1996; Mann *et al*, 1999) and problems explaining actions and reasons (Beatty *et al*, 1996)**
- **The ability to understand complex information and concepts (such as alcohol dependency and implications for behaviour) and difficulty in acquiring drink refusal strategies (Smith & McCrady, 1991)**
- **The ability to be able to change from one stream of thought to another with normal degrees of flexibility (difficulty in working in groups or following complex discussions) (Beatty *et al*, 1996)**
- **Within the first few weeks of abstinence there is likely to be increased proneness to make impulsive decisions and there is less awareness of the longer-term implications of decisions and actions (Weissenborn & Duka, 2003; Davies *et al*, 2005; Parks *et al*, 2010)**
- **Understanding risk related to actions and decisions (Blume *et al*, 2005)**
- **Reduced organisational skills (Fox *et al*, 2000; Parks *et al*, 2010), and planning (Weissenborn & Duka, 2003)**
- **Poor adherence to treatment programmes (Copersino *et al*, 2012)**
- **Lower confidence (Bates *et al*, 2006)**
- **Breakdown of interpersonal relationships (Patterson *et al*, 1988)**
- **Difficulty in remembering and working out the relationship between objects (perceiving and remembering the locations of objects relative to each other and in 2- and 3-dimensional space) with potential consequences for DIY, constructing things, working with complicated machinery and driving**

Box 8 Adaptations of routine alcohol treatment programmes to suit individual patients

- Delaying the introduction of educational programmes until the patient has made sufficient cognitive recovery (McCrady & Smith, 1986)
- Focus on supportive or enforced abstinence (McCrady & Smith, 1986). This may be appropriate if the person is too incapacitated to make decisions and may have to be placed in a protective environment
- Expect the person with cognitive impairment to take much longer to benefit from interventions (McCrady & Smith, 1986)
- Simplification of educational materials (McCrady & Smith, 1986)
- Development of learning texts and materials to ensure that one concept is understood and learned before going on to another (McCrady & Smith, 1986)
- Provide the same information through multiple sensory modalities (McCrady & Smith, 1986)
- Wear name tags and provide memory cues (McCrady & Smith, 1986)
- Allow for reduced levels of concentration (DeFranco *et al*, 1985) and difficulties in swapping from topic to topic (Beatty *et al*, 1996). Patients may be helped through simplifying both content and form of discussions and educational points within each contact, with an emphasis on focusing on one or two points
- Providing some 'rewards' relating to appropriate behaviour may be beneficial. These may be psychological or social but should be tailored to the individual and may help recall (Hochalter & Joseph, 2001)
- Providing increased time for individuals within contact sessions (VanDamme & d'Ydrewalle, 2008)
- Sessions may have to be adapted to cater for problems in remembering new information
- Getting the individual to repeat information as soon as it is given may be of some help (Kessels *et al*, 2007). Offering information in a number of ways, including verbal, written and diagrammatic methods may help. Memory cues (Morgan *et al*, 1990) and reminders will play an important role
- Particular emphasis in helping patients with cognitive impairment in planning and providing a timetable and structure (Acquired Brain Injury Services, 2011)
- Working out simple rules to apply when dealing with problems may offer some help (Bardenhagen *et al*, 2007). This may include five steps (D'Zurilla & Goldfried, 1971):
  identify the problem
  collect information about the problem
  generate solutions to the problem
  select and implement the solution
  evaluate the results
- Keeping drink management strategies very simple and easy to follow is likely to be important
- In the first few weeks, particular emphasis should be placed on reducing exposure to risk as a consequence of increased likelihood of impulsive decision-making (Weissenborn & Duka, 2003; Davies *et al*, 2005; Parks *et al*, 2010)
- Diary-keeping may help in terms of cuing memories as well as informing future planning and activities (Wilson *et al*, 2012)
- It is likely that problems in concentration, memory and understanding, planning and following complex instructions will influence the individual's engagement with the therapist and team. It may be necessary for the therapist/team to adopt an active engagement strategy to accommodate the needs of patients with cognitive impairment. This may involve more frequent visits, more guidance, transport assistance and social support. It is important for the clinician to conceptualise these issues as problems in learning rather than simply seeing them as 'motivational issues' (McCrady & Smith, 1986)

3 All new patients referred to alcohol treatment services have a cognitive assessment. A cognitive assessment should be nested within an assessment of the psychological and social needs of the individual. It may take the form of a number of structured examinations ranging from fairly brief ones such as the 6-CIT or the MMSE, through to more sophisticated interviews using the ACE-III or MoCA©.

4 Cognitive testing should be carried out early in the treatment programme, and subsequently after 3 months of abstinence. If there is residual cognitive impairment, then 6-monthly cognitive assessments should be undertaken over a follow-up period of up to 3 years.

5 Therapists should gain experience in mental capacity assessment as required by the MCA and AwIA.

6 Patients with severe cognitive problems or who are incapacitated to the degree that they are at risk should be referred for specialist ARBD assessment.

7 When there is a likelihood of Wernicke's encephalopathy and related symptoms, in-patient referral and i.v. thiamine should be considered.

8 All patients are assessed for risk of thiamine deficiency in the absence of Wernicke's encephalopathy-related symptoms and if there are significant risk factors then i.m. thiamine treatment is indicated.

9 All patients having received parenteral thiamine should be continued on oral thiamine.

10 Anyone receiving medically supported withdrawal should be prescribed oral thiamine even when no risk factors of Wernicke's encephalopathy are present.

11 Close liaison between alcohol treatment services and local 'specialist' services commissioned to cater for ARBD is recommended.

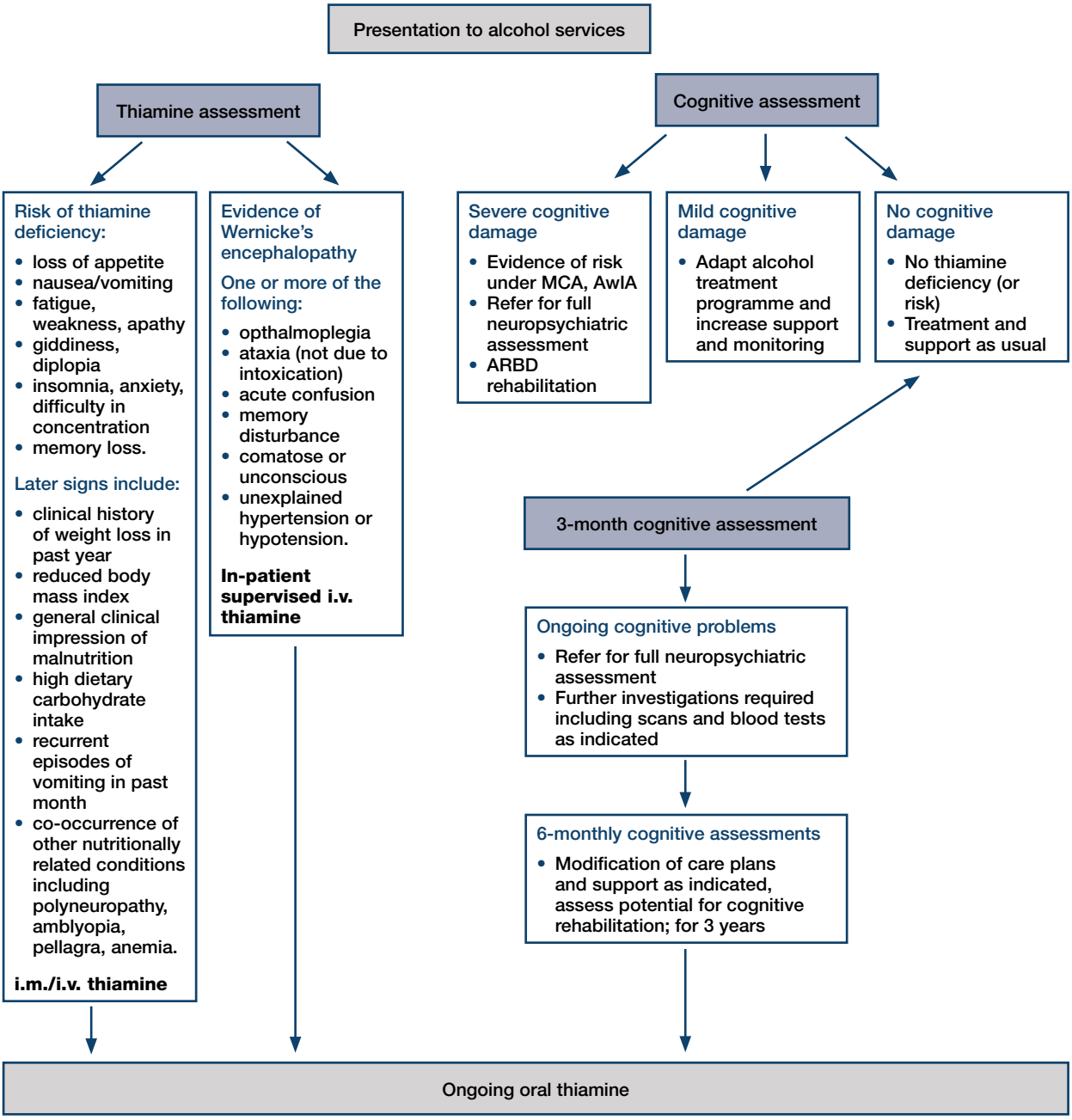

Fig 1 Management of alcohol-related brain damage (ARBD) within alcohol treatment services. AwIA, Adults with Incapacity (Scotland) Act 2000; i.m., intramuscular; i.v., intravenous; MCA, Mental Capacity Act 2005.

Screening and management of alcohol-related brain damage within the prison service

It is important when considering the provision of healthcare to this complex-needs group to describe the wider context of healthcare delivery within the prison system.

Recent developments of prison health services

During the latter part of the 20th century, provision of healthcare within prisons was severely criticised. In the Home Office paper *Patient or Prisoner?* inequity of provision of healthcare between those inside prison and those outside was highlighted (HM Inspectorate of Prisons, 1996). An argument for the equivalence of care between these two groups gathered momentum and a working party, set up between the Department of Health and the Home Office, formalised this argument in the paper *The Future Organisation of Prison Healthcare* (Joint Prison Service and National Health Service Executive Working Group, 1999). A further Department of Health document *Changing the Outlook* (Department of Health, 2001) set out the timetable for the transfer of commissioning responsibility to primary care trusts. This process came to fruition in April 2006. All prison healthcare is now delivered by the NHS through services commissioned by local commissioning arrangements.

The limitations of prison healthcare provision

It is important to recognise the difficulties in dealing with such physically ill patients, both within prison and in hospital, and for doctors and clinicians working outside the prison to recognise the limitations of healthcare provision within the prisons. Prisons and hospitals have very different purposes: the former control and contain, whereas the latter care and treat. Healthcare workers within prisons are the guests of the prison. Healthcare opinions may suggest a move of an individual to a certain prison with specific healthcare provision, but the ultimate decision to move the prisoner is that of the prison governor.

The majority of healthcare in prison is delivered on an out-patient basis to prisoners located on normal location (i.e. in normal cells on the wings in the prison). A small minority of prisoners are moved to the healthcare unit within prison where they can have more in-depth observation by medical staff. Such healthcare units are usually staffed by primary care nurses with input from general practitioners (GPs) and secondary mental health services. There is no equivalent to such healthcare units in the community. It is important to recognise that such healthcare units do not fulfil all the

functions of a hospital. Patients are accommodated in cells rather than wards or side rooms and are subject to the same discipline as other prisoners within the prison. Intense physical observation and anything but the most basic physical care is extremely difficult in such circumstances. For those who are physically very unwell, transfer to the local general hospital under prison escort may be indicated. However, supervising prisoners in the general hospital setting can be difficult: it may cause disruption to the hospital staff and extra expense to the prison service, but is nevertheless at times essential.

Screening

All prisoners receive a primary and secondary medical screen on reception into prison. The primary screen is undertaken immediately on entry to prison and is designed to identify healthcare problems which require immediate intervention. The secondary screen takes place within the first week and considers a broader group of non-urgent healthcare problems. Thus, identification of alcohol withdrawal may be indicated in the primary screen, whereas identification of the sequelae of chronic alcohol misuse would be more appropriately targeted in the secondary screen.

Commonly used screening tools, such as the Cage questionnaire (Mayfield *et al*, 1974) and the AUDIT tool (Babor *et al*, 1992) are employed in prison. It is interesting to note that they require the cooperation of the prisoner. In one study of remand prisoners the proportion identified with the AUDIT tool as having a probable alcohol problem increased from 19 to 60% and those rated as probably alcohol dependent increased from 11 to 43% when comparing assessment made on the day of reception and 2 weeks later. It is thought that these increases were due to improved cooperation at the second screening (Maggia *et al*, 2004). See Table 2 (p. 52) for levels of drinking in UK prisoners as discovered in Singleton *et al*'s (1998) study.

The close association between ARBD and traumatic brain injury is well established (Wilson *et al*, 2012). As there is a high prevalence of traumatic brain injury in prison populations, screening for both ARBD and traumatic injury is advised so as to inform appropriate assessment and rehabilitation.

Substance misuse services in prisons

Services for drug users, particularly heroin addicts, are relatively well delivered within the prison. The recently introduced integrated drug treatment service (IDTS) aims to offer opiate replacement maintenance therapy for all prisoners with opiate dependence serving sentences of 24 weeks or less. Drug counselling is also available through Counselling Assessment Referral Advice Through Care (CARAT) services.

Services for those with alcohol dependence are less well developed. However, there are opportunities for prisoners to attend Alcoholics Anonymous meetings and in some prisons to undertake short interventions relating to their alcohol problems.

Prescription of benzodiazepine detoxification regimes for those withdrawing from alcohol are commonplace. Diversion of such sedative medication is a significant problem in prison and such medication is given to the prisoner at the clinic hatch and their consumption of it is observed.

Clinical psychological services within the prison service are relatively underdeveloped. There are a number of forensic psychologists within the prison, although their focus is not specifically clinical: they undertake risk assessments and deliver treatment programmes relating to offending.

Prisoners with ARBD and indeterminate sentences

The prison population is divided into three groups:

1. non-sentenced remand prisoners
2. those sentenced to determinate sentences (with a fixed release date)
3. those who have received life sentences.

The last group includes: those who have received mandatory life sentence for the conviction of murder; those who have received a discretionary life sentence, where their offence was of a serious nature, they are thought to be of unstable

Table 2 Drinking among UK prison population (Singleton *et al*, 1998)		
	Hazardous drinking in the year prior to detention, %	
	Remand prisoners	Sentenced prisoners
Male	58	63
Female	36	39

character and the consequences of their offence were significant (sexual or violent); and a third group, those imprisoned for public protection (IPP). IPP sentences are given to those who have been convicted of a serious offence which would attract a penalty of 10 years or more and in whom there are concerns regarding ongoing risks to the public. There are currently approximately 11 000 life sentence prisoners. The sentence of imprisonment for public protection came into effect in April 2005. The numbers detained under this legislation have risen exponentially (there were just over 1000 made in 2006 and just over 6000 in March 2012; Srtickland *et al*, 2013). The current prison population in England and Wales is approximately 85 000 (The Howard League for Penal Reform, 2014).

