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Rapid Evidence Review: The relationship between alcohol and mental health problems

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Foreword

In developing its future programme of grant-funded research, Alcohol Change UK wished to explore what is known, and what is yet to be understood, in a series of key areas, as follows:

Topic one	The role of alcohol in intimate partner relationships
Topic two	The impact of alcohol on the human brain
Topic three	Alcohol interventions and the criminal justice system
Topic four	The relationship between alcohol and mental health problems
Topic five	Drinking problems and interventions in black and minority ethnic communities
Topic six	Digital interventions to reduce alcohol-related harm

These areas were selected through stakeholder engagement and consultation, as well as 'horizon-scanning' the research, policy and practice environment to identify where particular gaps appeared.

Rapid evidence reviews were commissioned on the six topics and their findings will allow Alcohol Change UK to synthesise knowledge on this particular range of subjects. This will help inform its own work, as well as leading to outward-facing publications that will allow the public, practitioners and policy-makers to better understand the research in these key areas.

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Queens University Belfast in partnership with our stakeholders will expand the demonstrable contribution that our research brings to society.

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This report was funded by **Alcohol Change UK**. Alcohol Change UK works to significantly reduce serious alcohol harm in the UK. We create evidence-driven change by working towards five key changes: improved knowledge, better policies and regulation, shifted cultural norms, improved drinking behaviours, and more and better support and treatment.

Find out more at alcoholchange.org.uk.

Opinions and recommendations expressed in this report are those of the authors.

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Executive summary

Background

The relationship between mental health disorders and alcohol misuse is complex, with the potential for multiple variations of diagnoses and mutually dependent problems (Baigent, 2012). There is a level of inconsistency in the definitions of comorbid mental health and co-occurring substance use disorders including Alcohol use Disorders (AuDs). In addition, there are multi-faceted and complex associations between AuDs and the various psychiatric disorders and these relationships are nuanced in terms of direction and symptomology. The term 'dual diagnosis' implies that there are only two clinical problem areas when in fact there are usually several, all of which are specific to the individual and manifest in varying and multiple combinations. These may include a range of domains, including personal, familial and social, physical health, mental and emotional health, involvement in the criminal justice system and accommodation. Therefore, it may be more useful to conceptualise this group as having 'complex needs' and subsequently reflect on working models and strategies which are flexible and tailored to the needs of the individual.

The high prevalence of coexisting mental health and substance use problems within mental health services is recorded in a number of studies in the United Kingdom (UK). The rates of co-occurring disorders recorded within UK mental health and addiction services vary between 30 and 85% (Schulte, 2008; Weaver et al., 2003; NICE, 2016) Evidence from a National Institute for Health and Care Excellence (NICE) review of prevalence of co-occurring conditions across secondary mental health settings indicated that the prevalence rate of co-occurring disorders was 34.3%, although due to heterogeneity of the sample it was stated that the result should be treated with caution (NICE, 2016). In order to respond to the myriad of problems engendered by comorbid AuDs and mental health disorders, a combination of service models have been developed in the UK and on an international basis. The majority of models of service delivery can be categorised as serial, parallel or integrated with the latter viewed as the most beneficial for service users and patients. Furthermore, interventions are also characterised by the many and varied range of pharmacological and psychosocial treatment modalities. Therefore, this review sought to provide an overview of policy, service delivery and treatment models to consider the context of treatment and the effectiveness of interventions relevant to individuals with comorbid conditions.

Aims

The Rapid Evidence Assessment (REA) considered two primary research aims:

1. To examine the effectiveness of psychosocial and pharmacological interventions for adults (18+) with comorbid alcohol use and mental health problems.
2. To identify the general policy framework for co-occurring substance use disorders and Alcohol Use Disorders (AuDs), assessment models, care plans and guidelines for practice within the UK. In addition, there was a specific focus on models of treatment delivery within the UK and international contexts.

Methods

A dualistic approach to the review was employed in accordance with the two primary aims of the review. First, a rapid review employing a systematic approach to searching, appraising and reviewing the results was used to identify the evidence base as regards interventions for comorbid alcohol use disorders and mental health disorders. Second, there was a broad literature review of UK policy frameworks and guidance documents which considered assessment and care planning and models of treatment service delivery in the UK. The section was augmented with international literature from the United States and European sources.

Findings

Findings suggest that there is a strong association between AuDs and mental health disorders including: depression, anxiety, bipolar disorder, personality disorder and schizophrenia. Across the UK, the policy framework for substance use disorders and mental health comorbidity is inconsistent and is even more fragmented as regards alcohol-specific co-occurring disorders. In England, the last comprehensive guide to policy and practice was published by the Department of Health in 2002; whilst in Northern Ireland there has been a gap in specific policy guidance for comorbid substance use and mental health disorders since 2005. However, the Welsh government produced a recent comprehensive policy framework which addressed the specific needs of people with comorbid disorders in 2015. Similarly, Scotland may not have a recent specific policy framework document related to comorbidities but it does make a substantial reference to comorbid disorders in a number of mental health and alcohol policy frameworks (Scotland Mental Health Strategy 2017-2027, Scottish Government 2018, Alcohol framework, 2018).

According to the evidence, all levels of assessment and care planning in working with comorbid disorders must be tailored to the complex individual needs of the service user (and carers where appropriate), be developed in full partnership with the service user (where possible) and founded on a non-judgemental, empathic and person-centred approach. In addition, shunting of service users between mental health and substance disorder services is often apparent with a lack of clarity about case management responsibility. NICE (2016) guidance also recommends that initial goals for alcohol and mental health comorbidities may be agreed on the basis of a harm reduction approach but that the ultimate goal for this specific service user grouping should be abstinence.

Three models of service delivery were identified from the literature: serial, parallel and integrated. Whilst the integrated service model demonstrates more efficacious treatment outcomes (Mangrum et al., 2005; Muser et al., 2003; McCoy et al., 2003), it is not entirely clear how many treatment providers in the UK currently provide an integrated service for concomitant AuDs and mental health disorders. However, there is the suggestion that the majority of treatment models in the UK and the United States tend to work within the parameters of the serial and parallel models. In Europe, there is substantial heterogeneity in the range of treatment models offered for co-existing disorders, although it is noted that the wide range of options may also act as barrier to treatment provision as some providers may lack the skills and expertise to address the needs incurred by both AuDs and mental health disorders.

Results from the current rapid structured review of interventions for alcohol use problems/disorders and comorbid mental health conditions showed mixed results for both pharmacological and psychosocial intervention studies. Naltrexone was the most commonly administered pharmacological intervention, and was most beneficial when combined with other drugs (for example Sertraline and Disulfiram) than when used alone. The combination was successful at treating alcohol use and psychiatric symptoms

compared to placebo (Petrakis et al., 2005, Pettinati et al., 2011). Similar to Naltrexone, when Sertraline was used alone it was less successful at treating comorbid conditions (Gual et al., 2003). In addition, combinations of lorazepam and Dilsulfiram demonstrated promising outcomes with reductions in alcohol use and psychiatric symptoms. Conversely, single application of Acamprosate was reported to be the least effective in the treatment of comorbid conditions (Tolliver et al., 2012; Ralevski et al., 2011). Whilst the majority of the studies were randomised controlled trials (RCTs), there was some evidence of methodological design flaws, including lack of appropriate control groups, small sample sizes and high attrition rates.

Cognitive behavioural therapy (CBT) was reported as an effective psychosocial intervention in treating at least one aspect of comorbid problematic alcohol use and psychiatric conditions (Toneatto & Calderwood, 2015; Morely et al., 2016; Brown et al., 2011). Moreover, computer-based CBT outcomes were similar, if not more effective than therapist-based CBT for a reduction in depressive symptoms and alcohol use (Agyapong et al., 2013; Deady et al., 2016; Kay-Lambkin et al., 2008) and a non-significant reduction in alcohol-related problems only (Geisner et al., 2016). On the other hand, outcomes from a motivational interviewing (MI) based intervention were not significantly different when compared to a 'brief advice' intervention. However, both groups experienced improvements in comorbid conditions. Only one study reported a specific integrated intervention administrating a pharmacological agent and psychosocial support. Although it reported a small sample and no control or comparison group, Lamotrigine and an individual relapse prevention programme demonstrated a significant reduction in problematic alcohol use and psychiatric symptoms.