The management of prisoners with ABRD who receive life sentences is quite problematic. All prisoners given life sentences have a sentence plan drawn up after receiving their sentence which details how their offending behaviour will be addressed and what they will have to achieve to be released into the community under licence. Much of the offence-related work, anger management and sex offender work is of a cognitive–behavioural orientation. Those who have significant deficits due to ARBD may be unable to fulfil the necessary courses to progress through their sentence plan and ultimately be released into the community. The life sentence prisoners (including those sentenced to IPP) who experience ARBD may find themselves in a 'catch 22' situation. They are unable to engage in the necessary work and therefore unable to prove that they are no longer a risk, and are stuck with no prospect of release.

The Mental Health Act 1983 does not allow for the detention of individuals purely for disorders of addiction. However, it does allow for detention for those disorders which are secondary to such addictions such as ARBD. Furthermore, the Act allows for the transfer of prisoners to hospital for assessment and treatment prior to trial and sentencing. It is therefore very important to consider transfer to hospital for assessment and treatment of prisoners with ABRD who may be sentenced to indeterminate detentions.

If the treating doctor believes the prisoner should be transferred to hospital as a matter of urgency, then Section 48 of the Mental Health Act is appropriate. Alternatively, reports could be made to the court requesting admission for assessment and treatment under Section 36. Finally, for those who have already been convicted of a crime it is possible to have an interim order (under Section 38) which allows for a trial period of assessment and treatment prior to sentencing.

There are community disposals available to the courts in place of prison sentences (community orders with conditions of treatment). These require a treating consultant to deliver a package of care in the community which would form part of the conditions of such a community order.

Preparation for release of prisoners with ARBD

There is an obligation on primary care services and secondary mental health services within the prison to identify those with ongoing alcohol use disorders and consequences thereof, to liaise with the appropriate services in preparation for their release into the community. In some instances, where alcohol misuse and its consequences are directly related to the risk of future offending (violent or sexual), there would be liaison with the MAPPA panel (a multi-agency vehicle which aims to identify high-risk individuals and reduce their risks, monitor them closely and minimise the risk of them reoffending in the future).

Summary

The identification and management of ARBD within a prison setting is associated with significant problems, despite the probability of a high prevalence

rate. Some rudimentary screening systems are usually in place to facilitate the identification of heavy drinkers. These can be used to identify people at high risk and may be useful in signposting individuals to additional support in the management of their alcohol misuse. Enforcement of abstinence in a prison setting will lead to some improvement over time and the needs of the individual can be reassessed as appropriate.

Recommendations

1. Alcohol withdrawal may need to be conducted under care of the local hospital.
2. Primary and secondary screening should incorporate alcohol-screening instruments.
3. Individuals identified as having alcohol-related problems should be signposted to appropriate support facilities.
4. People with alcohol-related problems should be reassessed in terms of needs prior to release from prison and referred to appropriate external agencies including the MAPPA panel.

Screening and care in acute hospital-based medical and surgical settings

The majority of patients presenting with severe ARBD will present through the acute hospital, frequently admitted in an acute confusional state and warranting an alcohol withdrawal regime. As a consequence of acute physical complications, many patients are admitted into acute medical or surgical wards. They are rarely referred for psychiatric assessment as a consequence of cognitive dysfunction, unless there are acute behavioural problems. Consequently, a screening mechanism is recommended to trigger appropriate referral to specialist services.

The development of a screening and diagnostic programme may face a number of issues. Some of these include:

1. Managing stigma.
2. Designing a screening/diagnostic process which is simple and quick to deliver.
3. Undertaking screening and diagnosis within a very small 'window' of time. The patient in an acute medical ward should be screened for cognitive damage when physically stabilised to reduce the chance of picking up acute and subacute confusional states relating to either withdrawal from alcohol or concomitant physical illnesses. The time frame is limited by the extreme pressure to discharge patients from acute medical/surgical care as soon as physically well.
4. Identifying a clinical organisation/member of staff to conduct the screening.
5. Providing a funded pathway of care that facilitates the relatively quick discharge of the patient from the acute ward so as not to cause inappropriate use of acute medical/surgical beds while patients are waiting on protracted discharge planning and funding arrangements.
6. Providing a mechanism by which incapacitated patients may be protected from further adverse exposure to alcohol so that ongoing assessment of capacity and damage can be undertaken in a protective and stable environment.

Managing stigma

Stigma remains a problem in the world of mental illness. In the absence of service provision, many acute hospital wards and mental health services will not have addressed the problem of how to identify and manage people with ARBD. This has potential significance in the context of the MCA which clearly places responsibilities for care of incapacitated individuals on provider units. Introduction of new service initiatives must be seen to be collaborative, based on education, facilitative and not threatening to service providers to overcome these issues.

Time limitation

The process of screening and assessment must be designed to accommodate (inasmuch as is possible) the relatively fast turnover found in acute hospital environments. Consequently, any

screening process needs to be done as soon as the patient is considered physically stabilised. It is quite likely that a person can be discharged within a day or two of physical stabilisation and if not identified as at risk, may well return home to continue alcohol misuse, which makes assessment of cognitive state very difficult.

Identifying a clinical organisation/member of staff to conduct the screening

There are a number of alternatives, depending on the profile of service delivery. In the absence of established service provision, the utility of these options has not been tried and tested. In the first instance, many acute hospital trusts may have alcohol liaison staff based on the wards. These clinicians will have some valuable skills, and are already integrated into routine ward life and have the advantage of being recognised as part of the service provision by generic services with established pathways of referral. The generic psychiatric liaison service provides another option, depending on expertise and immediacy of response. One more option worthy of consideration is to embed the initial screening into generic nursing and junior medical staff on the ward. This is quite difficult as it may involve introducing new procedures in the context of a busy clinical environment. However, many junior doctors will be familiar with simple screening instruments such as the MMSE. An alternative is to have screening as part of an in-reach service, funded through the mental health services and conducted by individuals working with ARBD in community and other settings.

Designing a simple and quick-to-deliver screening/diagnostic process

The nature of the process will be informed by what resources are available, brevity and utility. The Wirral (Wilson *et al*, 2012) has adopted a two-phase approach in which high-risk patients are initially identified by the alcohol liaison nurse/psychiatric liaison services and generic nurses on the acute hospital wards, using general information concerning the patient and not requiring a formal cognitive examination. A further assessment is conducted by the ARBD team consultant. If the second assessment is delayed then one of the other members of the ARBD team will carry out an interim assessment and record it in the clinical notes. The whole process is achieved within 5 working days of referral.

This approach is pragmatic, utilising readily accessible hospital records (in this case computerised), adopting a fairly flexible approach to alcohol misuse assessment and not involving anything other than a 'lay' interpretation of 'confusion', not requiring any psychometric or instrumental assessments. It has been employed in the context of a service specifically commissioned to reduce the use of secondary care beds by people with ARBD. There are obvious disadvantages in that this approach will only identify severe levels of ARBD in people who have been frequent users of acute hospital services and will potentially identify people with non-permanent changes in cognition.

Alternative screening may include the use of the MMSE or equivalent brief instruments such as the 6-CIT. It has already been noted that most of these instruments do not incorporate frontal lobe testing and may only pick up more severe forms of ARBD. Alternative primary or secondary instrumentation may include slightly more sophisticated profiles including aspects of frontal lobe testing such as the MoCA© or the ACE-III. Other options include using such instruments as the MMSE in combination with simple frontal lobe testing instruments such as the Frontal Assessment Battery (Dubois *et al*, 2000).

As already indicated, these 'screening' instruments should be supplemented by a clinical diagnostic process which should include investigations to exclude vascular disease (Oslin & Carey, 2003), and a more comprehensive neuropsychological/psychosocial assessment, albeit conducted in a relatively short period of time in an acute medical or in-patient setting. One of the more important aspects of this is the assessment of capacity in terms of informing care planning and discharge

arrangements, including the capacity to make informed decisions concerning further exposure to alcohol.

Accident and emergency units

Accident and emergency departments also offer a key venue through which people with ARBD may be identified. However, problems in undertaking screening in this environment are particularly challenging. The turnaround of patients is particularly fast, with many patients being discharged within a few hours. One of the major issues that may be considered is the assessment of capacity, invoking the MCA (England and Wales) or, in Scotland, the AwIA legislation, which may provide a window of opportunity to undertake a cognitive assessment.

Immediate management

There are a number of steps through which patients are likely to flow:

- physical stabilisation in acute hospital setting
- rapid identification through screening and establishing a diagnosis
- assessment under appropriate legal framework when indicated (MCA, AwIA)
- discharge to appropriate environment for further assessment over 3 months
- development of a care plan suitable for the rehabilitative needs of the individual if required.

Many severely confused patients will require a safe and structured environment in which ongoing assessment can take place. Some of these patients may be socially, financially and physically vulnerable and some may be so cognitively impaired that they are incapacitated in making even simple day-to-day decisions. The acute confusional effect of long-term alcohol misuse may last for up to 3 months in the context of an uncomplicated case. A pathway of care should cater for these critical few months, allowing the clinical team to assess improvement and the possibility of longer-term damage. Institutions may provide an appropriate environment, depending on the need of the patient; however, where support is available and the risk is acceptable, the home environment may be an alternative.

Summary

Most patients with ARBD admitted to acute medical and surgical care are rarely recognised as having ARBD and are not referred to appropriate service providers that can facilitate care plans and follow-up. Hence screening is recommended for high-risk patients. Patients should have mental capacity assessments conducted in the context of cognitive examination and care plans adapted as appropriate. Referral pathways should be commissioned and funding made available for the rapid discharge from acute care into a safe and alcohol-free environment, where appropriate. During the first 3 months, cognitive improvement can be expected and patients should be reassessed. Longer-term active rehabilitation should be planned for those with residual cognitive disability, with a view to optimising independence and autonomy.

Recommendations

1. A simple screening instrument should be used to identify at-risk patients in acute hospital settings. This should be supported by a primary diagnostic process which includes appropriate physical and radiological (scanning) investigations, a psychosocial review (including examination of frontal lobe function), and engaging carers or family where appropriate.
2. Where indicated, the patient should be assessed in the context of the MCA (England and Wales) or AwIA (Scotland).
3. Owing to the very high turnover in acute hospitals it is advised that assessments should be undertaken as soon as a referral is made to the team, with relatively assertive 'in-reach' into hospital wards and accident and emergency departments.
4. Funding support should be designed to enable ready access to appropriate services and rapid discharge from acute medical wards.

5 The first 3 months of abstinence are associated with considerable cognitive and behavioural improvement. During this period, the incapacitated patient should be protected from alcohol exposure and other risks until able to make and manage their own decisions.

6 Ongoing assessment of capacity, clinical status, cognition and behaviour should be continued over the first 3 months with a view to construction of an appropriate care plan, ARBD rehabilitation, referral to other agents (e.g. alcohol treatment services) or discharge as appropriate.

Pregnancy and fetal alcohol spectrum disorder

Fetal alcohol spectrum disorder (FASD) is a group of disorders where prenatal alcohol exposure causes congenital damage to the central nervous system and other systems and organs of the fetus that subsequently leads to a number of adverse health consequences. These disabilities, characterised by physical, cognitive and behavioural impairments, include a continuum of developmental disorders that are clustered together under an umbrella term of FASD. Four separate conditions are recognised within the continuum: fetal alcohol syndrome (FAS), partial fetal alcohol syndrome (PFAS), alcohol-related neurodevelopmental disorder (ARND) and alcohol-related birth defects. From this group, FAS is the only disorder coded in ICD-10 as fetal alcohol syndrome (dysmorphic) Q86.0 (World Health Organization, 1992). It was coded previously in ICD-9, clinical modification (ICD-9-CM) as alcohol affecting fetus or newborn via placenta or breast milk 760.71 (Popova *et al*, 2012). The DSM-5 includes a diagnostic category 'neurobehavioural disorder associated with prenatal alcohol exposure' in section 3, 'Conditions for further study' (American Psychiatric Association, 2013).

Despite ancient references and interest in the medical community in the 1700s and 1800s, it was not until 1973 that the term fetal alcohol syndrome was first coined in the medical literature. Jones *et al* (1973) were among the first to advance scientific knowledge in their submission of 'Pattern of malformation in offspring of chronic alcoholic mothers' to *The Lancet*. The research compiled cases of children with prenatal alcohol exposure in terms of cognitive impairment, growth deficiencies and morphological abnormality.

Prevalence and healthcare costs

Despite increased public and media interest in FASD, doctors and other health professionals are unable to access prevalence figures of these conditions in the UK as these are not routinely collected or recorded by the British Paediatric Surveillance Unit (British Medical Association, 2007). However, there is general consensus arising from separate research studies carried out in different countries that the figure for FAS is 1 in 1000, with FASD being 3–4 times higher. Internationally, prevalence rates vary widely from 0.5 to 40.0 per 1000 live births, with American studies reporting ranges of 0.5–2 and 10 per 1000 live births for FAS and ARND respectively (May & Gossage, 2001). Canadian studies report comparable prevalence with 1–6 per 1000 live births (Chudley *et al*, 2005). Much higher rates of 39.2 per 1000 (May & Gossage, 2001) and 40+ per 1000 are found in certain high-risk communities in South Africa (Rosenthal *et al*, 2005). This level of discrepancy in quoted prevalence rates may be linked to variable diagnostic convergence and the methodological variations, including potential observer bias from participation of clinicians with a special interest in FASD (Druschel & Fox, 2007).

Lack of clarity in formulating a reliable diagnosis is one of the reasons for existing difficulty in quantifying the scope of the problem associated with FASD. Although paediatric dysmorphologists or geneticists are best equipped to diagnose FAS (which has lower incidence), psychiatrists and other mental health professionals treat the majority of FASD lifelong problems, including comorbid

conditions such as ADHD and conduct disorder. Cases of misdiagnosed FASD as bipolar affective disorder and pervasive developmental disorders of childhood are also commonplace.

FASD is associated with a vast number and wide range of health conditions and an increased mortality rate, as compared against the general population (Burd *et al*, 2008). As a result of the increased morbidity, FASD is a substantial burden to society in relation to the healthcare costs involved in caring for affected individuals. In the USA, Klug & Burd (2003) estimated that the prevention of one case of FAS each year for 10 years would result in out-patient and in-patient healthcare costs savings of US$129 000, and the prevention of one case each year for 20 years would decrease these expenditures by US$492 000. The healthcare cost associated with FASD are multifaceted in their nature and affect areas of special education, community social services, juvenile legal services and law enforcement. For example, in one American study of 253 people with FAS or fetal alcohol effects, 60% reported ever being charged, convicted or in trouble with the authorities for any of a list of criminal behaviours, and 42% of adults had been incarcerated for a crime (Streissguth *et al*, 1996). The indirect costs – such as productivity losses of people with FASD and their caregivers – are harder to estimate, as they require longitudinal studies.