Conclusion

Results from both the policy/guidance and interventions components of the review indicate the complex issues and the problems faced by vulnerable individuals who have comorbid AuDs and mental health disorders. It is clear that the multi-faceted problems reach far beyond the dual diagnosis label to include many and varied combinations of mental and physical health problems. National and regional UK Governments have tried to address some of the complex and multi-layered issues via a number of policy framework and guidance documents. The somewhat sporadic UK Government documentation on co-occurring disorders has been usefully supplemented by published material from expert commentators, practitioners and community-based or voluntary sector mental health and substance use disorder organisations. From the policy review, it is clear that the development of a UK national policy framework for working with comorbid mental health and substance use disorders is overdue and should specifically address the issues of morbidities related to AuDs. In addition, whilst the interventions review indicated some level of success for CBT, and other psychosocial and mixed modality drug interventions as first line treatment options for comorbid AuDs and mental health disorders, it is apparent that the majority of studies are marred by weak research design. It is also clear that studies with high-quality design and rigorous methodological approaches should be developed to examine the efficacy of pharmacological, psychosocial and integrated treatments for comorbid disorders.

Introduction

The nature and prevalence of co-occurring alcohol use disorders and mental health conditions is increasing within mental health and substance use disorder services. Moreover, the concomitant problems for individuals, families and communities are becoming ever more complex and the absence of a coordinated approach in some regions of the UK are further exacerbating poor outcomes for patients and service users. The relationship between mental health disorders and alcohol misuse is complex, with the potential for variable combinations of diagnoses and mutually dependent problems (Baigent, 2012). Staff working in psychiatric and addiction service settings frequently encounter the challenges involved in treating these patients and balancing the management of risk with the promotion of patient empowerment.

One common understanding of dual diagnosis is the presence of comorbid alcohol misuse in an individual with at least one psychiatric disorder (WHO, 1995). It is not recognised in the diagnostic classifications and so is not considered to be a formal psychiatric diagnosis. Definitions can vary with some excluding the most prevalent psychiatric conditions in practice, such as anxiety and personality disorders (Marshall & Farrell, 2006; Drake, 2007). To complicate matters further, both psychiatric and alcohol use disorders have their own spectrum of severity and diagnostic classification (Chrome & Myton, 2004; Thoma & Daum, 2013). This lack of a consistent definition makes communication difficult and limits useful comparison of the evidence-base (Canaway & Merkes, 2010).The term dual diagnosis implies that there are only two clinical problem areas when in fact there are usually several, all of which are specific to the individual and manifest in varying and multiple combinations. These may include inter-related domains, for example, personal responsibility, social contact, managing physical health, mental and emotional health, daily lifestyle, relations, crime and accommodation. Therefore, it may be more useful to conceptualise this group as having ‘complex needs’ and thus consider and reflect on working models and strategies which are flexible and tailored to the needs of the individual. Due to the range of terms used to define a diagnosis of both mental health disorders and alcohol use disorders (AuDs) by authors, expert commentators and researchers from a range of health and social care backgrounds, the following report will use alternate terminology to describe the complex marriage of a range of comorbidities. This will include co–occurring/coexisting disorders, comorbid disorders, multiple morbidities and to a lesser extent dual diagnosis as it is now widely accepted that the term dual diagnosis is considered inadequate when discussing the complexities inherent to combined mental health and AuDs. It is also apparent that the diagnosis of both disorders may have originally been associated with combination of alcohol disorders and more severe and enduring mental illnesses (SMIs), for example schizophrenia and bipolar disorders. However, the recent rise in numbers of complex morbidities that are related to AuDs such as anxiety and depressive disorders is reflected in the literature and therefore the review considers a range of SMIs including anxiety and mild to moderate depressive disorders.

Nature and Prevalence

From the prevalence figures described below, it is clear that alcohol-related harms and comorbidities have increased in the majority of the four UK nations. In England, there were 337,870 hospital admissions due to alcohol in 2017/18. This figure has not changed greatly since 2016/17 although over a ten-year period, it is 15% higher than 2007/2008 figures (NHS Digital, 2019). In addition, there were 5,483 alcohol-specific deaths, 6% higher than in 2016 (ONS, 2019). Figures from Wales show that in 2017-18, hospital admissions for alcohol-specific conditions were 2.4 times higher than for illicit drug use.

There were also 540 alcohol deaths in 2017 which represents an increase of 7.1% from 2016 (Welsh Government, 2019). Scottish statistics indicate that there were 1,265 alcohol-related deaths in 2016, an increase of 10% in comparison with 2015. Furthermore, there were 36,235 alcohol-related hospital admissions in 2016/17 (NSS, 2017; NRS, 2019).

The high prevalence of coexisting mental health and substance use problems within mental health services is well-documented via recorded prevalence rates in various UK studies. The rates of co-occurring disorders recorded within UK mental health and addiction services range between 30 and 85% (Schulte, 2008; Weaver et al., 2003; NICE, 2016). In a national survey Schulte et al. (2008) estimated that 32% of service users who were engaged with mental health and addiction services in England recorded a dual diagnosis although almost 50% did not receive assessments for both mental health conditions and substance use problems and joint protocols for treatment remained unstructured. Delgadillo et al. (2012) found 70% of a sample from community substance use treatment were also diagnosed with common mental health disorders. Evidence from a NICE review of the prevalence of co-occurring conditions across secondary mental health settings (NICE, 2016) highlighted rates of between 11.7% and 61.2% for substance use/misuse/dependence within the past year. A combination of data from nine relevant studies indicated that the prevalence rate of co-occurring disorders was 34.3%, although due to the heterogeneity it was stated that the result should be treated with caution (NICE 2016). In the UK it is estimated that over 33% of psychiatric patients with severe and enduring mental illness have a substance misuse problem including an alcohol use disorder, whilst over 50% of clients currently accessing drug and alcohol services have a mental health problem (University of Manchester, 2015).

Co-occurring Substance use with Specific Mental Health Disorders

Alcohol use disorders (AuDs) are associated with a range of mental health difficulties including: depression, anxiety, bipolar disorder, personality disorder and schizophrenia (PHE, 2016). In 2014/15, there were 203,700 hospital admissions for mental disorders related to alcohol use and this accounted for 19% of hospital admissions in that period in the UK (PHE, 2016).

Evidence suggests that there is a causal linkage between alcohol use disorders and depression where an increased use of alcohol is positively correlated with an increased risk of depression (Boden, 2011; Kuria, 2012; Van den berg, 2014). The association between alcohol dependence and depression may be attributable to the depressive effects of ethanol and it is widely expected that in this specific comorbidity dyad, indicators of depression often lessen or cease with abstinence (Pary & Patel, 2017).

Presentation of dually diagnosed AuDs and anxiety disorders is relatively common and is often synonymous with a range of complex factors. Symptoms of anxiety often present as a result of withdrawal from a number of substances including alcohol. Conversely, anxiety disorders are a risk factor for the development of substance use disorders and may exacerbate the symptomology of a range of anxiety disorders. Accurate diagnosis and care planning requires a person centred and individualised approach to treatment to provide the best treatment outcomes for service users. Furthermore, standard interventions for anxiety disorders or AUDs may need to be amended and merged in ways to accommodate the precise needs of individuals who have the co-occurring disorders (Smith & Randall, 2012, Back & Brady, 2008).

The association between schizophrenia and comorbid alcohol disorders has been widely acknowledged by service users and practitioners. Alcohol has been reported as having

mediating effects on symptoms of the disorder, often precipitating a sedative effect on delusional beliefs, emotional blunting, and chaotic thought processes associated with schizophrenia. As substance use disorder is often seen in conjunction with a diagnosis of schizophrenia (paranoid, disorganised, residual, and undifferentiated) an individual who displays symptoms of the illness should also be evaluated for alcohol or drug use or dependence (American Centre of Addictions, 2019). There is also some evidence as regards the association between AuDs and bipolar disorders with experts purporting that alcohol use disorders are also highly prevalent in individuals who have been diagnosed with bipolar disorder (Cardoso et al., 2008). In a review by Farren et al. (2012) the authors reported that substance use disorders are associated with increased suicidal behaviour in people with a bipolar disorder. The risk of attempted suicide is almost double for these patients in comparison to bipolar patients who do not abuse alcohol (Farren et al., 2012).

Aims of the Review

The Rapid Evidence Assessment (REA) considered two primary research aims:

1. To examine the effectiveness of psychosocial and pharmacological interventions for adults (18+) with comorbid alcohol use and mental health problems.
2. To identify the general policy framework for co-occurring substance use disorders and Alcohol Use Disorders (AUDs), assessment models, care plans and guidelines for practice within the UK. In addition, there was a specific focus on models of treatment delivery within UK and international contexts.