Cause

Maternal alcohol consumption during pregnancy is an established cause of FASD, thus pointing to this group of patients as having environmentally induced developmental disabilities. Our society's accepted drug of choice, alcohol, is the most potent neurodevelopmental teratogen and one of the leading causes of functional birth defects in the world. Prenatal exposure to alcohol disrupts fetal brain development at any point in gestation. Exposure in the first trimester affects organ development and craniofacial development. Structural brain changes are most common, followed by cardiac (especially septal) defects, and skeletal, renal, ocular and auditory abnormalities. The quantity of alcohol and frequency of consumption do not directly correlate with occurrence of FASD and its severity, thus it has been hypothesised that this causative relationship is mediated by other factors. Since the original description of the syndrome in the 1970s, mounting evidence about the impact of maternal alcohol consumption and its effects has been advanced through autopsy, rodent models, longitudinal, structural and functional imaging studies, but much still remains to be understood about the role of epigenetics in causation of FASD and the nature of cellular changes that take place during organogenesis. The maternal risk factors are considered to be important in our conceptualisation of FASD and include advanced maternal age, undernutrition, low socioeconomic status, frequent binge drinking, psychiatric diagnosis and high gravidity and parity (Abel & Hannigan, 1995).

Presentation

Infants affected by FASD show intellectual impairment and difficulties in learning, memory, problem-solving and attention as well as experiencing additional problems with mental health and social interactions. Children have a pattern of defects including prenatal and postnatal growth deficiency, small head size and facial abnormalities, allowing for recognition of the disorder in infancy (Hanson *et al*, 1976). Typical facial abnormalities are characterised by small eyelid openings, a smooth ridge on the upper lip (absence of a philtrum), and a thin upper lip border (Warren *et al*, 2011). Research has examined the diagnostic heterogeneity of this group, with some studies reporting a significant relation between general cognitive functioning, postnatal growth deficiency and facial abnormalities (Ervalahti *et al*, 2007), and others revealing that the majority of children with prenatal alcohol exposure may not present with the physical abnormalities necessary for a diagnosis of FAS, yet represent a profile with significant neurodevelopmental impairments. The presence or absence of facial dysmorphology, or growth features, does not clinically correlate with neuropsychiatric sequelae or structural brain damage in FASD (Streissguth & O'Malley, 2000).

FASD is not just a childhood disorder; difficulties that emerge in childhood often are reflective of a convergence of genetic, neurophysiological and environmental factors that persist into adulthood

(Nash *et al*, 2013). There is also a predictable long-term progression of the disorder into adulthood, with increased risk for mental health disorders and poor social functioning, and in which maladaptive behaviours present the greatest challenge to management (Streissguth *et al*, 1991).

High rates of mental disorders within the FASD and perinatal alcohol exposure population were found to be consistently reported for both externalising and internalising disorders and this is seen as a result of increased vulnerability to common psychiatric disorders rather than as a direct consequence of having FASD. Disorders such as ADHD, early childhood trauma, post-traumatic stress disorder, reactive attachment disorder, mood and anxiety disorders, social communication disorders, substance use disorders and psychosis are commonly associated with FASD.

Management

Interventions for individuals with FASD suffer universally from a serious lack of rigorous scientific investigation and robust clinical trial data. A systematic evaluation of randomised controlled and quasi-experimental studies of interventions in FASD in people under the age of 18 (Premji *et al*, 2007) demonstrated a paucity of research and emphasized the need for further studies. However, the current understanding of the neuropsychological and neurobehavioural profile of FASD has facilitated the development of guidelines for interventions that may be useful in the management of children, adults and affected families with FASD including psychoeducational, psychosocial, pharmacological and novel approaches such as nutritional and physical therapies.

Professionals must be mindful of the enduring cognitive and social blueprint that each child represents, varying by multifactorial genetic and teratogenic manifestations from perinatal alcohol exposure. It is thus essential that treatment plans be targeted at a family systems level, incorporating person-centred approaches specific to the individual's areas of difficulty for each stage of development. All treatment programmes should start with psychoeducation for the family on the manifestations of FASD, the associated risks, neurobehavioural profile and available interventions. Interventions should draw from evidence-based practice and address the specific needs of each individual. Interventions addressing the neurocognitive and social aspects of the disorder should focus on a strengths-based model to compensate for the identified weaknesses in each individual. Family strategies have been focusing on resilience-amplifying interventions and working on enhancing family coping strategies (Wilton & Plane, 2006). The efficacy of a parent-assisted children's friendship training (CFT) versus a delayed treatment control (DTC) was assessed for 100 children with FASD (O'Connor *et al*, 2006). Children aged 6–12 years in the CFT group showed clear evidence of improvement in their knowledge of appropriate social behaviour, and CFT resulted in improved social skills and fewer problem behaviours compared with DTC, with gains maintained at 3-month follow-up.

There is no specific pharmacological treatment for FASD, but most psychotropic groups are used generically for the treatment of active symptoms of comorbid psychiatric disorders. In the literature the evidence of the wide use of psychostimulants in FAS, PFAS and ARND was reviewed by O'Malley & Hagerman (1998) and O'Malley & Nanson (2002). They concluded that the response to standard psychostimulant medication used for ADHD might be unpredictable because individuals with FASD have disturbed brain neurochemistry and oversensitive corpus callosum. The prescribing for this fragile, neurologically compromised population is made especially difficult due to polypharmaceutical use, paradoxical responses to medication, contraindications on the basis of medical or neurological issues and higher likelihood of drug adverse effects.

Clinical implications

This report draws attention to an urgent need for population- and clinic-based studies that will accurately establish the true prevalence of FASD within the UK population. In capturing the size of the problem associated with FASD, we need to develop comprehensive and sound methods for calculating the economic impact of FASD on British society. It is hoped that the results of carefully designed cost utilisation studies will inform healthcare commissioners and policy makers of

the extent of economic burden that FASD places on the British healthcare system.

It is clearly evident that we need to increase our capacity to provide preventative public education services for at-risk population, as FASD is a completely preventable group of conditions. Universal prevention approaches can be used to protect entire populations through education and the implementation of public health policy. Doctors should screen patients about the frequency and amount of their alcohol use and encourage women of childbearing age who are consuming alcohol to use contraception and to plan their pregnancies after stopping alcohol use. Similar is the case with retinoic acid derivatives, lithium, sodium valproate and other teratogenic agents that are avoided or cautiously prescribed for sexually active women of childbearing age. We also need to be mindful of popular misconceptions about 'safe' amounts of alcohol used during pregnancy. Anecdotal evidence suggests that educated women abstain for a period during early stages of pregnancy due to the misconception that it is safe to begin drinking after the first trimester.

We call for the development of early diagnostic services to individuals of any age exposed to alcohol prenatally. By improving the recognition of FASD and by providing early and accurate diagnostics we will be decreasing the healthcare utilisation costs by affected individuals. A proper early diagnosis has the additional benefit of targeted alcohol misuse treatment for identified mothers in order to prevent recurrent cases of FASD. We are mindful of these targeted interventions to be recommended in a way that would avoid further stigmatisation of mothers with alcohol dependence. We stress the need for prevention and early interventions to be implemented to minimise the manifestation of disabilities associated with prenatal alcohol exposure.

This report recommends FASD-specific training and professional development initiatives to be endorsed and rolled out by the recognised training programmes and professional bodies representing doctors of all disciplines, nurses, psychologists, addiction counsellors and other involved professionals. The Royal College of Psychiatrists would like to seize the opportunity in developing training manuals on the assessment of risk drinking and on referral and intervention methods for health practitioners who treat women of childbearing age. The work on the early childhood neurodevelopmental assessment for the differential diagnosis of FASD has already begun by the multidisciplinary team representing national network on Childhood Onset Neuropsychiatric Conditions and Early Life Brain Injury (CONCEBI) under the auspices of the Royal College of Psychiatrists. We are also making links with our colleagues from the Royal College of Paediatrics and Child Health to develop a joint guide on screening children for FASD and to propose changes to the recording of FASD by the British Paediatric Surveillance Unit. It is envisaged that with time the full range of FASD diagnoses will be coded in the ICD/DSM diagnostic manuals, thus helping to recognise and diagnose FASD more accurately.

This report highlights that there is a potential demand for specialist psychiatric and psychological healthcare services in this population. Understanding the complexities of FASD-related presentations arising from the interplay between neurobiological, environmental and adaptive factors requires a range of skills and clinical expertise. No one discipline can meet the trajectory of need related to FASD in children and youth, and it is our view that dedicated child and adolescent neuropsychiatric/neuropsychological teams should play a central role in the initial assessment and diagnosis of these conditions, as early identification and intervention for children with complex neuropsychiatric presentation, including FASD, will enhance the likelihood of positive outcomes.

Specialist centres will offer a high level of expertise and care to those who need this level of input. Shared care arrangements (care shared between a specialist centre and local hospital and community services) enable specialist clinicians to focus on assessment and setting of treatment plans while allowing the treatment to be carried out in a more local setting. The concept of a network of care is particularly important for these specialist services and they should establish vertical and lateral care pathways with primary care health teams, early interventions teams, child and adolescent mental health teams, disability services and other relevant service providers. Similar adult services have a lifelong role in meeting the care needs of this vulnerable group.

Summary

In conclusion, these outlined clinical implications alongside societal driven arguments should be used as a strong evidence base demonstrating the healthcare need of the FASD population. We need to use our current epidemiological and scientific understanding of FASD to design and implement more effective prevention and intervention programmes that address these issues across the spectrum of possible public health approaches. We hope that the available best evidence will build the platform for healthcare and utilisation requirements for decision makers formulating policies on FASD services.

Recommendations

1. The dangers of alcohol consumption during pregnancy should be routinely explained to all that are either planning pregnancy or are expectant.
2. Physicians should routinely ask about prenatal alcohol exposure as part of history-taking in patients who appear to be displaying ADHD symptomatology but who may have FASD.
3. Treatment plans should be targeted towards families, emphasising early education.
4. Interventions should be tailored to the needs of the individual: specific interventions of known efficacy include parent- or carer-assisted CFT.
5. Child and adolescent neuropsychiatric/neuropsychological teams should play a central role in the initial assessment and diagnosis of these conditions, and the development of specialisation and specialist centres should be considered to facilitate early diagnosis and intervention.

Examples of service provision

NHS Adult ARBD Service: Fife, Scotland

A recent report into ARBD, *The Picture in Fife* (O'Brien, 2011), identified the need to develop an ARBD service that could assess and 'case manage' people affected by the condition. The service has been developed, delivered and managed by the NHS Central Fife Mental Health Clinical Service. It is a community-based service using an assertive outreach model of care. The service was piloted in the Levenmouth area only in 2011/2012 and, following evaluation, was rolled out across other areas of Fife. As a case management service the team work closely with any existing support services. The core members of the ARBD team are mental health nurses who develop and coordinate each referred individual's assessment and care plan, working in close partnership with colleagues from the multidisciplinary team including psychiatry, occupational therapy, addictions services, social work service, housing, homelessness services and voluntary sector agencies.

Aims and objectives

1. To establish appropriate service provision for this vulnerable client group.
2. To provide care coordination for people affected by ARBD.
3. To develop and promote partnership working across traditional service boundaries.
4. To work in partnership with other services in developing an integrated approach to delivering an ARBD service.
5. To raise awareness of the difficulties faced by those with ARBD when trying to access mainstream services.
6. To become a source of specialist advice, training and information for other services on ARBD.
7. To complement and coordinate existing services, not replace them.

Role of the ARBD nursing team

The ARBD case management service is nurse led; the nursing team is managed by a team leader supported by three staff nurses. The team is responsible for delivering an ARBD case management service that is responsive to the individual's identified needs, including recognising that care planning and coordination arise from the assessment process and the importance of an integrated service approach to assessment of needs. The case management model facilitates the integration of input from different agencies.

- People with ARBD need a range of services crossing traditional boundaries between medical and social care. To facilitate this, the nursing team regularly meets with colleagues from partner agencies to review current patients' care plans.
- There is an open referral system: anyone can refer an individual for assessment to the team by completing a referral form.
- The team supports a range of therapeutic interventions designed to maximise an individual's potential to live as independently as possible.
- Care plans are holistic and patient-centred. The aim is to try to address all aspects of the person's functioning, and various team members may be involved in this, utilising their individual and varied skills.

- Multidisciplinary care planning is standard with a robust review process; the team use the care programme approach (CPA) for ongoing care, at least until the person is settled.
- Coordination facilitates the integration of input from different agencies.
- Provision is made available for those who continue to drink; particular skills are required for engaging with this challenging group of people and a harm minimisation approach is used.
- Carer support is a vital component of the work carried out by the team.

Service delivery and location

The service operates from 09:00 to 17:00, Monday to Friday; however, a degree of flexibility, depending on need, is built in. The service does not operate on public holidays.

The main base of the service is the Whyteman's Brae Hospital, Kirkcaldy, but the nursing team see individuals in a variety of community settings, including the patient's own accommodation.

Referral process

The service operates an open referral system where anyone can refer. Referrals can be made by completing a referral form, which is then sent to the ARBD nursing team.

Information required on referral: name, date of birth, gender, address, GP, marital status, referred by and date, other agencies involved, and brief details of current presentation including history of alcohol use. The person referred must fulfil two criteria: there must be history of alcohol dependence/harmful drinking, and evidence of cognitive impairment (i.e. inaccurate memories, confabulation, disorientation, inability to screen out irrelevant information, attention deficits, difficulty with planning and executing plans, poor judgement, difficulty processing new information, poor motivation, self-neglect, disinhibited/impulsive behaviour).

When the referral form is received by the ARBD nursing team an appointment is made to visit the person referred. The nursing team will complete a preliminary investigative assessment and establish whether the two admission criteria are met. The team will discuss new referrals with colleagues from partner agencies.

The person's GP will be informed and asked to provide salient information to assist in the assessment of current physical and mental health, including any recent test results, scan reports, etc. Any known information about persons referred will be gathered by a member of partner agencies and collated by the ARBD nursing team. The ARBD nursing team and partners from other agencies will discuss each referral and identify the person's needs. The referrer, if appropriate, will be kept informed of the outcome of the referral.

The nursing team will continue to visit the person referred regularly and complete a number of baseline assessments. Each person referred will be reviewed at agreed regular intervals by all involved services and the care plan and risk management plan updated each time.

Once the person's condition is stabilised, they will be discharged from the case management service and all relevant parties will be informed.

Evaluation

With no dedicated service provision for this marginalised patient group and in light of the key findings, an ARBD service has been developed. It is a nurse-led, community-based service, delivered and managed by the NHS Central Fife Mental Health Clinical Service, which utilises an assertive outreach model of care and the Tidal Model of mental health nursing (www.tidal-model.com). The initial pilot service was delivered in the Levenmouth area of Fife: an area of multiple deprivations. The team had a number of key aims and objectives, listed earlier.