Methodology

A Rapid Evidence Assessment (REA) method was used to identify, select and analyse the literature relevant to this review on mental health and alcohol use/alcohol use disorders. REAs provide a rigorous, open and effective means of evaluating what is known and are particularly suited to projects where the potential literature is very broad but where the themes from the evidence are needed to inform policy direction. The key stages of a REA are to develop search strategies and identify appropriate databases, screen the results against agreed inclusion criteria, assess the quality of the included results, extract the key findings from the included results, and provide a synthesis of the key themes to inform the discussion and recommendations of the review. The Government Social Research Service and the Evidence for Policy and Practice Information and Co-ordinating Centre (2013) recommend a REA when there is a need to decide on a policy direction based on the best available evidence but despite there being a wide range of literature there are ongoing debates and questions. The current methodology was informed by discussion with the Drug and Alcohol Research Network (DARN) and The Mental Health Advisory Group members, both based at the School of Education and Social Sciences at Queens University Belfast. A dualistic approach to the review was utilised according to the primary aims identified above. First, a rapid review employing a systematic approach to searching, appraising and reviewing the results was used to identify the evidence-base as regards interventions for comorbid alcohol use disorders and mental health disorders. Secondly, there was a broad literature review of UK policy frameworks and guidance documents which considered assessment and care planning, and models of treatment service delivery in the UK. The section was augmented with international literature from United States and European sources. The key phases of the REA for this review are summarised below.

Identifying the literature

Databases

Studies were identified using the following electronic databases: International Bibliography of the Social Sciences (IBSS), PsycINFO, Scopus, Social Care Online (SCIE), Social Science Citation Index, ERIC and Medline.
Pertinent national and international drug and alcohol and mental health websites, key UK government reports and guideline documents were also accessed to identify policy frameworks, guidelines and extant literature relevant to the topics of mental health and alcohol use disorders. During searches it became apparent that some significant messages, with regards to mental health and alcohol specifically, were embedded in policy documents and other reports which considered mental health disorders alongside an overview of both alcohol use and drug use.

Search strategy

Search strategies were developed and refined in collaboration with clients, key stakeholders and a specialist librarian. The search terms (or similar phrases) included 'alcohol misuse', 'mental health', 'comorbidities' and 'intervention' and were limited to publications between January 2002 to May 2019, involving adults and written in the English language (see Appendix A for primary search strategy).

Inclusion and Exclusion Criteria

Criteria were compiled according to the two primary aims (see table one).

Table 1: Exclusion and Inclusion Criteria

Aim One: An examination of psychosocial and pharmacological **interventions** for adults with comorbid alcohol use and mental health problems.	**Aim Two**: Analysis of the policy frameworks, care plans and clinical guidelines for practice within the UK and models of treatment delivery within UK and international contexts.
Inclusion Criteria Peer-reviewed Journals English Language Quantitative and mixed methods research Substance / Alcohol use /misuse or disorder Mental illness disorder or psychiatric disorder Dual Diagnosis / comorbidities /AuDs and Mental Health Disorders Interventions Psychosocial or pharmacological **Exclusion** Participants under 18 years Policy or framework document	**Inclusion Criteria** UK government and regional policy documents on aspects of the care continuum for comorbid conditions UK clinical guidelines UK and international literature on service models of treatment **Exclusion** International policy documents International literature on assessment and care planning

Screening methods

The results of all search strategies for the interventions component of the review were imported to the screening tool, Rayyan (Ouzzani et al., 2016). Using clearly defined

inclusion criteria, all papers were screened by two members of the research team using title and abstract initially. Any disagreements were referred to a third review author in the team. Accessible full text copies were then screened by two research team members to assess their eligibility for inclusion in the study.

Data extraction

A developed data extraction tool was used to capture all necessary information for the intervention review including: (1) type of study (2) participants (3) intervention (4) clinical outcomes (5) clinical scales (6) clinical facility (7) timeframe of intervention (8) key results (9) limitations (table 2).

Quality appraisal

Quality of interventions evidence was assessed using the Cochrane Risk of Bias Tool (CRBT; Higgins et al., 2011) for intervention studies using randomised methodologies (see appendix B). The CRBT has six domains including sequence generation, allocation concealment and blinding (personal, participants and outcomes, incomplete data, selective outcome reporting and 'other sources of bias'). The CRBT is designed to be comprehensive in evaluating randomisation and blinding (Armijo-Olivo et al., 2012). The Evidence Project Risk of Bias tool was used to assess studies using non-randomised methodologies. The Evidence Project Risk Bias tool (EPRBT) includes five key domains including study design (pre-post intervention data, control or comparison group, cohort), comparison of groups (comparison groups equivalent on socio-demographics and comparison groups equivalent at baseline on outcome measure), sampling (random assignment of participants to the intervention, random selection of participants for assessment), control for potential confounders and follow up rate of 80% or more. The EPRBT is applicable for pre-post design or cohort studies and can be used without adaptation (Kennedy et al., 2019; see appendix B).

Data synthesis

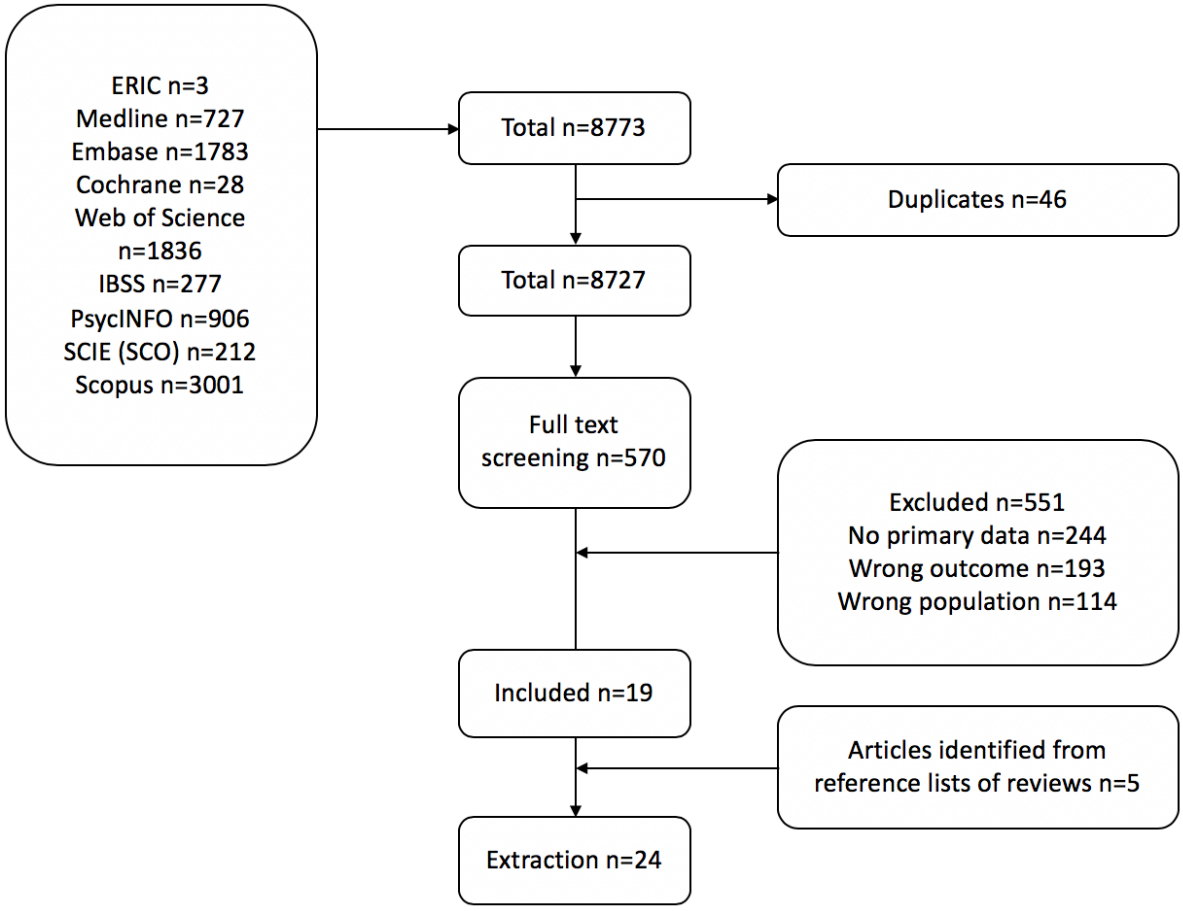
The intervention findings were discussed narratively due to the nature of the outcome assessments and quality of reporting for the interventions. A categorisation of data and descriptive summary are provided. The policy documents and frameworks section of the review was themed according to the following headings: policy frameworks (UK), assessment models (UK), care planning (UK), treatment models (International and UK).

Included evidence

Included studies for Interventions Review

After removing duplicates (n=46), 8,727 articles were identified for title and abstract screening. 8,157 articles were later excluded based on title and abstract. The remaining 570 articles were included for full text screening. Subsequently, 551 articles were later excluded, and 19 articles were included for extraction. In addition, reference lists of fourteen reviews were examined, identifying a further five studies. In total, 24 studies were included for extraction in this rapid review.