The methods of evaluating the project included data collection and measuring a number of outcomes, including:

- physical health status (including height, baseline weight, nutritional status, etc.)
- dependence on and current alcohol use, using the Severity of Alcohol Dependency Questionnaire (SAD-Q) (Stockwell *et al*, 1983)
- Quality of Life Enjoyment and Satisfaction Questionnaire – Short Form (Q-LES-Q-SF) (Endicott *et al*, 1993)

- ACE-III
- Number of episodes of unplanned care.

People with ARBD require a range of services crossing traditional boundaries between medical and social care, and the case management model facilitated the integration of input from different agencies. The nursing team met with colleagues from partner agencies to review current patients' care plans and discuss new referrals, initially on a fortnightly basis, but latterly this was reduced to monthly meetings.

Multidisciplinary and multi-agency care planning was standard. Effective coordination facilitated the integration of input from different agencies and a robust review process, modelled on the CPA, was carried out at least until the person was settled. The care plans were holistic, recovery-focused and patient-centred. They aimed to address all aspects of the person's functioning, including supporting them to reduce alcohol use; however, we also supported the policy that those who continued drinking would not be excluded from accessing the case management service. In these cases, a harm minimisation approach was adopted and particular skills – such as non-judgemental attitude, emphatic approach and persistence – were required for engaging with this challenging group of people.

Carer support has been a vital component of the work carried out by the team. This ranged from one-to-one support to a carers' event.

Outcomes

The following assessments were completed on admission to the service, at agreed regular intervals and on discharge and used to measure outcomes and evaluate the pilot. The data collected evidenced the success of the model.

1. **Health Passport:** physical health status, including height, baseline weight, nutritional status, etc. There were no deaths during the course of the project.
2. **SAD-Q:** dependence on alcohol and current alcohol use; all patients scored less after involvement with the ARBD service, indicating reduced alcohol use.
3. **Q-LES-Q-SF:** evidence that on admission to the service patients scored themselves very poorly satisfied with quality of life, enjoyment and satisfaction. On discharge, they articulated good or very good satisfaction and enjoyment in most categories, showing a marked difference in life enjoyment and satisfaction.
4. **Validated ACE-III:** assessment of cognitive function on admission and discharge. The data highlighted significant improvement in cognitive functioning on discharge.
5. **Number of episodes of unplanned care:** hospital admissions have been significantly reduced. In financial terms this has generated estimated savings of £112 000 to NHS Fife in the year the pilot has been operational (June 2011/May 2012) compared with the previous 12-month period.
6. **Number of attendances at accident and emergency:** visits to secondary care accident and emergency departments significantly reduced.
7. **Nursing model:** testimonies of improved quality of life recorded in patients' case notes.

The ARBD case management service implemented the Tidal Model as a framework for the process of nursing. The model is recovery-focused and helps the nurse and the patient deal with the real problems of living and ensures that time with the patient is maximised. The service engages with a group of people often marginalised by society and aims to address that through use of the multidisciplinary care pathway developed by the team. Directly linked to NHS Scotland HEAT target three (the four HEAT performance targets are: health improvement, efficiency and governance, access to services, and treatment appropriate to individuals; www.scotland.gov.uk/About/Performance/scotPerforms/partnerstories/NHSScotlandperformance), the service has reduced the number and lengths of admissions and improved physical health in this patient group.

The ARBD team have developed and delivered multidisciplinary training to acknowledge and challenge existing attitudes and behaviours in the workplace and to reduce stigma. The team received funding to establish a carers' support and information group and a very successful carers' conference was held.

In December 2011 the team won two national awards for practice innovation and development, including the overall award from the Scottish Mental Health Nursing Forum in recognition of the innovative ARBD model piloted with this marginalised population group.

Conclusions

This pilot ARBD service has held other agencies accountable for care. It has established care pathways as well as communication pathways that previously were fractured and patchy. The awareness-raising/educational sessions have equipped multiple staff members to change their approach to this patient group who now receive a flexible, needs-led service which encourages continued engagement.

Feedback from patients, carers and partner agencies reinforces improved quality of life and satisfaction.

The nurses have developed specialist knowledge and skills as well as the attitudes necessary to help patients and carers affected by ARBD. Patients remain in contact with nurses despite ongoing difficulties abstaining from alcohol, whereas previously these patients were discharged from services. The case management model has successfully achieved the desired outcomes – it has improved people's quality of life, reduced alcohol use and the evidence proves that it is cost effective. It has maximised the opportunity of patients living independently in their own homes, protecting and improving their mental and physical health, where previously placement in a long-term care facility would be the inevitable outcome.

Further funding was secured from the Fife area Alcohol and Drug Partnership in April 2013, enabling wider roll-out of the service to selected areas in Central and West Fife.

NHS/Local Authority Adult ARBD Service: Wirral, England

The ARBD service in Wirral was commissioned in 2009 as a consequence of the commissioners being made aware of the problems faced by the local acute hospital in the discharge and prevention of readmission of patients identified as experiencing long-term alcohol misuse with significant cognitive damage. The aim of the service is to:

- improve the quality of life of people presenting with ARBD
- enhance and facilitate rapid discharge from acute hospital care as soon as the patient is physically stabilised
- reduce the likelihood of unplanned readmission.

Population and referrals

The service is embedded within the Wirral early onset dementia team (adult cognitive assessment team), utilising the expertise of a team with experience of managing patients of working age with a wide range of dementias. The team services a population of 310 000. It is designed to cater for patients with severe ARBD who have recently been withdrawn from alcohol. Most of the referrals are directly from in-patient wards in the acute hospital. The service will also take referrals from community sources provided the patient has undergone recent withdrawal and has significant cognitive damage. The team offers support and advice to local alcohol treatment services and community mental health teams in the management of patients who are already under treatment and have cognitive damage as a result of ARBD. Notably, the team does not have expertise in management of alcohol treatment or withdrawal but works closely with established alcohol services. The team receives approximately three ARBD referrals a month.

The team

The early onset dementia team was enhanced by one full-time equivalent (FTE) nurse practitioner (band 6) and one FTE social worker to cover the additional work imposed through catering for patients with ARBD. The nurse, social worker and team are integrated into the full adult cognitive assessment team consisting of: two FTE social workers, one-and-a-half FTE nurses, one nurse auxiliary, one team secretary, and 2 days of consultant psychiatrist. Currently the team carries approximately 50 patients with ARBD.

Principles of service delivery

In the absence of established specialised institutions catering for ARBD, the team has adopted a flexible approach in developing services. This is underpinned by a five-phase rehabilitation programme, designed to cater for individual patient needs and an assertive outreach approach in supervising the care of individuals irrespective of where they are placed (in institutions or domestic environment). Care packages are individually commissioned. This model has enabled the team to build expertise in targeted nursing homes, residential settings, supported living arrangements and home help agencies, enabling a continuum of rehabilitation across a variety of levels of independence.

The five phases of rehabilitation (Wilson *et al*, 2012) are:

- **Phase 1:** acute physical treatment and stabilisation, usually carried out in acute hospital settings
- **Phase 2:** stabilisation in a safe environment
- **Phase 3:** a 2- to 3-year rehabilitation programme of increasing independence and autonomy
- **Phase 4:** adapting the environment to cater for residual cognitive deficits
- **Phase 5:** providing structure and social support to reduce relapse into alcohol misuse.

Referral criteria

A simple screening instrument was locally developed and examined in the context of 20 consecutive referrals. The initial screening is designed to identify patients who are 'confused', have a history of multiple hospital contacts and/or problems in previous delayed discharges and a clear history of heavy alcohol misuse over a number of years. This initial screening was adapted from Oslin's criteria (Oslin & Carey, 2003) and piloted on a small sample of 20 patients with ARBD in an acute hospital context. Further evaluation has not been undertaken.

Screening for referral to the ARBD service requires the patient to be abstinent at referral and that all three criteria are met:

- probable history of heavy, long-standing alcohol drinking: 35 standard drinks (35 units or more) per week for men and 28 standard drinks (28 units or more) for women (Oslin & Carey, 2003) for at least 5 years
- confusion, memory problems, doubt about capacity and concerns about risk on discharge after withdrawal/physical stabilisation
- three or more admissions into hospital and/or accident and emergency in 1 year probably associated either directly (withdrawal, unconscious) or indirectly (trauma, organ disease etc.) with alcohol ingestion, or one or more delayed discharges from general hospital wards in the past 12 months (defined as patients staying on the acute medical/surgical ward because of social and/or psychiatric problems).

The screening instrument is not clinically validated and its use should not be generalised until further validations are carried out. Its use runs the risk of not capturing all patients with ARBD and it is only likely to pick up very severe cases and patients with other causes of cognitive impairment. However, in the context of a team which also caters for individuals with dementia and other cognitive problems referred through other criteria, this was thought to be acceptable.

Service evaluation

The service is subjected to ongoing annual evaluation. All patients are assessed using the Health of the Nation Outcome Scales (HoNOS) for acquired brain injury and the utilisation of secondary care in-patient beds was recorded. Ongoing cognitive evaluations have been conducted using the ACE-III.

A consecutive series of 38 cases referred to the service had the following HoNOS profile:

- 12 with severe intellectual problems, hardly capable of the simplest tasks, with very poor memory, attention problems and hardly able to learn new information
- 17 with moderate intellectual problems, including disorientation, attention problems, organisational difficulties and difficulty in thinking clearly
- 9 had either circumscribed intellectual deficits or milder impairment characterised by disorientation, difficulty in prioritising tasks,

organisational issues and definite problems in learning new information.

A review of mental health and physical conditions in a consecutive series of 48 patients demonstrated a significant comorbidity including convulsions, multiple neurological syndromes, trauma, and heart, gastrointestinal and liver conditions. Depression, aggression and psychoses were common; in 25% of cases there was either concomitant cerebrovascular disease or a history of head trauma.

In reviewing a consecutive series of 41 patients, group-average HoNOS scores fell in all domains, apart from an increase in depression scores. There was an 85% reduction in use of hospital bed days when comparing the 3 years prior to referral to the service with post-referral.

Of 57 consecutive patients reviewed more recently, 36 patients are in non-institutional care (sheltered accommodation, supported living, domestic care). Of these: 5 have uncontrolled drinking of which 1 has a personality disorder but is stable in the community in supported living; 4 have died in the community (having been abstinent); and 27 are well and abstinent. Twenty-one patients are in institutional care and 9 of these are profoundly ill (multiple mental and physical illnesses), 3 have died in institutions, 6 are under assessment and probably will be rehabilitated, and 3 are in active rehabilitation and will leave the institution.

Conclusions

There is an approximate 10% mortality rate and 10% relapse into chaotic alcohol misuse. There is a significant (85%) reduction in acute bed hospital days and increase in all HoNOS scores apart from emergent depression scores. Of 57 patients most recently surveyed, 9 are likely to stay in institutional settings and have significant cognitive damage, complicated by concomitant functional mental illnesses. Thirty-six patients (63%) have either been through or are expected to go through the programme, with reducing care costs and final establishment in community settings which include: unsupported living at home, supported living at home, living in flats with wardens, and supported living in settings designed to cater for adults with mental health problems. Significant minorities of patients have now taken on voluntary jobs and it is hoped some will return to paid work. The team continues to provide advice and support to general adult mental health teams and the alcohol treatment services in the management of patients who maintain capacity and have milder degrees of cognitive damage due to alcohol misuse and thiamine deficiency.

Recommendations

1. A small team, nested within another team with expertise in the assessment and management of working-age adults with cognitive damage, can provide a service that will reduce bed occupancy and enhance quality of life of patients with severe ARBD.
2. The team can offer advice, support and training to other services managing patients with less severe ARBD.
3. The team can build expertise in private and voluntary sector institutions and organisations to enable patients with severe ARBD to be rehabilitated within a local geographical area.

Adult ARBD team: Glasgow

Setting up the team

The Glasgow ARBD team began operation in June 2006, but there had previously been discussions between NHS Greater Glasgow and Glasgow City Council over some years. In 1998 it was recognised that there were a number of patients with ARBD in both elderly and adult beds in mental health, and there were noted concerns from the Mental Welfare Commission about a lack of monitoring of ARBD patients in the community. While there were plans to develop beds and resources, it may have been that plans were to an extent galvanised by contemporary research around 2003/2004.

In 2004 the *Fuller Life* report (Cox *et al*, 2004) was published. Compiled by an expert group of professionals, the report noted the implications for the stigma associated with ARBD ('self-inflicted') but very importantly it also highlighted the potential for recovery. The recommendation was to adopt

a person-centred approach to service delivery, balancing service requirements with patient rights while retaining flexibility. Contemporary research had indicated that there may be significant numbers of individuals with alcohol-related cognitive impairment in the homeless population in Glasgow.

With the 1999 Greater Galsgow Health Board Mental Health Strategy came allocated monies to develop a specific ARBD service which would support, and provide liaison between, addiction and mental health. Assessment was to be a main focus of the team in recognition of the diversity of need, the age range, and the level of cognitive impairment in this patient population. The team would sit under the umbrella of secondary services within addiction services, but (uniquely in that area) there was provision for a social care component in the team, again reflecting the range of health and social care needs. Working in conjunction with existing care managers, the team would supplement existing provision. It would be resourced to provide intensive input to a manageable case-load to develop strong therapeutic relationships and to maximise rehabilitation gains. The longer-term goals were recovery focused, aimed at reducing care home admissions and promoting independent living.

The ARBD team

The disciplines represented in the ARBD team are in line with recommendation in the *Fuller Life* report. The 2014 staffing is:

- team leader
- senior addiction nurses × 2
- senior addiction workers × 1 (vacant post)
- social care officers × 4
- occupational therapy × 1
- psychiatry × 5 sessions
- psychology × 8 sessions
- admin 2 × full time.

The original remit of the multidisciplinary ARBD team was:

- to promote optimal functional recovery and maximise potential for independent living in those individuals with newer or more recent onset of ARBD
- to provide intensive assessment and rehabilitation for up to 2 years – working in tandem with existing care managers
- to assist others to work with this client group, to provide training and share knowledge about ARBD – to function as a resource
- to provide patient and carer involvement.

Since there were existing services for dementia and brain injury, the team would work with those individuals whose cognitive impairment was resultant from heavy drinking and prolonged thiamine deficiency. (There are comprehensive services for acquired brain injury, however, there are no formal links between these and ARBD services. This is in part due to the fact that ARBD services are provided through mental health, whereas brain injury services are delivered through acute [physical] health.) For that group, continued drinking causes impairment to worsen, so to be able to engage with rehabilitation patients would require being abstinent from alcohol. (It is important also to stress that continuing good nutritional intake is equally relevant.) There was no upper age limit for referrals and the team operated an 'open' referral system.