Figure 1: Rapid review flow chart



Findings

Research Aim One - Review of Interventions

1 To examine the effectiveness of psychosocial and pharmacological interventions for adults (18+) with comorbid alcohol use and mental health problems.

Study measures

All studies included participants with comorbid disorders involving an alcohol use disorder and mental health disorders. Studies utilised a wide range of standardised and non-standardised measures (n=52). The most common alcohol outcome assessment included the Substance Abuse Calendar/Timeline Follow-Back Interview (TFLB; Sobell & Sobell, 1992) and the Obsessive Compulsive Drinking scale (OCDS; Anton et al., 1995). The most common psychiatric outcome assessment was the Hamilton Depression Rating Scale (HAM-D; Bech et al., 1979) and the Brief Psychiatric Rating Scale (BPRS; Overall et al., 1962).

Settings

The majority of studies were out-patient based (Rubio et al., 2006; Deady et al., 2016; Kay-Lambkin et al., 2008; Morley et al., 2016; Toneatto & Calderwood, 2015; Brown et al., 2011; Andrisano-Ruggieri et al., 2016; James et al ., 2004; Brady et al., 2005; Brown et al., 2009; Brown et al 2014; Bogenschutz et al., 2016; Di Nicola et al., 2017; Gual et al., 2003; Hernandez-Avila et al., 2004; Martinotti et al 2008; Petrakis et al., 2005; Pettinati et al., 2010; Ralevski et al., 2011; Tolliver et al.,2012; Salloum et al., 2005) which involved health service research departments or addiction clinics based in hospitals, psychiatric and community mental health settings. One study recruited in patients within a hospital setting (Baker et al., 2002) and two studies took place in service user homes (Ralevski et al., 2011; Agyapong et al., 2013).

Interventions

Twenty-four studies which considered interventions of comorbid conditions were included in the rapid review. Three intervention domains were identified: psychosocial, pharmacological and integrated drug treatment and psychosocial treatment interventions. Ten studies used only psychosocial interventions involving one or more of the following: group therapy, motivational interviewing (MI) or cognitive behavioural therapy (CBT). Thirteen studies involved only a pharmacological intervention. One study conducted an integrated treatment intervention using pharmacological and psychosocial components (see table two).

Table 2: Studies Included in the Intervention Review

Authors	Design	Participants	Intervention	Clinical Outcomes	Clinical Scales	Clinical facility	Timeframe	Results	Limitations
Integrated interventions for alcohol and mental health problems									
Rubio et al. (2006)	Pre-post open label trial	N=28 (10 female) Mean age 36.5 years 18-65 years	Lamotrigine and individual relapse-prevention programme	Alcohol use Psychiatric symptoms	SADS VASC TLFB CDT HAM-D YMRS BPRS ECG	Outpatient	Baseline, 2, 4, 6, 8, 10, 12 weeks	Significant improvement was observed in psychiatric scores ($p < 0.01$). Craving and alcohol consumption also significantly decreased ($p < 0.001$).	No control or comparison Other medications taken
Psychosocial interventions for alcohol and mental health problems									
Agyapong et al. (2013)	RCT	EG n=24 46% male mean age 48 years CG n=24 46% male mean age 49 years	Mobile phone text messages vs brief text message	Alcohol use Depression	CAD BDI-II	Home	Baseline, 6 months	Benefits of text message intervention were not sustained beyond the period of 3 months.	Small sample Attrition at follow up CBT for both groups as well
Andrisano-Ruggieri et al. (2016)	Pre-post design	n=7 43% male Age range 35-57 years	Group counselling CBT sessions	Alcohol use Psychiatric symptoms	MALT PANSS	Outpatient	Baseline, 6 months	The PANSS and MALT scores indicated there was no significant reduction of the alcohol use or psychiatric symptoms after treatment.	Limited data analysis Small sample No control group or comparison

Baker et al. (2002)	RCT	EG n=79 75% male Mean age 31.71 years CG n=81 75% male Mean age 30.05 years	MI vs BI	Alcohol and Drug use Psychiatric syndromes	OTI BSI	Inpatient	Baseline, 3, 6 and 12 months	Both groups improved over time on alcohol and psychiatric symptoms however this was not significant different at 12 months.	Heterogeneous sample Attrition at follow up
Brown et al. (2011)	RCT	n= 151 67% male mean age 40.8 years	CBT-D vs TAU	Alcohol use Depression	BDI MHRSD TLFB	Outpatient	Baseline, 6 weeks, 3, 6, 12 months	Significant improvement for all patient on alcohol use and depression. No difference between groups on abstinence; depression significantly lower for treatment group only at 6-week follow up (p=.05). Not significant for MHRSD.	Baseline treatment
Deady et al. (2016)	RCT	EG n=60 40% male Mean age 21.85 years CG n=44 41% male Mean age 21.59 years	Online CBT/MI vs online control	Alcohol use Depression	PHQ-9 TOT-AL	Outpatient	Baseline, 3 & 6 months	Improvement in depression symptoms (p<.001) and alcohol use outcomes (p<.001) however gains not maintained at follow-up.	Attrition at follow up Small sample size Error in randomisation
Geisner et al. (2016)	RCT	N=311 (EG n= 76)37.6% male Mean age 20.14 years	Online CBT/MI vs TAU	Alcohol use Depression	AUDIT BDI-II DDQ RAPI PHQ-9	University	Baseline, 1 month	There were no significant differences across the study conditions for any of the outcome measures however alcohol intervention resulted in	Non-patient sample Attrition at follow up

								a reduction in alcohol related problems in those with a lower depressed mood compared to controls.	
James et al. (2004)	RCT	EG n=29 71.9% male mean age 28.50 years CG n=29 71.0% males, mean age 26.87 years	Group-based CBT vs one session	Alcohol and drug use Psychiatric symptoms	POLYTOT SADS AUDIT GSI DAST CPZ BPRS	Outpatient	Baseline, 6 weeks	Significant reductions treatment group observed in psychopathology (p<.01), CPZ (p<.01), alcohol and illicit substance use (p<.001), severity of dependence and hospitalisation.	Short follow up Attrition at follow up Small sample Study design
Kay-Lambkin et al. (2008)	RCT	n=97 46% male Mean age 35.37 years	Therapist led SHADE therapy vs Computer delivered SHADE therapy vs control	Alcohol and drug use Depression	BDI-II OTI SCID-RV	Outpatient	Baseline, 3, 6, 12 months	Depression responded better to intensive SHADE intervention compared to BI alone. Therapist lead treatment demonstrated a strong short-term beneficial effect which was matched by computer-based treatment at 12-month follow-up. Problematic alcohol use responded well to BI alone and even better to the intensive MI/CBT intervention.	Baseline treatment Small sample size Heterogeneous sample
Morley et al. (2016)	RCT	n=37 (46% male) mean age 41 years	CBT vs TAU	Alcohol use Psychiatric symptoms	TLFB, OCDS ADS ADIS-IV DASS-21	Outpatient	Baseline, 3, 12, 16 and 24 weeks	Significantly higher abstinence for treatment group on abstinence and days to relapse (heavy drinking; p<.05) over usual care (BI) and days until relapse (any drinking; p<.01). No	Short follow up Small sample

								significant difference in depression between groups.	
Toneatto & Calderwood (2015)	RCT	n=123 61% male mean age 39.43 years	CBT plus anxiety sessions vs CBT sessions	Alcohol use Psychiatric symptoms	TFLB SCL90 BAI	Outpatient	Baseline, 6 months (average 10 months)	Significant reduction of quantity and frequency of alcohol misuse (p<.001) and anxiety (p<.001). However, no advantage of extra anxiety sessions.	Small sample Attrition at follow up Other medications taken Heterogeneous sample
Pharmacological interventions for alcohol and mental health problems									
Bogenschutz et al. (2016)	Pre-post open label trial	n=41 39% male Mean age 41.66 years	Disulfiram and Lorazepam (combined)	Alcohol use Anxiety disorder	TLFB, CIWA-Ar HAM-A HAM-D MINI	Outpatient	Baseline, 1, 2, 4, 6, 8, 10, 12, 16, 28 weeks	Combined treatment of alcohol use showed significant increases in percent abstinent days (p<.0005) during treatment and at 24-week follow-up. Large reductions in anxiety, depression, and craving were observed during treatment, and improvement remained significant at 24 weeks.	Pilot study Small sample No control group or comparison Sample heterogeneity (medications; drug use and other comorbid syndromes) Missing data
Brady et al. (2005)	RCT: double blind placebo-controlled trial	EG n=49 3 57% male Mean age 6.7 years CG n=45 51% male	Sertraline vs Placebo	Alcohol use PTSD	CAPS SCID TLFB OCDS ASI HAM-D	Outpatient	Baseline, 12 weeks	Significant reduction in drinking or depression for both groups but not significantly different. Lower alcohol disorder (AD) and early onset PTSD had greater reduction in AD with	Small sample Other comorbid diagnoses Baseline treatment

		Mean age 36.6 years						active treatment (<.001). More severe AD and later onset of PTSD had significantly reductions in drinking (p<.05).	Attrition at follow up
Brown et al. (2009)	RCT: double blind placebo-controlled trial	EG n=20 50% male Mean age 39.8 years CG n=23 52.2% male Mean age 43.2 years	Naltrexone vs Placebo	Alcohol use Bipolar disorder	MINI HAM-D IDS-SR YMRS PACS PRD-111 ASI GGT	Outpatient	Baseline, 12 weeks	No significant differences between groups.	Small sample Attrition at follow up Baseline treatment
Brown et al. (2014)	RCT: double blind placebo-controlled trial	EG n=44 61.4% male Mean age 43.4 years CG n=44 56.8% male Mean age 39.7 years	Quetiapine s Placebo	Alcohol use Psychiatric symptoms	HRSD IDS-SR, YMRS, CIWA-Ar, PACS, PRD-III, AIMS, SAS, BARS, TLFB, AST, ALT, GGT, UDS	Outpatient	Baseline, 12 weeks	No significant difference in craving and alcohol use. No difference in psychiatric symptoms expect IDS-SR in favour of treatment group (p=.07).	Small sample Heterogeneity (medications) Low adherence
Di Nicola et al. (2017)	Pre-post Naturalistic study	n=65 64.6% male Mean age 44.17 years	Nalmefene	Alcohol use Psychiatric symptoms	HDD, TAC, CGI-S, VASc OCDS, BPRS, HAM-D YMRS	Outpatient	Baseline, 24 weeks	Nalmefene reduced drinking and craving in alcohol use disorder patients with and w/o comorbidity (p<.001).	No control group or comparison Small sample Sample heterogeneity (medications; other comorbid syndromes) Study design

Gual et al. (2003)	RCT: double blind placebo-controlled trial	n=83 53% male mean age 47 years	Sertraline vs placebo	Alcohol use Depression	HRSD, MADRS, DD HDD	Outpatient	Baseline, 24 weeks	No significant differences between groups on alcohol or depression outcomes. Significant difference when groups were stratified into severe or moderate MADRS. Improvement (p=.038) and remission (p=.042) was reported for those with severe depression only.	Small sample Low baseline scores Attrition at follow up
Hernandez-Avila et al. (2004)	RCT: double blind placebo-controlled trial	EG n=21 47.6% male Mean age 43.1 years CG n=20 50% male Mean age 42.7 years	Nefazodone vs Placebo	Alcohol use Psychiatric symptoms	TLFB, HAM-D, SAI, PSQI	Outpatient	Baseline, 10 weeks	Depression and anxiety reduced significantly over time (p=.01; p=.04). Treatment group had significantly greater reduction in HDD than placebos (p=.003).	Small sample Attrition at follow up Low baseline scores
Martinotti et al. (2008)	Pre-post open label trial	N=28 71% male Mean age 32.2 years	Quetiapine (anti-psychotic)	Alcohol use Psychiatric symptoms	EuropASI, OCDS, VAS, CIWA-Ar, BPRS, YMRS, HRDS, CGI, AST, ALT, GGT	Outpatient	Baseline, 16 weeks	Significant reduction alcohol use (p=.005), OCDS (p<.001) and craving (p=.018). Significant improvement in depressive symptoms (p<.001) and BPRS (p=.001).	Small sample Heterogeneity sample (psychiatric diagnoses) Study design No control
Petrakis et al. (2005)	RCT with open label	n=254 97.2% male mean age 47 years	Disulfiram vs placebo OR Naltrexone alone OR Placebo OR Disulfiram and Naltrexone	Alcohol use Psychiatric symptoms	OCDS GGT HSCL TLFB CAPS	Outpatient	Baseline, 12 weeks	69.7% of all subjects achieved complete abstinence during the trial. Active medication groups had significantly better drinking outcomes than those given placebo (p=.02), more	Predominately male sample Attrition at follow up Study design

								consecutive days of abstinence (p=.04) and a significant reduction of psychopathology for (<.02).	
Pettinati et al. (2010)	RCT: double blind placebo-controlled trial	n=170; 64.7% male mean age 43.4 years	Sertraline OR Naltrexone OR Sertraline and Naltrexone OR placebo	Alcohol use Depression	ASI, TLFB, HAM-D, SCID-D (subscale)	Outpatient	Baseline, 14 weeks	More patient receiving sertraline plus naltrexone combination achieved abstinence from alcohol (p=.001), had delayed relapse to heavy drinking (p=.003), reported fewer SAE (p<.02) and tended to not be depressed by the end of treatment.	Heterogeneous sample (alcohol and drugs) Attrition at follow up Baseline treatment Placebo not described Short follow up
Ralevski et al. (2011)	RCT: double blind placebo-controlled trial	n=23 83% male mean age 50.73 years	Acamprosate vs Placebo	Alcohol use Psychiatric symptoms	TLFB OCDS PANSS	Home	Baseline, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 weeks	Acamprosate was not more effective than placebo as all participants reduced drinking (non significant. Treatment group had improved psychiatric symptoms (non significant).	Small sample Attrition at follow up Placebo not described
Salloum et al. (2005)	RCT: double blind placebo-controlled trial	EG n=29 72% male Mean age 37 years CG n=30 77% male mean age 38 years	Lithium and Valproate vs Lithium and placebo	Alcohol use Bipolar disorder	BRMS, HRSD, TLFB	Outpatient	Baseline, 12 weeks	Significantly reduced alcohol consumption (p=.02) and longer period to relapse (p=.048) in both groups.	Small sample Attrition at follow up Heterogeneity (comorbid mental health problems)

Tolliver et al. (2012)	RCT: double blind placebo-controlled trial	EG n=14 71.4% male mean age 40.8 years CG n= 1656.3% male Mean age 43.7 years	Acamprosate vs Placebo	Alcohol use Psychiatric symptoms	MINI GGT CDT ALT/ AST TLFB OCDS MADRS YMRS CGI-S/I GGT	Outpatient	Baseline, 1, 2, 3, 4, 5, 6, 7, 8 weeks	Acamprosate was not significantly different at endpoint compared to placebo for alcohol consumption or psychiatric symptoms.	Small sample Attrition at follow up Placebo not described

(see appendix C for list of screening tools used)

Findings – Psychosocial Studies

Ten studies were identified using a psychosocial intervention. Three studies conducted CBT based interventions. Toneatto and Calderwood (2015) compared CBT sessions with CBT and additional anxiety sessions. This study reported significant reductions of quantity and frequency of alcohol use ($p<.001$) and anxiety ($p<.001$) in both groups. However, extra anxiety sessions were not deemed advantageous. Morley and colleagues also reported a beneficial effect of specialised CBT including days to relapse decrease ($p<.05$) compared to brief individualised motivation enhancement therapy (Morley et al., 2016). However, there was no significant differences for depression and anxiety scores. Brown et al. (2011) conducted an RCT whereby patients were assigned to receive eight individual sessions of CBT-D which included a coping with depression course modified for use with alcohol patients as well as focusing on daily mood monitoring, pleasant activities, constructive thinking, and social skills and assertiveness.

After six weeks, no differences were found between CBT-D and an individualised relaxation training programme relating to abstinence, however, on one measure of depression, scores were significantly lower for treatment group at 6-week follow up ($p=.05$). However, a limitation of this study is that all patients received the standard group therapy which is CBT based which may have influenced outcomes. One study used motivational interviewing (MI) with inpatients and demonstrated short-term benefits in reducing alcohol consumption and depressive/anxiety symptoms compared to brief information relating to reducing substance abuse. At the three-month follow up juncture there was a significant reduction in alcohol use ($p\leq.01$) and depression indicators ($p\leq.001$) although these results were not replicated at 6 and 12-month follow up time frames (Baker et al., 2002).
Two studies used group-based interventions. Andrisano-Ruggieri et al. (2016) conducted group counselling for 6 months; validated tools indicated there was no reduction of the psychiatric symptoms after treatment at follow up (6 months after study finished). Furthermore, the study findings were undermined by poor reporting of findings and a weak design. James et al. (2004) conducted manualised group-based interventions. This included the following topics for six weeks (1) psycho-education on drug use and mental health; (2) reasons for use; (3) reasons to change; (4) harm reduction strategies; (5) coping with high-risk situations and assertiveness training; and (6) planning for the future which encompassed peer support, motivational enhancement strategies, harm minimisation and relapse prevention paradigms. At follow up (three months), significant reductions in favour of treatment group was observed in psychopathology ($p<.01$), alcohol and illicit substance use ($p<.001$) and severity of dependence and hospitalisation. However, methodological issues include heterogeneity in the sample, blinding and randomisation concerns.