Lessons learned in the first 2 years

Many of the original referrals were recognised by the professionals in the team as having been previously referred to other services. This highlighted gaps in the system – although sometimes poor engagement with services was a factor, there is extensive physical and mental health comorbidity and a range of complex needs in this population. Where services are designed around aetiology rather than need, gatekeeping can be an issue; this had significant implication for joint working. (Many were frustrated that the team did not take cases from them, but sought to work alongside them.) It became apparent also that addiction services were managing a number of continuing drinkers with a history of brain injury – traditional approaches to addiction often have limited efficacy for these individuals, yet needs remain complex and vulnerability is extreme.

There was a varied understanding of the diagnosis of ARBD, and there was no agreed diagnostic algorithm. Owing to pressures and time constraints

patients were often diagnosed very soon after they became abstinent from alcohol – in fact the diagnosis is dynamic and presentation often changes significantly in the months following abstinence. (When followed up later, it often appeared that alcohol had not been the main precipitating factor in perceived cognitive impairment.) Also, many patients were admitted to acute hospitals in crisis from social isolation and there was little or no collateral information about their presentation in the years prior to admission. Few cases referred seemed to be clear-cut Wernicke–Korsakoff syndrome (again, comorbidity is extensive) so even where a diagnosis had been made, this often had to be re-evaluated when considering rehabilitation potential.

The disciplines represented in the team were ideal for comprehensive assessment, and the smaller case-load allowed intensive input and engagement. Rapid and flexible response on an assertive outreach model meant assessing and meeting patient needs wherever they were living or placed, and the team was able to feed directly back into both Glasgow City Council and NHS systems.

Within the team neuropsychological assessment became the gold standard for detailed assessment of cognitive profile, providing clarity for differential diagnosis (is this ARBD, stroke, acquired brain injury, mixed aetiology?) and for evaluation of rehabilitation potential. This assessment is not available in acute hospitals, and it became clear that many patients could potentially be misdiagnosed or placed into a care pathway that did not meet their needs. This would often only become apparent at follow-up.

The implications of the experience and learning:

- ARBD should be a 'diagnosis of exclusion' – all other possible causes of cognitive impairment should be ruled out first
- criteria at the team were too tight; for example, the notion of actual date of onset was a complex one and referrals should not be excluded on this basis
- crisis admission to acute hospitals was often the only way that these very heavy drinkers achieved abstinence or were diagnosed
- accurate diagnosis for rehabilitation requires at least 6 weeks of abstinence
- with many referrals not being accepted, the team began to question whether the remit may actually met the needs of the ARBD population.

In response: broadening the remit of the ARBD team

The Mental Welfare Commission for Scotland published their report *Investigation into the Care and Treatment of Mr H* in 2006. Advocating the use of statutory legislation, the recommendation was that all local authorities look to earlier intervention and response to vulnerable individuals with alcohol-related cognitive impairment. In Glasgow, in the absence of defined care pathways there seemed to be potential for individuals to fall between services or to be discharged from hospital and return to heavy drinking. The ARBD team took the view that some drinkers are unable to engage in services as opposed to unwilling. Assertive follow-up found that many of those referred would engage with the team, but since they had returned to drinking, many were very much at risk of further cognitive damage, physical and mental health crisis, and re-admission to hospital. These individuals would be highly unlikely to attend appointments or present to services.

Accordingly the decision was taken to broaden the remit of the team, while retaining the original rehabilitation remit:

- to provide assessment of individuals suspected of having developed cognitive problems as a result of heavy drinking
- to support care plans aimed at facilitating harm reduction, detoxification, diagnosis and assessment of capacity where appropriate
- where referrals were inappropriate, support referral on or advise on care planning and management
- to support early legislative intervention to reduce alcohol-related harm, and to try to move patients out of a cycle of crisis presentations to a range of already over-burdened services
- to provide assessment for suitable resettlement of those in longer-term care
- to provide tailored training packages to those who work, come into contact or live with drinkers.

Table 3 Glasgow adult ARBD team current case-load (data from April 2014)						
Case-load by age, years						
	25–34	35–44	45–54	55–64	65+	Total
Male	1	10	27	29	23	90
Female	0	3	10	16	5	34
Total	1	13	37	45	28	124
Average age at time of referral, years						
Male	56					
Female	56					

ARBD, alcohol-related brain damage.

Table 4 Glasgow adult ARBD team referrals by source since 2006	
Source	%
Community addiction teams	27
Acute	25.5
Social work	12
Community mental health teams	7.5
Psychiatry	7.5
Acute addiction liaison	6.5
Third sector[a]	3
General practitioners	3
Care homes	2
Secondary services[b]	2
Homelessness	2
Others	2

ARBD, alcohol-related brain damage.
a. For example, Scottish Association for Mental Health, Addaction and Penumbra.
b. Including addiction occupational therapy or addiction psychology.

Some key roles and functions of the team

- Harm reduction and prevention
- Assessment and liaison
- Confirmation of diagnosis
- Psychiatric assessment and follow-up
- Neuropsychological assessment
- Rehabilitation – developing rehabilitation plans and supporting their implementation
- Support and advice in relation to placement and re-settlement if appropriate
- Support to placement providers and service commissioners
- Training is provided to all four tiers of service provision within addictions, but above all the target population is those who provide 'front-line' services to, or come into contact with, heavy drinkers. This then includes colleagues in social work and NHS services across the range, acute hospitals, voluntary sector agencies, home care providers, primary care, carers and friends and families. Packages can be developed to address specific requirements (e.g. Glasgow Caledonian University MHO Course, acute hospitals) with psychiatry, psychology, occupational therapy, nursing and social care officers also offering specific input to professional peers.

ARBD placements in Glasgow

Glasgow City Council commission a number of supported accommodation placements (eight provided by Scottish Association for Mental Health (S.A.M.H.) and eight by Penumbra) and a number of supported living placements (eight provided by S.A.M.H., hours to dedicated tenancies by Penumbra) to support and facilitate recovery for individuals with ARBD. There are also supported accommodation placements with a harm reduction focus for individuals with ARBD who wish to continue to drink alcohol, provided by Loretto Care. A number of care home placements are provided by a private provider (Thistle Healthcare), however, not all are commissioned by the Council.

Addiction services directly commission ten care home placements in Crannog Care home in

Drumchapel (provided by the Mungo Foundation) for individuals who have more severe cognitive impairment. (This unit is a home for life and while specific cognitive rehabilitation for this group would be less likely to produce difinitive outcomes, the unit still works with a rehabilitative focus to enhance quality of life.) December 2013 saw the opening of a dedicated 22-bed rehabilitation unit provided by Loretto Care and again specifically commissioned by addiction services. Service provision will be at a level between care home and supported accommodation, offering the safety and protection of a highly supported environment while allowing graded exposure to greater independence (e.g. budgeting, food preparation, activities of daily living). A period of intensive support immediately post-diagnosis (or abstinence) will optimise potential for recovery and rehabilitation.

Future challenges and considerations

To date the Glasgow ARBD team's work has largely been concentrated in the Glasgow City Council area. The dedicated service provision in Glasgow would seem to have provided fairly unique opportunities when compared to other areas of the country.

Addiction services (in line with other service areas in NHS Greater Glasgow and Clyde) are currently involved in a service-wide review, which will offer an opportunity to ensure models of drug and alcohol services which will best meet the needs of the public for the future. A significant part of this review will be the consideration of how best to take forward provision for ARBD across the whole health board area.

Appendix: Alcohol-related brain damage patient and public information leaflet

Short-term effects of long-standing alcohol misuse on the brain

- Long-term heavy drinking (average of 35 units or more a week for females and 50 units or more for males, for 5 years) is likely to lead to changes in the brain which will affect memory and reasoning ability. In most cases, the individual will be unaware of this, but it is likely to be noted by friends, family and employers.
- Heavy alcohol use of this nature will also make the individual prone to 'furring' of the arteries in the brain which can lead to more permanent damage and may even lead to strokes.
- In most cases, the brain will take up to 3 months to recover from drinking this amount over this length of time, provided alcohol is completely avoided.

More permanent effects of long-standing alcohol misuse on the brain

- Long-term alcohol misuse and the changes in the brain often make it difficult for the individual to look after themselves properly. In particular, they do not take in enough vitamins through regular meals.
- Long-term alcohol misuse tends to prevent vitamin B1 (thiamine) from being absorbed through the gut, even if enough is being taken in meals.
- Thiamine and other vitamins are necessary for the brain to operate properly. When a patient has not had enough vitamins there is likely to be more permanent brain damage.

The nature of the brain damage caused by vitamin deficiency and alcohol misuse

Memory is particularly damaged

Short-term memory People with this problem will be able to undertake and keep up with normal conversations and at first glance, appear to have no problems with memorising what has been said. However, after a few minutes, they will start to forget things that have been discussed or have taken place.

Long-term memory People will lose memories from the more recent past and depending how seriously they are affected may lose up to 25 years' worth of memories.

False memories (confabulation) When people have memory problems their brain automatically tries to make sense of the world and fill in the gaps in their memory. The person may experience 'memories' of events that have not happened. They are unable to recognise that these are false memories as they are as real to the person as events and memories that really did happen. People with these memory problems will often get mixed up and appear at times quite confused.

Reasoning, emotional difficulties and changes in behaviour

- Vitamin deficiency and alcohol misuse frequently affect the front part of the brain that is the main seat of reasoning and decision-making. The affected person is unlikely to be aware of these problems.
- The person will have difficulty in sorting out problems and understanding the implications of decisions, particularly problems and tasks involving complicated decisions such as financial planning and arranging things.
- Other people will notice that the person will have problems in controlling impulses and managing risks. This can cause difficulties in social settings and bursts of emotion or difficult behaviour.
- The person is likely to have problems in understanding the emotional needs of other people; this may lead to arguments and break up of relationships.

Treatment and help

- Changes in memory, reasoning, emotion and behaviour can advance to the degree that a person is unable to look after themselves and these changes can be permanent, resulting in the person needing long-term care. In severe cases this is called Korsakoff's syndrome.
- If a long-term, heavy alcohol drinker or their friends or family realise that they are running into memory problems, it is very important that they look for help urgently to avoid permanent brain damage. Treatment will include help with stopping drinking and vitamin treatment (which in severe cases may need to be by injection).
- In cases in which there are long-standing memory problems and changes in reasoning, emotions and behaviour, professional assessment is required. Most individuals can benefit from rehabilitation and can dramatically improve over 2–3 years. However, some people may have brain damage for longer periods, if not the rest of their lives.

References

Abel E, Hannigan J (1995) Maternal risk factors in fetal alcohol syndrome: provocative and permissive influences. *Neurotoxicology and Teratology*, **17**: 445–62.

Acker C (1986) Neuropsychological deficits in alcoholics: the relative contributions of gender and drinking history. *British Journal of Addiction*, **81**: 395–403.

Agabio R (2004) Thiamine administration in alcohol dependent patients. *Alcohol and Alcoholism*, **40**: 155–6.

Alexander-Kaufman K, Cordwell S (2007) A proteome analysis of the dorsolateral prefrontal cortex in human alcoholic patients. *Proteomics – Clinical Applications*, **1**: 62–72.

Alexander-Kaufman K, Harper C, Wilce P, *et al* (2007) Cerebellar vermis proteome of chronic alcoholic individuals. *Alcoholism, Clinical and Experimental Research,* **31**: 1286–96.

Alfonso-Loeches S, Pascual-Lucas M, Blanco AM, *et al* (2010) Pivotal role of TLR4 receptors in alcohol-induced neuroinflammation and brain damage. *Journal of Neuroscience*, **30**: 8285–95.

Alterman AI, Holahan JM, Baughman TG, *et al* (1989) Predictors of alcoholics' acquisition of treatment related knowledge. *Journal of Substance Abuse Treatment*, **6**: 49–53.

American Psychiatric Association (1994) *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)*. APA.

American Psychiatric Association (2013) *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)*. APA.

Amodio P, Pellegrini A, Amista P, *et al* (2003) Neuropsychological-neurophysiological alterations and brain atrophy in cirrhotic patients. *Metabolic Brain Disease*, **18**: 63–78.

Anderson JJM, Flanigan C, Jauher PJ (1999) Knowledge of alcohol related problems in clinical staff in psychiatric community resource centres in Glasgow. *Health Bulletin*, **57**: 162.

Acquired Brain Injury Services (2009) *Annual Report 2008–2009*. ARBIAS (http://www.arbias.org.au/about-us/annual-reports.html).

Acquired Brain Injury Services (2011) *Looking Forward: Information and Specialised Advice on Alcohol Related Brain Impairment* (4th edn). ARBIAS.

Babor T, Higgins-Biddle J, Saunders J, *et al* (1992) *The Alcohol Use Disorders Identification Test: Guidelines for Use in Primary Care, Second Edition*. Department of Mental Health and Substance Dependence, World Health Organization.

Baddeley AD, Wilson BA (1994) When implicit learning fails: amnesia and the problem of error elimination. *Neuropsychologica*, **32**: 53–68.

Baddeley AD, Kopelman MD, Wilson BA (2002) *Handbook of Memory Disorders (2nd edn)*. Wiley.

Bardenhagen FJ, Oscar-Berman M, Bowden SC (2007) Rule knowledge aids performance on spatial and object alternation tasks by alcoholic patients with and without Korsakoff's amnesia. *Neuropsychiatric Disease and Treatment*, **3**: 907–18.

Bartels C, Kunert H, Stawicki S, *et al* (2007) Recovery of hippocampus-related functions in chronic alcoholics during monitored long-term abstinence. *Alcohol and Alcoholism*, **42**: 92–102.

Bates M, Bowden S, Barry D (2002) Neurocognitive impairment associated with alcohol use disorders: implications for treatment. *Experimental and Clinical Psychopharmacology*, **10**: 193–212.

Bates ME, Pawlak AP, Tonigan JS, *et al* (2006) Cognitive impairment influences drinking outcome by altering therapeutic mechanisms of change. *Psychology of Addictive Behaviors*, **20**: 241–53.

Beatty WW, Hames KA, Blanco CR, *et al* (1996) Visuospatial perception, construction and memory in alcoholism. *Journal of Studies on Alcohol*, **57**: 136–43.

Bjork J, Momenan R, Smith A, *et al* (2008) Reduced posterior mesofrontal cortex activation by risky rewards in substance-dependent patients. *Drug and Alcohol Dependence*, **95**: 115–28.

Blansjaar BA, Takens H, Zwinderman AH (1992) The course of alcohol amnestic disorder: a three-year follow-up study of clinical signs and social disabilities. *Acta Psychiatrica Scandinavica*, **86**: 240–6.

Blume AW, Schmaling KB, Marlatt GA (2005) Memory, executive cognitive function, and readiness to change drinking behaviour. *Addictive Behaviours*, **30**: 301–14.

BMA Board of Science (2008) *Alcohol Misuse: Tackling the UK Epidemic*. British Medical Association.

Boeijinga PH, Parot P, Soufflet L, *et al* (2004) Pharmacodynamic effects of acamprosate on markers of cerebral function in alcohol-dependent subjects administered as pretreatment and during alcohol abstinence. *Neuropsychobiology*, **50**: 71–7.

Boughy L (2007) *Alcohol Related Brain Damage: A Report of the Learning Captured from Carenza Care in North Wales*. Care Services Improvement Partnership/ Alzheimer's Society Working Group.

Bowden SC, Whelan G, Long C, *et al* (1995) The temporal stability of the WAIS–R and WMS–R in a

heterogeneous sample of alcohol dependent clients. *Clinical Neuropsychologist*, **9**: 194–7.

British Medical Association (2007) *Fetal Alcohol Spectrum Disorders: A Guide for Healthcare Professionals*. BMA.

Brooke P, Bullock R (1999) Validation of a 6 item cognitive impairment test with a view to primary care usage. *International Journal of Geriatric Psychiatry*, **14**: 936–40.

Burd L, Klug MG, Bueling R, *et al* (2008) Mortality rates in subjects with fetal alcohol spectrum disorders and their siblings. *Birth Defects Research Part A*, **82**: 217–23.

Cagnin A, Taylor-Robinson SD, Forton DM, *et al* (2006) In vivo imaging of cerebral 'peripheral benzodiazepine binding sites' in patients with hepatic encephalopathy. *Gut*, **55**: 547–53.

Caine D, Halliday GM, Kril JJ, *et al* (1997) Operational criteria for the classification of chronic alcoholics: identification of Wernicke's encephalopathy. *Journal of Neurology, Neurosurgery & Psychiatry,* **62**: 51–60.

Chanraud S, Martelli C, Delain F, *et al* (2007) Brainmorphometry and cognitive performance in detoxified alcohol-dependents with preserved psychosocial functioning. *Neuropsychopharmacology*, **32**: 429–38.

Chick J (1989) Delirium tremens. *BMJ*, **298**: 3–4.

Chudley AE, Conry J, Cook JL, *et al* (2005) Foetal alcohol spectrum disorder: Canadian guidelines for diagnosis. *CMAJ*, **172**: S1–21.

Cocchi R, Chiavarini M (1997a) Raven's coloured matrices in female alcoholics before and after detoxification: an investigation on 73 cases. *International Journal of Intellectual Impairment*, **11**: 45–9.

Cocchi R, Chiavarini M (1997b) Raven's coloured matrices in male alcoholics before and after detoxification: a research on 225 subjects. *International Journal of Intellectual Impairment*, **10**: 157–60.

Cook C, Hallwood P, Thomson A (1998) B Vitamin deficiency and neuropsychiatric syndromes in alcohol misuse. *Alcohol and Alcoholism*, **33**: 317–36.

Copersino ML, Schretlen DJ, Fitzmaurice GM, *et al* (2012) Effects of cognitive impairment on substance abuse treatment attendance: predictive validation of a brief cognitive screening measure. *American Journal of Drug and Alcohol Abuse*, **38**: 246–50.

Cox S, Anderson I, McCabe L (eds) (2004) *A Fuller Life: Report of the Expert Group on Alcohol Related Brain Damage*. Dementia Services Development Centre, University of Stirling.

Cummings JL (1995) Anatomic and behavioural aspects of frontal-subcortical circuits. *Annals of the New York Academy of Sciences*, **769**: 1–13.

Cutting J (1978) A reappraisal of alcoholic psychoses. *Psychological Medicine*, **8**: 285–96.

David A, Fleminger S, Kopelman MD, *et al* (2009) *Lishman's Organic Psychiatry* (4th edn). Blackwell.

Davies SJC, Pandit SA, Feeney A, *et al* (2005) Imbalance between neuroexcitatory and neuroinhibitory amino acids causes craving for ethanol. *Addictive Behaviors*, **29**: 1325–39.

DeFranco C, Tarbox AR, McLauglin EJ (1985) Cognitive deficits as a function of years of alcohol abuse. *American Journal of Drug and Alcohol Abuse*, **11**: 279–93.

DeLeon G, Jainhill N (1981) Male and female drug abusers: social and psychological status two years after treatment in a therapeutic community. *American Journal of Alcohol Abuse*, **8**: 595–600.

DeLeon G (1984) Program-based evaluation research in therapeutic communities. *National Institute on Drug Abuse Research Monograph Series*, **51**: 69–87.

Department of Health (2001) *Changing the Outlook: A Strategy for Developing and Modernising Mental Health Services in Prisons*. Department of Health.

Department of Health (2009) *Local Routes: Guidance for Developing Alcohol Treatment Pathways*. Department of Health.

Department of Health, National Treatment Agency for Substance Misuse (2006) *Models of Care for Alcohol Misusers (MoCAM)*. Department of Health.

Druschel CM, Fox JD (2007) Issues in estimating the prevalence of fetal alcohol syndrome: examination of 2 counties in New York State. *Pediatrics*, **119**: 384–90.

Dubois B, Stachevsky A, Litvan I (2000) The FAB: a Frontal Assessment Battery at bedside. *Neurology*, **55**: 1621–6.

Duka L, Welzel M, Nakoviks H, *et al* (2010) Effects of repeated withdrawal from alcohol on recovery of cognitive impairment under the abstinence and rate of response. *Alcohol and Alcoholism*, **45**: 541–7.

Dyson J (2007) Experiences of alcohol dependence: a qualitative study. *Journal of Family Health Care*, **17**: 211–4.

D'Zurilla TJ, Goldfried MR (1971) Problem solving and behaviour modification. *Journal of Abnormal Psychology*, **78**: 107–26.

Elleswei E (2000) Caring with people with alcohol related brain injury. *Signpost*, **4**: 12–3.

Endicott J, Nee J, Harrison W, et al (1993) Quality of Life Enjoyment and Satisfaction Questionnaire: a new measure. *Psychopharmacology Bulletin*, **29**: 321–6.

Ervalahti N, Korkman M, Fagerlund A, *et al* (2007) Relationship between dysmorphic features and general cognitive function in children with foetal alcohol spectrum disorders. *American Journal of Medical Genetics Part A*, **143A**: 2916–23.

Fals-Stewart W (1992) Using subtests of the Brain Age Quotient to screen for cognitive deficits among substance abusers. *Perceptual and Motor Skills*, **75**: 244–6.

Fals-Stewart W, Lucente S (1994) The effect of cognitive rehabilitation on the neuropsychological status of patients in drug abuse treatment who display neurocognitive impairment. *Rehabilitation Psychology*, **39**: 75–94.

Fernandez-Lizarbe S, Pascual M, Guerri C (2009) Critical role of TLR4 response in the activation of microglia induced by ethanol. *Journal of Immunology*, **183**: 4733–44.

Ferran J, Wilson K, Doran M (1996) The early onset dementias: a study of clinical and service need. *International Journal of Geriatric Psychiatry*, **11**: 863–9.

Forsberg LK, Goldman MS (1985) Experience-dependent recovery of visuospatial functioning in older alcoholic persons. *Journal of Abnormal Psychology*, **94**: 519–29.

Forsberg LK, Goldman MS (1987) Experience-dependent recovery of cognitive deficits in alcoholics: extended transfer of training. *Journal of Abnormal Psychology*, **96**: 345–53.

Fox AM, Coltheart M, Solowij N, *et al* (2000) Dissociable cognitive impairment in problem drinkers. *Alcohol and Alcoholism*, **35**: 52–4.

Franchi S, Sacerdote P, Moretti S, *et al* (2010) The effects of alcoholism pharmacotherapy on immune responses in alcohol-dependent patients. *International Journal of Immunopathology and Pharmacology*, **23**: 847–55.

Freud A (1937) *The Ego and the Mechanisms of Defense*. Hogarth Press & Institute of Psycho-Analysis (revised edn: 1966 (USA), 1968 (UK)).

Ganzelves PGJ, Geus BWJ, Wester AJ (1994) Cognitive and behavioural aspects of Korsakoff's syndrome: the effect of special Korsakoff wards in a general hospital. *Tijdschrift voor Alcohol*, *Drugs en Andere Psychotrope Stoffen,* **20**: 20–31.

Giancola PR, Zeichner A, Yarnell JE, *et al* (1996) Relation between executive cognitive functioning and the adverse consequences of alcohol use in social drinkers. *Alcoholism: Clinical and Experimental Research*, **20**: 1094–8.

Giles GM (1994) The status of brain injury rehabilitation. *American Journal of Occupational Therapy*, **48**: 199–205.

Glass I (1991) Alcoholic brain damage: What does it mean to patients? *British Journal of Addiction*, **86**: 819–21.

Goldman R, Goldman M (1988) Experience-dependent cognitive recovery in alcoholics: a task component strategy. *Journal of Studies on Alcohol*, **49**: 142–8.

Goldman-Rakic PS (1987) Circuitry of primate prefrontal cortex and regulation of behaviour by representational memory. In *Handbook of Physiology, Volume 5* (eds F Plum, V Mountcastle): pp. 373–417. American Physiological Society.

Gonzàlez-Quintela A, Dominguez-Santalla MJ, Pérez LF, *et al* (2000) Influence of acute alcohol intake and alcohol withdrawal on circulating levels of IL-6, IL-8, IL-10 and IL-12. *Cytokine*, **12**: 1437–40.

Goodwin DW, Crane JB, Guze SB (1969) Phenomenological aspects of the alcoholic 'blackout'. *British Journal of Psychiatry*, **115**: 1033–8.

Grant I, Adams KM, Reed R (1986) Intermediate-duration (subacute) organic mental disorder of alcoholism. In *Neuropsychiatric Correlates of Alcoholism* (ed. I Grant): pp. 37–60. American Psychiatric Press.

Gupta S, Warner J (2008) Alcohol-related dementia: a 21st–century silent epidemic? *British Journal of Psychiatry*, **193**: 351–3.

Hachinski VC, Iliff LD, Zilhka E, *et al* (1975) Cerebral blood flow in dementia. *Archives of Neurology*, **32**: 632–7.

Hannestad J, Gallezot JD, Schafbauer T, *et al* (2012) Endotoxin-induced systemic inflammation activates microglia: [11C]PBR28 positron emission tomography in nonhuman primates. *Neuroimage*, **63**: 232–9.

Hanson J, Jones KL, Smith DW (1976) Foetal alcohol syndrome: experience with 41 patients. *JAMA*, **235**: 1458–60.

Harding A, Halliday G, Caine D, *et al* (2000) Degeneration of anterior thalamic nuclei differentiates alcoholics with amnesia. *Brain*, **123**: 141–54.

Harper CG, Giles M, Finlay-Jones R (1986) Clinical signs in the Wernicke-Korsakoff complex: a retrospective analysis of 131 cases diagnosed at autopsy. *Journal of Neurology, Neurosurgery and Psychiatry,* **49**: 341–5.

Harper C, Gold J, Rodriguez M (1989) The prevalence of the Wernicke-Korsakoff syndrome in Sydney, Australia: a prospective necropsy study. *Journal of Neurology, Neurosurgery and Psychiatry,* **52**: 282–5.

Harper C, Fornes P, Duyckaerts C, *et al* (1995) An international perspective on the prevalence of the Wemicke-Korsakoff Syndrome. *Metabolic Brain Disease*, **10**: 17–24.

Harper C, Kril J, Sheedy D, *et al* (1998) Neuropathological studies: the relationship between alcohol and aging. In *Alcohol Problems and Aging: NIAAA Research Monograph No. 33.* (eds ESL Gomberg, AM Hegedus, RA Zucker). National Institute on Alcohol Abuse and Alcoholism.

Harper C (2009) The neuropathology of alcohol-related brain damage. *Alcohol and Alcoholism*, **44**: 136–40.

Harvey R, Rossor M, Skelton–Robinson M, *et al* (1998) *Young Onset Dementia: Epidemiology, Clinical Symptoms, Family Burden, Support and Outcome*. Imperial College School of Medicine.

Haussinger D, Schliess F (2009) Pathogenic mechanisms of hepatic encephalopathy. *Gut*, **57**: 1156–65.

He J, Crews FT (2008) Increased MCP-1 and microglia in various regions of the human alcoholic brain. *Experimental Neurology*, **210**: 349–58.

He X, Sullivan EV, Harper CG, *et al* (2007) Interaction of thiamine deficiency and voluntary alcohol consumption disrupts rat corpus callosum ultrastructure. *Neuropsychopharmacology*, **32**: 2207–16.

Heinrichs RW, Levitt A, Arthurs A, *et al* (1992) Learning and retention of a daily activity schedule in a patient with alcoholic Korsakoff's syndrome. *Neuropsychological Rehabilitation*, **2**: 43–58.

Heinssen RK (1996) The cognitive exoskeleton: environmental interventions. In *Cognitive Rehabilitation for Neuropsychiatric Disorders* (eds PW Corrigan, SC Yudofsky): pp. 395–423. American Psychiatric Press.

Hermann D, Weber-Fahr F, Sartorius A, *et al* (2012) Translational magnetic resonance spectroscopy reveals excessive central glutamate levels during alcohol withdrawal in humans and rats. *Biological Psychiatry*, **71**: 1015–21.

Hillman A, McCann B, Walker NP (2001) Specialist alcohol liaison services in general hospital improve engagement in alcohol rehabilitation and treatment outcome. *Health Bulletin*, **59**: 420–3.

HM Inspectorate of Prisons (1996) *Patient or Prisoner? A New Strategy for Health Care in Prison*. Home Office.

Hochalter AK, Joseph B (2001) Differential outcomes training facilitates memory in people with Korsakoff and Prader-Willi syndromes. *Integrative Physiological and Behavioral Science*, **36**: 196–204.

Holmes C, Cunningham C, Zotova E, *et al* (2009) Systemic inflammation and disease progression in Alzheimer disease. *Neurology*, **73**: 768–74.

Hutchinson MR, Zhang Y, Brown K, *et al* (2008) Non-stereoselective reversal of neuropathic pain by naloxone and naltrexone: involvement of toll-like receptor 4 (TLR4). *European Journal of Neuroscience*, **28**: 20–9.

Ihara H, Berrios GE, London M (2000) Group and case study of the dysexecutive syndrome in alcoholism without amnesia. *Journal of Neurology, Neurosurgery and Psychiatry*, **68**: 731–7.

Irwin MR, Olmstead R, Valladares EM, *et al* (2009) Tumor necrosis factor antagonism normalizes rapid eye movement sleep in alcohol dependence. *Biological Psychiatry*, **66**: 191–5.

Jacques A, Stevenson G (2000) *Korsakoff's Syndrome and Other Chronic Alcohol Related Brain Damage: A Review of the Literature*. Dementia Services Development Centre, University of Stirling.

Jacques A, Anderson K (2002) *A survey of views on assessment, management and service provision for people with Korsakoff's syndrome and other chronic alcohol-related brain damage in Scotland*. Dementia Service Development Centre, University of Stirling.

Joint Prison Service and National Health Service Executive Working Group (1999) *The Future Organisation of Prison Health Care*. HM Prison Service & NHS Executive.

Jones GA (1989) Alcohol abuse and traumatic brain injury. *Alcohol Health and Research World*, **13**: 105–9.

Jones K, Smith D, Ulleland C, *et al* (1973) Pattern of malformation in offspring of chronic alcoholic mothers. *Lancet*, **301**: 1267–71.