Four studies used technology-based CBT interventions (Agyapong et al., 2013; Deady et al., 2016; Geisner et al., 2016; Kay-Lambkin et al., 2008). Agyapong et al., (2003) implemented a three-month recovery support intervention in the form of text messaging. Participants received two daily text messages promoting good mental wellbeing, dealing with stress, promoting abstinence from alcohol, dealing with cravings, promoting adherence with medication and providing general support for three months, followed up at six months. At three months, positive effects for abstinence and depression were reported. However, compared to controls, who received fortnightly ‘thank you’ text messages, the effects were not sustained beyond the three month period (Agyapong et al., 2013). Limitations relate to a small sample despite low attrition at follow up. Deady et al., (2016) conducted an RCT comparing two online computer interventions: The Deal Project and Healthwatch. The Deal Project involved an online CBT and MI intervention

implemented via a website that required the completion of ten modules (4x1 hour) over 4 weeks. Healthwatch involved 12 online attention control modules, whereby patients read information about various health concerns and completed surveys (for example about physical and mental health activity) which acted as a control. Results for the Deal intervention indicated that there were significant reductions in severity of depression symptoms ($p \leq .001$) and reduction in number of drinks per week ($p \leq .001$) compared to control group. However, authors refer to limitations including randomisation concerns.

Geisner et al., (2016) also conducted an online CBT intervention. The intervention involved online computer sessions of personalised feedback and psycho-education compared to treatment as usual (TAU) which involved a treatment resource, providing information on depression and substance use but did not view any personalised feedback or intervention materials. Despite no significant differences across the study conditions for any of the outcome measures, participants in the intervention group showed a reduction in alcohol-related problems at follow up compared to the control group. It is important to note that unlike other studies in this review, this sample included college students and were not from a patient population. Kay-Lambkin et al., (2008) also conducted an RCT using integrated CBT and MI provided by trained therapists compared to a computer delivered intensive therapy programme entitled 'SHADE'. The therapist-led intervention consisted of ten individual sessions of therapy, one week apart, delivered by a psychologist. These sessions incorporated cognitive behavioural therapy (CBT) and motivational interviewing (MI) components. The computer-led intervention was identical to the therapist-led intervention but also included interactive components such as video demonstrations and in-session exercises. In addition, a third group receiving no treatment acted as control. The computer-based treatment had the largest treatment effect followed by combined CBT and MI for depression scores and a reduction in problematic alcohol use. However, this was an underpowered study due to the small sample size across three groups (n=97). In addition, a brief CBT session was provided to all participants at baseline before randomisation which may have influenced results.

Findings - Pharmacological Studies

Thirteen studies were identified using a pharmacological intervention for comorbid mental health conditions and problematic alcohol use. Although Naltrexone was the most commonly administered drug it was assessed in various ways.

Naltrexone (drug to combat alcohol craving) was compared against placebo, combined with or compared to other drugs. Brown et al. (2011) conducted a double blind RCT comparing Naltrexone and placebo however there were no significant differences between groups relating to alcohol use and psychiatric symptoms after 12 weeks. Nalmefene, a derivative of Naltrexone, was administered to patients with alcohol and drug problems with and without a psychiatric comorbidity. Nalmefene was reported to have significantly reduced drinking and craving in alcohol use disorder patients (Di Nicola et al., 2017; $p < .001$) but there was no difference between those with and without comorbidity. This was a pre-post naturalistic design study and no control or comparison was provided.

Petrakis et al. (2005) conducted a 12-week open label RCT comparing Naltrexone, Disulfiram (produces an acute sensitivity to drinking alcohol) alongside combined Naltrexone and Disulfiram and placebo arms. Active medication groups had significantly more consecutive days of abstinence ($p = .04$), however, 69.7% of all subjects achieved complete abstinence during the trial. Active medication groups also had significantly less cravings ($p = .02$) and obsessive alcohol thoughts ($p = .02$) compared to those treated with placebo. There was also a significant reduction in paranoid ideation ($p = .02$) for those

receiving medication. However, caution should be taken in generalisation given this was a mixed study design (blinding and open label), an overrepresentation of males (97%) and high attrition at follow up.

A double blind RCT by Pettinati et al. (2011) indicated that Naltrexone combined with Sertraline (anti-depressant) was more effective than used as separate interventions. Patients reported more abstinence days for the combined drugs (p<.001), did not drink as heavily (p<.001) and reported a longer time before relapse (p=.003) and were more likely to not be depressed by the end of treatment, however, this was not statistically significant. Other issues include attrition at follow up, short follow up and inclusion of patients with multiple substance abuse problems. Interestingly, Gual et al. (2003) reported no significant differences between groups on abstinence or depression who were given either Sertraline or placebo. However, 72% remained abstinent during the 24-week trial. In addition, those with severe depression were more likely to improve (p=.038) and experience remission of comorbid depression (p=.042)Similarly, Brady et al. (2005) in a double blind RCT placebo trial administrated Sertraline and placebo, finding no significant differences between groups, however, those with early onset of PTSD had a greater reduction (p<.001) in alcohol use with active treatment. Hernandez-Avila et al.(2004) also used the anti-depressant Nefazodone which significantly reduced heavy drinking days (p=.003), depression (p=.01) and anxiety (p=.04) compared to a placebo. However, both studies had small samples and had high attrition at follow up.
Mixed findings are reported by two studies using Quetiapine (anti-psychotic) compared to placebo (Martinotti et al., 2008; Brown et al., 2014). Despite the small sample and pre post-test design, Martinotti et al. (2008) reported a significant reduction in alcohol use (p=.005) and cravings after 16 weeks, as well as a significant improvement in psychopathology (p<.001) within the treatment group. Brown et al. (2014) conducted an intention to treat, double blind RCT and found no significant difference in alcohol use or cravings after 12 weeks. Whilst the authors did find an improvement in psychiatric symptoms this was only recorded via one outcome measure (IDS-SR; p=.007) in favour of the treatment group. Salloum et al. (2005) conducted a double blind RCT using Lithium (anti- psychotic) and Valproate (anti-convulsant) compared to lithium and placebo to reduce alcohol use with comorbid bipolar disorder. Both groups reported a significant reduction in alcohol use and a longer time to relapsing after 12 weeks. However, this study described high attrition at follow up.

Bogenschutz et al. (2016) conducted an open label pre-post design study combining Disulfiram and Lorazepam (drug used to treat anxiety) to treat individuals with alcohol dependence and an anxiety disorder with or without co-occurring major depression. Results highlighted that this was successful in reducing alcohol use and anxiety (Bogenschutz et al., 2016). There were significant increases in percentage of abstinent days (p<.0005) during treatment and at 24-week follow-up. Significant reductions were also found in anxiety, depression, and craving during treatment and improvement remained significant at 24 weeks (p<.05). However, no control group was used, and the sample size was small (n=41). Acamprosate (used to reduce urges to drink alcohol) was used in two double blind RCT studies and was found to have no effect on alcohol use (Ralevski et al., 2011; Tolliver et al., 2012) when compared to placebo. In addition, no significant differences were reported for mood outcomes and despite a reduction in schizophrenic symptoms this was not significantly different. Methodological issues include a small sample size and attrition at follow up.

Findings – Integrated Studies

One study implemented an integrated treatment (Rubio et al., 2006). A 12-week open label RCT used Lamotrigine (a drug treatment for depression in adults with bipolar

disorder) in combination with a weekly relapse-prevention programme. The programme involved patients attending weekly interviews as regards their consumption, craving and to analyse psychopathological symptoms. The study reported significant improvement in depression, mood and psychiatric symptoms ($p<.01$). In addition, craving and alcohol consumption significantly reduced during treatment ($p<.001$; Rubio et al., 2006). Despite this, the psychosocial component was not clearly described preventing replication, a range of prescribed drugs were used by patients and no control group included.

Research Aim Two - Review of Policy and Treatment Models

The second research aim in the review focused on the general policy framework for dual diagnosis, assessment models, care plans and guidelines for practice within the UK. In addition, there was a specific focus on models of service delivery within UK and international contexts.

Policy Framework (UK)

In England, Government policies for alcohol and mental health have developed in a separatist fashion over the past few decades. A series of strategies including the National Service Framework for Mental Health (NHS, 1999) and No Health without Mental Health (HM Government, 2011) made very little reference to alcohol or drug comorbid conditions. However, the Five Year Forward view for Mental Health (Mental Health Taskforce, 2016) did make a brief recommendation on funding which should be used locally for those regions that could demonstrate integration of assessment and care planning alongside treatment for those individuals with comorbidity. Similarly, there is a lack of focus on comorbidity in The Government's Alcohol Strategy (HM Government, 2012). The 2012 document included only two paragraphs to note the association between alcohol and mental health but did not provide any recommendations as to how issues could be addressed in policy or practice.