Ke ZJ, Wang X, Fan Z, *et al* (2009) Ethanol promotes thiamine deficiency-induced neuronal death: involvement of double-stranded RNA-activated protein kinase. *Alcoholism: Clinical and Experimental Research*, **33**: 1097–103.

Kessels RPC, van Loon E, Wester AJ (2007) Route learning in amnesia: a comparison of trial-and-error and errorless learning in patients with the Korsakoff syndrome. *Clinical Rehabilitation*, **21**: 905–11.

Kessels RPC, Kopelman MD (2012) Context memory in Korsakoff's syndrome. *Neuropsychology Review*, **22**: 117–31.

Klug MG, Burd L (2003) Fetal alcohol syndrome prevention: annual and cumulative cost savings. *Neurotoxicology and Teratology*, **25**: 763–5.

Kok AF (1991) Developments in the care of Korsakoff patients.*Tijdschriftvoor Alcohol, Drugs en Andere Psychotropic Stoffe,* **17**: 3–9.

Kopelman MD (1991) Alcoholic brain damage. In *International Handbook in Addiction Behaviour* (ed. I Glass): pp. 141–51. Routledge & Kegan Paul.

Kopelman MD (2002) Disorders of memory. *Brain*, **125**: 2152–90.

Kopelman MD, Fleminger S (2002) Experience and perspectives on the classification of organic mental disorders. *Psychopathology*, **35**: 76–81.

Kopelman MD (2008) Retrograde memory loss. In *Handbook of Clinical Neurology, Vol 88, 3rd Series: Neuropsychology and Behavioral Neurology* (eds G Goldenberg, BL Miller): pp. 185–202. Elsevier.

Kopelman MD, Thomson A, Guerrini I, *et al* (2009) The Korsakoff syndrome: clinical aspects, psychology and treatment. *Alcohol and Alcoholism*, **44**: 148–54.

Korsakoff SS (1889) Psychic disorder in conjunction with peripheral neuritis (transl 1955, M Victor, PI Yakovlev). *Neurology*, **5**: 394–406.

Kraepelin E (1913) *Psychiatrie – Ein Lehrbuch für Studierende und Aerzte* (8th edn), Vol 3. Barth.

Kril JJ, Harper CG (2012) Neuroanatomy and neuropathology associated with Korsakoff's syndrome. *Neuropsychology Review*, **22**: 72–80.

Krupitsky EM, Rudenko AA, Burakov AM, *et al* (2007) Antiglutamatergic strategies for ethanol detoxification: comparison with placebo and diazepam. *Alcohol: Clinical and Experimental Research*, **31**: 604–11.

Krystal JH, Petrakis IL, Krupitsky E, *et al* (2003) NMDA receptor antagonism and the ethanol intoxication signal: from alcoholism risk to pharmacotherapy. *Annals of the New York Academy of Sciences*, **1003**: 176–84.

Laso FJ, Vaquero JM, Almeida J, *et al* (2007) Chronic alcohol consumption is associated with changes in the distribution, immunophenotype, and the inflammatory cytokine secretion profile of circulating dendritic cells. *Alcohol: Clinical and Experimental Research*, **31**: 846–54.

Leclercq S, Cani PD, Neyrinck AM, *et al* (2012) Role of intestinal permeability and inflammation in the biological and behavioral control of alcohol-dependent subjects. *Brain, Behavior, and Immunity*, **26**: 911–8.

Lennane KJ (1986) Management of moderate to severe alcohol related brain damage (Korsakoff's syndrome). *Medical Journal of Australia*, **145**: 136–43.

Ling J, Luczakiewicz K, Heffernan T, *et al* (2010) Subjective ratings of prospective memory deficits in chronic alcohol users. *Psychological Reports*, **106**: 905–17.

Lingford-Hughes AR, Acton PD, Gacinovic S, *et al* (1998) Reduced levels of GABA-benzodiazepine receptor in alcohol dependency in the absence of grey matter atrophy. *British Journal of Psychiatry*, **173**: 116–22.

Lingford-Hughes A, Welch S, Nutt DJ (2004) Evidence-based guidelines for the pharmacological management of substance misuse, addiction and comorbidity: recommendations from the British Association for Psychopharmacology. *Journal of Psychopharmacology*, **18**: 293–335.

Lingford-Hughes AR, Wilson SJ, Cunningham VJ, *et al* (2005) GABA-benzodiazepine receptor function in alcohol dependence: a combined 11C-flumazenil PET and pharmacodynamic study. *Psychopharmacology*, **180**: 595–606.

Lingford-Hughes AR, Welch S, Peters L, *et al* (2012) BAP updated guidelines: evidence-based guidelines for

the pharmacological management of substance abuse, harmful use, addiction and comorbidity: recommendations from BAP. *Journal of Psychopharmacology*, **26**: 899–952.

Lishman WA (1981) Cerebral disorder in alcoholism: syndromes of impairment. *Brain*, **104**: 1–20.

Lishman WA (1998) *Organic Psychiatry: The Psychological Consequences of Cerebral Disorder* (3rd edn). Blackwell Science.

Lokensgard JR, Chao CC, Gekker G, *et al* (1998) Benzodiazepines, glia, and HIV-1 neuropathogenesis. *Molecular Neurobiolology*, **18**: 23–33.

Lucas SM, Rothwell NJ, Gibson RM, *et al* (2006) The role of inflammation in CNS injury and disease. *British Journal of Pharmacology*, **147** (suppl 1): S232–40.

Lundquist G (1961) Delirium tremens: a comparative study of pathogenesis, course and prognosis with delirium tremens. *Acta Psychiatrica Scandinavica*, **36**: 443–66.

Luria AR (1973) *The Working Brain: An Introduction to Neuropsychology*. Basic Books.

Ma JJ, Truswell AS (1995) Wernicke-Korsakoff syndrome in Sydney hospitals: before and after thiamine enrichment of flour. *Medical Journal of Australia*, **163**: 531–4.

MacRae R, Cox S (2003) *Meeting the Needs of People with Alcohol Related Brain Damage: A Literature Review on the Existing and Recommended Service Provision and Models of Care*. University of Stirling.

Maggia B, Martin S, Crouzet C, *et al* (2004) Variation in AUDIT (Alcohol Use Disorder Identification Test) scores within the first weeks of imprisonment. *Alcohol and Alcoholism*, **39**: 247–50.

Mair WGP, Warrington EK, Weiskrantz L (1979) Memory disorder in Korsakoff's psychosis: a neuropathological and neuropsychological investigation of two cases. *Brain*, **102**: 783.

Malcolm R, Roberts JS, Wang W, *et al* (2000) Multiple previous detoxifications are associated with less responsive treatment and heavier drinking during an index outpatient detoxification. *Alcohol*, **22**: 159–64.

Malloy P, Noel N, Longabaugh R, *et al* (1990) Determinants of neuropsychological impairment in antisocial substance abusers. *Addictive Behaviors*, **15**: 431–8.

Mann K, Gunther A, Stetter F, *et al* (1999) Rapid recovery from cognitive deficits in abstinent alcoholics: a controlled test-retest study. *Alcohol and Alcoholism*, **23**: 567–74.

Mann K, Kiefer F, Spanagel R, *et al* (2008) Acamprosate: recent findings and future research directions. *Alcoholism: Clinical and Experimental Research*, **32**: 1105–10.

Mardini H, Saxby B, Record CO (2008) Paper and pencil or computer assessment of minimal encephalopathy: effect of nitrogen challenge and liver transplant. *Gastroenterology*, **135**: 1582–90.

Mardini H, Smith FS, Record CO, *et al* (2011) Magnetic resonance quantification of water and metabolites in the brain of cirrhotics following induced hyperammonaemia. *Journal of Hepatology*, **54**: 1154–60.

Mardini H, Record C (2013) Pathogenesis of hepatic encephalopathy: lessons from nitrogen challenges in man. *Metabolic Brain Disease*, **28**: 201–7.

Marshall SA, McClain JA, Kelson ML, *et al* (2013) Microglial activation is not equivalent to neuroinflammation in alcohol-induced neurodegeneration: the importance of microglia phenotype. *Neurobiology of Disease*, **54**: 239–51.

Mason GF, Petrakis IL, de Graaf RA, *et al* (2006) Cortical-aminobutyric acid levels and the recovery from ethanol dependence: preliminary evidence of modification by cigarette smoking. *Biological Psychiatry*, **59**: 85–93.

Masson S, Mardini HA, Rose JD, *et al* (2008) Hepatic encephalopathy after transjugular intrahepatic portosystemic shunt insertion: a decade of experience. *QJM: An International Journal of Medicine*, **101**: 493–501.

May AP, Gossage JP (2001) Estimating the prevalence of foetal alcohol syndrome: a summary. *Alcohol Research and Health*, **25**: 159–67.

Mayes AR, Meudell PR, Mann D, *et al* (1988) Location of lesions in Korsakoff's syndrome: neuropsychological and neuropathological data on two patients. *Cortex*, **24**: 367–88.

Mayfield D, McLeod G, Hall P (1974) The CAGE questionnaire: validation of a new alcoholism screening instrument. *American Journal of Psychiatry*, **131**: 1121–3.

McCabe L (2006) *Working with People with Alcohol-Related Brain Damage*. Dementia Services Development Centre, University of Stirling.

McCrady BS, Smith DE (1986) Implications of cognitive impairment for the treatment of alcoholism. *Alcoholism: Clinical and Experimental Research*, **10**: 145–9.

McCreadie RG, Stewart M, Robertson L, *et al* (1991) The Scottish survey of old long-stay in-patients. *British Journal of Psychiatry*, **158**: 398–402.

Meek PS, Clark HW, Solana VL (1989) Neurocognitive impairment: the unrecognized component of dual diagnosis in substance abuse treatment. *Journal of Psychoactive Drugs*, **21**: 153–60.

Mental Welfare Commission for Scotland (2006) *Investigation into the Care and Treatment of Mr H*. MWCS.

Mental Welfare Commission for Scotland (2010a) *Our Overview of Mental Welfare in Scotland 2009–10*. MWCS.

Mental Welfare Commission for Scotland (2010b) *Safeguarding Rights and Welfare: Annual Report 2009–2010*. MWCS.

Migo EM, Mayes AR, Montaldi D (2012) Measuring recollection and familiarity: improving the remember/know procedure. *Consciousness and Cognition*, **21**: 1435–55.

Mimura M, Komatsu SC, Kato M, *et al* (2005) Further evidence for a comparable memory advantage of self-performed tasks in Korsakoff's syndrome and non-amnesic control subjects. *Journal of the International Neuropsychological Society*, **11**: 545–53.

Morgan J, McSharry K, Sireling L (1990) Comparison of a system of staff prompting with a programmable electronic diary in a patient with Korsakoff's syndrome. *International Journal of Social Psychiatry*, **36**: 225–9.

Moriarty KJ, Cassidy P, Dalton D, *et al* (2010) *Alcohol-Related Disease: Meeting the Challenge of Improved Quality of Care and Better Use of Resourses: A*

Joint Position Paper on Behalf of the British Society of Gastroenterology, Alcohol Health Alliance UK, British Association of the Study of the Liver. British Gastroenterology Society, 2010.

Morrison F, Pestell S (2010) The application of cognitive behaviour therapy to individuals with comorbid depressions and alcohol related brain damage. *Clinical Psychology*, **January**: 13–20.

Nash K, Stevens S, Rovet J, *et al* (2013) Towards identifying a characteristic neuropsychological profile for fetal alcohol spectrum disorders: 1. Analysis of the Motherisk FASD clinic. *Journal of Population Therapeutics and Clinical Pharmacology*, **20**: e44–55.

Nasreddine ZS, Collin I, Chertkow H, *et al* (2003) Sensitivity and specificity of the Montreal Cognitive Assessment (MoCA) for Detection of Mild Cognitive Deficits. *Canadian Journal of Neurological Sciences*, **30** (suppl 2): 30.

National Institute for Health and Clinical Excellence (2010) *Alcohol-Use Disorders: Diagnosis and Clinical Management of Alcohol-Related Physical Complications* (Clinical Guideline CG100). NICE.

National Institute for Health and Clinical Excellence (2011) *Alcohol-Use Disorders: Diagnosis, Assessment and Management of Harmful Drinking and Alcohol Dependence* (Clinical Guideline CG115). NICE.

Neuroscience Research Australia (2013) *Addenbrooke's Cognitive Examination–III (ACE–III)*. Available at: https://neura.edu.au/frontier/research/test–downloads (accessed January 2014).

Nicholas S (2010) Experiments on implicit memory in a Korsakoff patient by Claparede 1907. *Cognitive Neuropsychology*, **13**: 1193–9.

North L, Gillard-Owen L, Bannigan D, *et al* (2010) The development of a multidisciplinary programme for the treatment of alcohol related brain injury. *Advances in Dual Diagnosis*, **3**: 5–12.

Obernier JA, White AM, Swartzwelder HS, *et al* (2002) Cognitive deficits and CNS damage after a 4-day binge ethanol exposure in rats. *Pharmacology, Biochemistry, and Behavior*, **72**: 521–32.

O'Brien S (2011) *Alcohol Related Brain Damage (ARBD): The Picture in Fife 2011 Internal report*. NHS Central Fife Mental Health Clinical Service.

O'Connor MJ, Frankel F, Paley B, *et al* (2006) A controlled social skills training for children with foetal alcohol spectrum disorders. *Journal of Consulting and Clinical Psychology*, **74**: 639–48.

O'Malley KD, Hagerman RJ (1998) Developing clinical practice guidelines for pharmacological interventions with alcohol-affected children. In *Proceedings of a Special Focus Session of the Interagency Co-ordinating Committee on Foetal Alcohol Syndrome* (eds Centers for Disease Control and Prevention, National Institute of Alcohol Abuse and Alcoholism): pp. 145–77. Sep 10–11.

O'Malley KD, Nanson J (2002) Clinical implications of a link between fetal alcohol spectrum disorder and attention-deficit hyperactivity disorder. *Canadian Journal of Psychiatry*, **47**: 349–54.

Oslin DW, Carey MS (2003) Alcohol related dementia: validation of diagnostic criteria. *American Journal of Geriatric Psychiatry*, **11**: 441–7.

Parks M, Greenberg D, Nickel M, *et al* (2010) Recruitment of additional brain regions to accomplish simple motor tasks in chronic alcohol dependent patients. *Alcoholism: Clinical and Experimental Research*, **34**: 1098–109.

Pascual M, Blanco AM, Cauli O, *et al* (2007) Intermittent ethanol exposure induces inflammatory brain damage and causes long-term behavioural alterations in adolescent rats. *European Journal of Neuroscience*, **25**: 541–50.

Patterson BW, Parsons OA, Schaeffer KW, *et al* (1988) Interpersonal problem solving in alcoholics. *Journal of Nervous and Mental Disease*, **176**: 707–13.

Pfefferbaum A, Sullivan EV, Mathalon DH, *et al* (1997) Frontal lobe volume loss observed with magnetic resonance imaging in older chronic alcoholics. *Alcoholism: Clinical and Experimental Research*, **21**: 521–9.

Pitel AL, Beaunieux H, Witkowski T, *et al* (2008) Episodic and working memory deficits in alcoholic Korsakoff patients: the continuity theory revisited. *Alcohol Clinical and Experimental Research*, **32**: 1229–41.

Popoola A, Keating A, Cassidy E (2008) Alcohol, cognitive impairment and hard to discharge acute hospital inpatients. *Irish Journal of Medical Science*, **177**: 141–5.

Popova S, Lange S, Burd L, *et al* (2012) Health care burden and cost associated with fetal alcohol syndrome: based on official Canadian data. *PLoS ONE*, **10 August**: doi: 10.1371/journal.pone.0043024.

Premji S, Benzies K, Serrett K, *et al* (2007) Research-based interventions for children and youth with a foetal alcohol spectrum disorder: revealing the gap. *Child: Care, Health and Development*, **33**: 389–97.

Price J, Mitchell S, Wiltshire B, *et al* (1988) A follow up study of patients with alcohol related brain damage in the community. *Australian Drug and Alcohol Review*, **7**: 83–7.

Prigatano GP, Glisky EL, Konoff PS (1996) Cognitive rehabilitation after traumatic brain injury. In *Cognitive Rehabilitation for Neuropsychiatric Disorders* (eds PW Corrigan, SC Yodofsky): pp. 223–42. American Psychiatric Publishing.

Qin L, He J, Hanes RN, *et al* (2008) Increased systemic and brain cytokine production and neuroinflammation by endotoxin following ethanol treatment. *Journal of Neuroinflammation*, **5**: 10.

Raistrick D (2000) Management of alcohol detoxification. *Advances in Psychiatric Treatment*, **6**: 348–55.

Ramayya A, Jauhar P (1997) Increasing incidence of Korsakoff's psychosis in the east end of Glasgow. *Alcohol and Alcoholism*, **32**: 281–5.

Rinn W, Desai N, Rosenblatt H, *et al* (2002) Addiction denial and cognitive dysfunction: a preliminary investigation. *Journal of Neuropsychiatry and Clinical Neurosciences*, **14**: 52–7.

Roehrich L, Goldman MS (1993) Experience-dependent neuropsychological recovery and the treatment of alcoholism. *Journal of Consulting and Clinical Psychology*, **61**: 812–21.

Ron D, Wang J (2009) The NMDA receptor and alcohol addiction. In *Biology of the NMDA Receptor* (ed AM Van Dongen). CRC Press.

Ron MA, Acker W, Shaw GK, *et al* (1982) Computerised tomography of the brain in chronic alcoholism. *Brain*, **105**: 497–514.

Rosenthal J, Christianson A, Cordero J (2005) Fetal alcohol syndrome prevention in South Africa and other low-resource countries. *American Journal of Public Health*, **95**: 1099–101.

Rota-Bartelink A, Lipman B (2007) Supporting the long-term residential care needs of older homeless people with severe alcohol related brain injury in Australia: the Wicking Project. *Care Management Journals*, **8**: 141–8.

Royal College of Physicians (2001) *ALCOHOL – Can the NHS Afford It? Recommendations for a Coherent Alcohol Strategy for Hospitals, A report of a Working Party of the Royal College of Physicians*. RCP.

Royal College of Physicians (2003) *Psychological Support for People in Hospital: Information for Patients, Relatives and Carers*. RCP.

Royal College of Physicians (2009) *Evidence Submission to the Health Select Committee Inquiry into Alcohol*. RCP.

Schacter DL (1987) Implicit memory: history and current status. *Journal of Experimental Psychology: Learning, Memory and Cognition*, **13**: 501–18.

Schmidt K, Gallo J, Ferri C, *et al* (2005) The neuropsychological profile of alcohol related dementia suggests cortical and subcortical pathology. *Dementia and Geriatric Cognitive Disorders*, **20**: 286–91.

Scottish Executive (2006) *Delivering for Mental Health*. Scottish Executive.

Scottish Government (2009) *Tackling Alcohol Misuse*. Scottish Government.

Sechi G, Serra A (2007) Wernicke's encephalopathy: new clinical settings and recent advances in diagnosis and management. *Lancet Neurology*, **6**: 442–55.

Serdaru M, Hausser-Hauw C, Laplane D, *et al* (1988) The clinical spectrum of alcoholic pellagra encephalopathy. *Brain*, **111**: 829–42.

Smith DM, Atkinson RM (1995) Alcoholism and dementia. *International Journal of Addiction*, **30**: 1843–69.

Singleton N, Meltzer H, Gatward R (1998) *Psychiatric Morbidity among Prisoners in England and Wales*. TSO (The Stationery Office).

Smith I, Hillman A (1999) Management of alcohol Korsakoff syndrome. *Advances in Psychiatric Treatment*, **5**: 271–8.

Smith DE, McCrady BS (1991) Cognitive impairment among alcoholics: impact on drink refusal skill acquisition and treatment outcome. *Addictive Behaviours*, **16**: 265–74.

Staley JK, Gottschalk C, Petrakis IL, *et al* (2005) Cortical gamma-aminobutyric acid type A-benzodiazepine receptors in recovery from alcohol dependence: relationship to features of alcohol dependence and cigarette smoking. *Archives of General Psychiatry*, **62**: 877–88.

Staner L, Boeijinga P, Dane T, *et al* (2006) Effects of acamprosate on sleep during alcohol withdrawal: a double-blind placebo-controlled polysomnographic study in alcohol-dependent subjects. *Alcoholism, Clinical and Experimental Research*, **30**: 1492–9.

Stockwell T, Murphy D, Hodgson R (1983) The severity of alcohol dependency questionnaire: its use, reliability and validity. *British Journal of Addiction*, **78**: 145–55.

Streissguth A, Aase JM, Clarren SK, *et al* (1991) Foetal alcohol syndrome in adolescents and adults. *JAMA*, **265**: 1961–7.

Streissguth AP, Barr HM, Kogan J, *et al* (1996) *Understanding the Occurrence of Secondary Disabilities in Clients with Fetal Alcohol Syndrome (FAS) and Fetal Alcohol Effects (FAE)*. University of Washington.

Streissguth AP, O'Malley KD (2000) Neuropsychiatric implications and long-term consequences of foetal alcohol spectrum disorders. *Seminars in Clinical Neuropsychiatry*, **5**: 177–90.

Strickland P, Grimwood G (2013) *The Abolition of Sentences of Imprisonment for Public Protection*. House of Commons Library, Standard Note SN/HA/6086, 27 November.

Stringer AY, Goldman MS (1987) Experience-dependent recovery of block design performance in male alcoholics: strategy training versus unstructured practice. *Journal of Studies on Alcohol*, **49**: 406–11.

Sullivan E, Pfefferbaum A, Rosenbloom M, *et al* (2000) Longitudinal changes in cognition, gait and balance in abstinent and relapsed alcoholic men: relationship changes in brain structure. *Neuropsychology*, **14**: 178–88.

Sullivan EV, Pfefferbaum A (2005) Neurocircuitry in alcoholism: a substrate of disruption and repair. *Psychopharmacology*, **180**: 583–94.

Sullivan EV, Pfefferbaum A (2009) Neuroimaging of the Wernicke-Korsakoff syndrome. *Alcohol and Alcoholism*, **44**: 155–65.

Svanberg J, Evans J (2013) Neuropsychological rehabilitation in alcohol-related brain damage: a systematic review. *Alcohol and Alcoholism*, **48**: 704–11.

Syapin PJ, Alkana RL (1988) Chronic ethanol exposure increases peripheral-type benzodiazepine receptors in brain. *European Journal of Pharmacology*, **147**: 101–9.

Tarter RE, Edwards KL (1986) Multifactorial etiology of neuropsychological impairment in alcoholics. *Alcoholism: Clinical and Experimental Research*, **10**: 128–35.

Taylor D, Paton C, Kapur S (eds) (2012) *The Madusley Prescribing Guidelines in Psychiatry* (11th edn). Wiley Blackwell.

The Howard League for Penal Reform (2014) *Latest prison population figures: week ending Friday 11 April 2014*. Available at: http://www.howardleague.org/weekly-prison-watch/ (accessed April 2014).

Thomson AD (2000) Mechanisms of vitamin deficiency in chronic alcohol misusers and the development of the Wernicke-Korsakoff syndrome. *Alcohol and Alcoholism Supplement*, **35**: 2–7.

Thomson AD, Cook CHC, Torquet R, *et al* (2002) The Royal College of Physicians report on alcohol: guidelines for managing Wernicke's encephalopathy in the accident

and emergency department. *Alcohol and Alcoholism*, **37**: 513–21.

Thomson A, Guerrini I, Marshall E (2009) Wernicke's encephalopathy: role of thiamine. *Nutrition Issues in Gastroenterology*, **series 75**: 21–30.

Todd KG, Butterworth RF (1999) Early microglial response in experimental thiamine deficiency: an immunohistochemical analysis. *Glia*, **25**: 190–8.

Torvik A, Lindboe CF, Rogde S (1982) Brain lesions in alcoholics: a neuropathological study with clinical correlations. *Journal of the Neurological Sciences*, **56**: 233–48.

Tsai G, Coyle JT (1998) The role of glutamatergic neurotransmission in the pathophysiology of alcoholism. *Annual Review of Medicine*, **49**: 173–84.

Tsukahara M, Ishii K, Kimura Y, *et al* (2005) Visualizing activated microglias in Wernicke-Korsakoff syndrome by [11C]PK11195 and PET. *Journal of Cerebral Blood Flow and Metabolism*, **25**: S370.

Ukermann J, Daum I (2008) Social cognition in alcoholism: a link to prefrontal cortex dysfunction? *Addiction*, **103**: 726–35.

Umhau JC, Momenan R, Schwandt ML, *et al* (2010) Effect of acamprosate on magnetic resonance spectroscopy measures of central glutamate in detoxified alcohol-dependent individuals: a randomized controlled experimental medicine study. *Archives of General Psychiatry*, **67**: 1069–77.

Vallés SL, Blanco AM, Pascual M, *et al* (2004) Chronic ethanol treatment enhances inflammatory mediators and cell death in the brain and in astrocytes. *Brain Pathology*, **14**: 365–71.

VanDamme I, d'Ydewalle G (2008) Elaborative processing in the Korsakoff syndrome: context versus habit. *Brain and Cognition*, **67**: 212–24.

Vetreno RP, Hall JM, Savage LM, *et al* (2011) Alcohol-related amnesia and dementia: animal models have revealed the contributions of different etiological factors on neuropathology, neurochemical dysfunction and cognitive impairment. *Neurobiology of Learning and Memory*, **96**: 596–608.

Victor M, Adams RD, Collins GH (1971) The Wernicke-Korsakoff syndrome: a clinical and pathological study of 245 patients, 82 with post-mortem examinations. *Contemporary Neurology Series*, **7**: 1–206.

Victor M, Adams RD, Collins GH (eds) (1989) *The Wemicke-Korsakoff Syndrome and Related Neurological Disorders Due to Alcoholism and Malnutrition* (2nd edn). FA Davis.

Wagner Glenn S, Parsons OA, Sinha R, *et al* (1988) The effects of repeated withdrawals from alcohol on the memory of male and female alcoholics. *Alcohol and Alcoholism*, **23**: 337–42.

Wang D, Hazell AS (2010) Microglial activation is a major contributor to neurologic dysfunction in thiamine deficiency. *Biochemical and Biophysical Research Communications*, **402**: 123–8.

Ward RJ, Lallemand F, de Witte P (2009a) Biochemical and neurotransmitter changes implicated in alcohol-induced brain damage in chronic or 'binge drinking' alcohol abuse. *Alcohol and Alcoholism*, **44**: 128–35.

Ward RJ, Colivicchi MA, Allen R, *et al* (2009b) Neuro-inflammation induced in the hippocampus of 'binge drinking' rats may be mediated by elevated extracellular glutamate content. *Journal of Neurochemistry*, **111**: 1119–28.

Warren K, Hewitt B, Thomas J (2011) Foetal alcohol spectrum disorders: research challenges and opportunities. *Alcohol Research and Health*, **34**: (online publication).

Weinstein DD, Martin PR (1995) Psychiatric implications of alcoholism and traumatic brain injury. *American Journal on Addictions*, **4**: 285–96.

Weissenborn R, Duka T (2003) Acute alcohol effects on cognitive function in social drinkers: their relationship to drinking habits. *Psychopharmacology*, **165**: 306–12.

Wernicke C (1885) *Acute Haemorrhagic Superior Polioencephalitis*. Trans. and republished IA Brody, RH Wilkins (1968) *Archives of Neurology*, **19**: 228–32.

Wernicke C (1900) *Grundriss der Psychiatrie in klinischen Vorlesungen*. Thieme.

Werring D, Howard R, Leff A, *et al* (2009) Systemic conditions and neurology. In *Neurology: A Queen Square Textbook* (eds C Clarke, R Howard, M Rossor, *et al*): pp. 913–43. Wiley–Blackwell.

White AM, Matthews DB, Best PJ (2000) Ethanol, memory, and hippocampal function: a review of recent findings. *Hippocampus*, **10**: 88–93.

Wilson K (2011) Alcohol-related brain damage: a 21st-century management conundrum. *British Journal of Psychiatry*, **199**: 176–7.

Wilson K, Halsey A, Macpherson H, *et al* (2012) The psycho-social rehabilitation of patients with alcohol-related brain damage in the community. *Alcohol and Alcoholism*, **47**: 304–11.

Wilton G, Plane MB (2006) The family empowerment network: a service model to address the needs of children and families affected by foetal alcohol spectrum disorders. *Pediatric Nursing*, **32**: 299–306.

Wood B, Currie J, Breen K (1986) Wemicke's encephalopathy in a metropolitan hospital: a prospective study of incidence, characteristics and outcome. *Medical Journal of Australia*, **144**: 12–6.

Woodburn K, Johnstone E (1999) Ascertainment of a population of people with early onset dementia in Lothian, Scotland. *International Journal of Geriatric Psychiatry*, **145**: 362–7.

World Health Organization (1992) *The ICD-10 Classification of Mental and Behavioural Disorders: Clinical Descriptions and Diagnostic Guidelines*. WHO.

Ylvisaker M, Feeney TJ (1998) *Collaborative Brain Injury Intervention: Positive Everyday Routines*. Singular Publishing Group.

Zinn S, Stein R, Swartzwelder HS (2004) Executive functioning early in abstinence from alcohol. *Alcoholism: Clinical and Experimental Research*, **28**: 1338–46.

For full details of reports available and how to obtain them, contact the Book Sales Assistant at the Royal College of Psychiatrists, 21 Prescot Street, London E1 8BB (tel. 020 7235 2351; fax 020 3701 2761) or visit the College website at http://www.rcpsych.ac.uk/publications/collegereports.aspx