However, in retrospect an older document published by Department of Health England (2002) published a definitive Dual Diagnosis Good Practice Guide which highlighted that an integrated model of service provision should be implemented for dually diagnosed individuals rather than the serial or parallel models of practice. It highlighted that dual diagnosis services should be led by community health teams with a corollary role for substance misuse services to work in partnership to best fulfil the needs of the service users. This was also reflected in the Bamford report (2005) in Northern Ireland which also purported the integrated service model as the most beneficial for the delivery of series for this specific grouping.

The current Welsh Government policy 'Together for Mental Health: A Strategy for Mental Health and Wellbeing in Wales' (2012) recognises the problems that are experienced by individuals with co-occurring mental health problems and alcohol or drug abuse and also advocates an integrated service model for addressing the problems experienced by this service user group. Similarly, the Drugs and Alcohol Strategy for Wales 'Working Together to Reduce Harm' (2008) also stipulates that services must work together to prevent individuals who have a dual diagnosis from 'falling between the gaps' in service provision. The government in Wales also produced a comprehensive policy framework which specifically addresses the needs of people with comorbid disorders. The document highlights the recovery approach for mental health and substance misuse services, whist focusing on co production, addressing the specific needs of the individual, improving accessibility to services and ethos of person-centred care (Government of Wales, 2015).

In Scotland, the current Mental Health Strategy 2017-2027 (Scottish Government, 2017) underlines that relevant alcohol, drugs, mental health services and social services should work in partnership to ensure an holistic approach to addressing the needs of their service users who have a dual diagnosis. The document proffers two action points in relation to working with clients who have comorbid substance use and mental health disorders.

1. To employ evidence-based assessment and referral pathways for people with comorbid substance use and mental health diagnoses.
2. Introduce pilot programmes which are based on 'improved arrangements' for people with dual diagnosis (although it is not entirely clear whether this is evidenced-based or not), (Scottish Government, 2017).

Furthermore, Scotland's most recent joint strategy on alcohol and drug treatment underlines that the Government will consider structured methods and joint working for people who present with alcohol/drug and mental health comorbidities (Scottish Government, 2018). Scotland also has separate alcohol policy documents 'Changing Scotland's Relationship with Alcohol: A Framework for Action' (Scottish Government, 2009) and the recent 'Alcohol Framework 2018: Preventing Harm next steps on changing our relationship with alcohol' (Scottish Government, 2018). However, these framework documents focus more on reducing consumption, (including Minimum Unit Pricing) encouraging positive choices, education, awareness changing, and behaviour change with little reference to co-occurring disorders.

In Northern Ireland, the most notable regional policy review on dual diagnosis was published in 2005. The Bamford Report provided discussion on models of assessment and models of treatment for comorbid disorders. Since the publication of the report, there has been little reference made to comorbid substance use disorders and substance use in drug and alcohol and mental health policies in Northern Ireland. As regards drug and alcohol policy frameworks, the New Strategic Direction in Drugs and Alcohol 2011-2016 made brief reference to mental health as a specialist area within the framework with a recognition that there was need for further coordination between mental health, drug and alcohol use and suicide (DOH, 2016).

Assessment Models (UK)

The overview of the information below summarises general guidelines for comorbid mental health disorders with substance use problems (including alcohol) and indicates where there is specific policy reference to alcohol only comorbid diagnoses.

The DOH Good Practice Guide (2002) stipulated that the assessment process in relation to comorbid mental health and substance use disorders should be comprised of detection and screening (via self-report, lab tests and comprehensive data gathering), specialised assessment (through comprehensive, longitudinal use of validated assessment instruments and under continuous review) and risk assessment (including gauge of severity of substance use, consideration of adulterants, risk or overdose and/or suicide).

Assessment should also be tailored to the needs of specific vulnerable groups including women, young people, people who are homeless, those involved in the criminal justice system and people from ethnic minorities (DOH, 2002). Components of assessment are highlighted in the guide and whilst the document is outdated the main foundations of

assessment remain relevant to current practice. The information presented in table three also draws upon some of the guiding principles outlined by Rethink (2017).

Table 3: Assessment Components

Assessment Components
Identification and response to any emergency or acute problem
Assessment of patterns of substance misuse and degree of dependence/withdrawal problems
Assessment of physical, social and mental health problems
Evaluate the relationship between substance misuse and mental health problems
Consider the clients concerns as central to the assessment process which may seem intimidating to some individuals and may lead to disengagement
Consider any likely interaction between medication and other substances
Consider of a range of needs including medical and social care, food shelter, access to primary care and child care
Timelines can be useful to ascertain priorities for treatment and include assessment of treatment history
Determine an individual's expectation of treatment and their degree of motivation for change
Make an assessment of carer involvement and need
Undertake an assessment of knowledge of harm minimisation in relation to substance misuse
Utilize a strengths-based approach to assessment recognising the achievements of the individual
Consider the need for pharmacotherapy for substance misuse
Notification to the National Drug Treatment Monitoring System

(Source: DOH, 2002, p.18; Rethink, 2017 p.25)

Assessment in specialist alcohol services is guided by the NICE (2011) document on Diagnosis and Assessment of Harmful Drinking and Alcohol Dependence. It recommends that for those who have a significant comorbidity the assessment goals may initially be based on a harm reduction approach but ultimately abstinence from alcohol would be the preferred objective (NICE, 2011).

Guidance on severe mental illness and co-occurring substance use problems published by NICE (2016) indicated that assessment processes should be underpinned by a person-centred, empathic and non-judgemental approach based on respect and trust. The importance of the person-centred nature of the assessment was also reiterated in the NICE guidelines document on coexisting severe mental illness and substance misuse and service user experiences in mental health (NICE 2016). In addition, a report by Hawkins et al. (2013) indicated that service users felt that a good dual diagnosis assessment involves asking a range of relevant questions, actively listening to the responses, avoiding pre-conceived notions based on stereotypes or diagnoses, matching the needs of individuals to a range of treatment options, avoiding repetition of information gathering and utilising a person centred approach (Hawkings et al., 2013).

A number of regional NHS Trust Dual Diagnosis strategies also make reference to the principles of a person-centred approach (North East London, 2008; Somerset Partnership, 2017). There is also direction regarding where service users should be accommodated when presenting for assessment and it is recommended that the person should remain with the organisation of first contact, either the mental health team or the substance use team, until a comprehensive assessment has been undertaken. Where possible there should be a joint assessment across both agencies (North East London, 2008). However, regional documentation also specifies that the management of more severe mental health illnesses should remain with the mental health team from the point of assessment with management of disorders such as anxiety and moderate depressive disorders staying with the substance use specialist teams (Bamford, 2005; North East London Trust, 2008).

It is also recognised that it may be difficult to assess whether the substance use disorder or the mental health disorder is the main problem at the time of the initial assessment. For example, use of new psychoactive substances or stimulants may induce a temporary psychotic episode similar to that seen in schizophrenia presentations but it is usually the case that symptoms dissipate following a period of abstinence, unlike a psychotic illness where the symptoms will be prolonged and more variable. Likewise, symptoms of anxiety and depressive disorders indicated in some individuals with an alcohol use disorder *“may resolve following detoxification and standard treatment for alcohol dependence” (*Bamford, 2005 p.6).

Shunting of service users at the assessment stage is often apparent with a lack of clarity about which organisation is responsible for the management of care. Similarly, barriers as regards access to mental health agencies are reported when mental health teams exclude people whose problems are primarily with alcohol or drug use (Rethink, 2017).

Assessment of risk is core to a process which is simply not confined to the initial phases of engagement but should be revisited in conjunction with the client on a regular basis. Risk assessment is also significant in the protection of the individual from harm to self or others or to the wider community, although it is likely that individuals with a dual diagnosis are at risk of harming themselves either through self-harm or suicide (University of Manchester, 2018). Practitioners should not avoid asking about risk behaviours as some fear that highlighting risk behaviours may likely encourage the client to engage in such behaviours rather than protect them. However, it is only through full

and honest engagement with the client that their concerns may be voiced to enable an adequate support system which protects them and others whilst working in partnership to provide them with choice and autonomy in respect of most aspects of their care (Rethink, 2017).

Care Planning (UK)

A successful model of care planning in working with people who have a dual diagnosis of alcohol and severe mental illnesses (SMIs) or mood disorders should mirror the preceding assessment in terms of overarching values including respect, dignity and empowerment of the individual in all parts of the care planning process. It should always be based on a co-production approach and should specify the goals that are achievable, highlight which agency should be involved in what aspect of the individual's treatment plan, specify how and why information should be shared between agencies/partners, consider cultural ethnic specific issues and include a structured review date (Rethink, 2017).

In addition, NICE guidelines for Severe Mental Illness and Substance Use (2016) highlight that the care plan must also involve family carers, if the request is made by the individual, whilst ensuring that the care plan considers previous experiences and coping strategies and whether these identified strengths would enable them to recover more readily. It is also advised that goals should be agreed openly and in partnership with the individual and a concomitant partnership approach should also be operationalised at a structural level to include established and productive collaborative agency working. This will ultimately benefit the service user and address the specific needs of each individual in a holistic fashion to include accommodation, finances, and relationships. Crucially, service users should not be responsible for navigating between statutory and third sector services as regards mental health and substance use (NICE, 2016; Welsh Government, 2015).

Treatment Models (UK and International Models)

The UK and international literature which considers treatment models for dual diagnosed individuals is consistent in highlighting three primary service delivery approaches which are applicable to hazardous or dependent alcohol use and/or drug use disorders with co-occurring mental health disorders. First, the serial treatment model usually describes a care pathway whereby the individual's mental health disorder and substance use disorder are treated by separate services at different junctures, for example people may be treated for substance use disorders prior to the mental health team treating their anxiety, paranoid delusions or depression (Abou-Saleh, 2004).

Second, the parallel model involves treatment for comorbid disorders simultaneously but via separate treatment providers in different settings (EMCDDA, 2015). Third, a model of integrated treatment health is one whereby professionals working in one clinical setting provide comprehensive treatment for both disorders simultaneously with interventions that address both disorders (EMCDDA, 2015). Research data from international sources demonstrate that individuals with co-occurring mental illness and AuDs who receive treatment for both disorders simultaneously have better clinical outcomes (SAMHSA, 2005; IOM, 2005; Mangrum et al., 2005; Muser et al., 2003; McCoy et al., 2003). Despite the evidence, many care service programmes tend to identify and treat only one of the two co-occurring disorders which often creates fragmented care and results in negative care outcomes and also increased risk of relapse (Drake, 2007).

Within mental health settings, the co-occurrence of alcohol misuse is highly relevant as it can destabilise patients and contribute to increased rates of relapse, readmission to hospital, physical health problems, suicidality, violence and social instability (Drake, 2007). However, mental health workers often do not feel confident to manage the alcohol use disorder, and so the patient's care tends to be passed between substance use and mental health services. Clinical Guidance for alcohol use disorders (NICE, 2011) stipulates that for alcohol misuse and comorbid depression or anxiety disorders the clinician should treat the alcohol misuse first as this may precipitate reduction of anxiety and depression symptoms. In addition, if the symptoms do not reduce over a 30-34 week period the 2011 guidance highlights that the practitioner should refer to the appropriate NICE guidance for either disorder (See NICE, 2009[1]; NICE, 2011[2]). Furthermore, for those individuals who have an alcohol problem and a co-current serious mental illness (SMI) they should undergo comprehensive assessment, risk and assessment and treatment by a psychiatrist. In addition, people who have an SMI and alcohol problem should only be referred to psychological treatment if they have abstained from or have significantly reduced their alcohol intake (NICE, 2011a).

In the United States integrated approaches to treatment that incorporate coordinated, systematic treatment of both co-occurring conditions within one programme are recommended as best practice for comorbid treatment (SAMHSA, 2005; IOM, 2005; Drake et al., 2001). The Affordable Care Act, passed in 2010 and fully implemented in 2014, calls for increased integration and coordination of behavioural health services, as clients diagnosed with both SUD and mental illness are overrepresented in treatment samples (Croft & Parish, 2013). However, the need for advancement is evident as when assessing dual diagnosis capability in 256 mental health and substance use disorder treatment programmes across multiple state systems in the United States McGovern et al., (2014) found that only approximately 18% of addiction treatment and 9% of mental health programmes met criteria for dual diagnosis capable services. Despite the development of training materials, such as SAMHSA's (2013) Substance Abuse Treatment for Persons with Co-occurring Disorders, only a small minority of mental health and addiction treatment programmes offer integrated mental health care services (McGovern et al., 2014). It is currently recognised that persons with co-occurring disorders often have complex clinical needs that require integrated treatment in "primary care, human services, housing, criminal justice, education and related fields" (SAMHSA/COCE, 2005, p.3). However, currently there are multiple barriers to treatment in the United States that result in a lack of collaboration and integration between care delivery systems for mental illness and SUDs which results in high attrition rates and low compliance (Krawczyk et al., 2017). In a national sample assessing the association of psychiatric comorbidity with treatment completion among clients admitted to substance use treatment programs in the United States it was evident that clients with psychiatric comorbidity have lower SUD treatment retention (Krawczyk et al., 2017).

In Europe, expertise centres and consortiums have been established in a number of countries to enable organisations to more effectively implement integrated treatment. However, there are many differences in approaches, not only between European countries but also between different regions of the same country (van Wamel, et al., 2015). Some countries, such as Finland, Italy, the Netherlands, Norway and Spain, have special facilities, including acute inpatient dual diagnosis units, dual diagnosis residential communities, and dual diagnosis programmes in both mental health and drug user

[1] NICE (2009) Depression the treatment and management of Depression in Adults, NICE clinical guideline 90.

[2] NICE (2011) Generalised panic disorder and panic disorder (with or without agoraphobia) in adults: management in primary, secondary and community care NICE clinical guideline 113.

outpatient centres which indicates attempts to move towards a more integrated model of treatment. EMCDDA, (2015) sourced specific data as regards treatment services for comorbid SUDs and mental illness in Europe and have suggested that despite vast heterogeneity in treatment approaches a general approach can be extrapolated (EMCDDA, 2015). Addiction treatment services are provided both by specialised centres and as part of general healthcare services (e.g. psychosocial services and psychiatric hospitals). They provide a range of service delivery options which can be applied to help address a client's treatment and social needs. Treatment centres provide counselling, outreach work, psychotherapy, aftercare and reintegration programmes. Inpatient psychosocial interventions are provided in both specific and generic facilities (i.e. drug use centres and mental health centres), offering short- and long-term treatment, often combined with inpatient detoxification (EMCDDA, 2015). However, Ness et al. (2014) suggests that these differentiations in treatment facilities may be a barrier to the provision of appropriate treatment services for clients with comorbid disorders. Furthermore, other difficulties are related to the fact that treatment services may lack sufficient combined expertise to treat both types of disorders (Sacks et al., 2013).

Conclusions

The term dual diagnosis is misleading as it implies the existence of only two disorders. Definitions of co-existing alcohol and mental health disorders can vary according to professional context and there may be some exclusion of the most prevalent mood disorders such as anxiety or depression. Subsequently, this may have an impact on the level of service provision afforded to the service user.

The rate of alcohol-related harms and morbidity have increased in most regions of the UK nations over the last few years. Moreover, there are multi-faceted and complex associations between AuDs and the various psychiatric disorders and these relationships are nuanced in terms of direction and symptomology. However, it is clear that there is a strong link between mental health disorders including depression, anxiety, bipolar disorder, personality disorder and schizophrenia. The evidence highlights that there is a strong association between AuDs and depression where increased alcohol intake may precipitate depression or exacerbate already existing symptoms. Furthermore, it is evident that there is a more reciprocal relationship between AuDs and anxiety, where withdrawal from the substance may intensify anxiety or individuals may attempt to ameliorate symptoms of anxiety via increased alcohol usage. As regards schizophrenia or schizoid affective disorders, alcohol has been reported as having sedative effects on symptoms of the disorders. Also, evidence suggests that there is a higher rate of suicide in people who have been diagnosed with AuDs and bipolar disorder.

Across the UK, the policy framework for substance use disorders and mental health comorbidity is inconsistent and even more so in relation to alcohol-specific co-occurring disorders. In England the last comprehensive guide to policy and practice was published by the Department of Health in 2002, whilst in Northern Ireland there has been a gap in specific policy guidance for comorbid substance use and mental health disorders since 2005. Conversely, in Wales the government produced a recent comprehensive policy framework which addressed the specific needs of people with comorbid disorders in 2015. Likewise, whilst Scotland may not have a recent specific policy framework document related to comorbidities, it does make a substantial reference to comorbid disorders in a number of mental health and alcohol policy frameworks (Scottish Government 2017; 2018).

According to the evidence, all levels of assessment and care planning in working with comorbid disorders must be tailored to the complex individual needs of the service user (and carers where appropriate), be developed in full partnership with the service user (where possible) and founded on a non-judgemental, empathic and person-centred approach. Risk assessment is also an integral part of the care pathway and practitioners should provide an open and honest environment through which service users are enabled to voice their concerns and in doing so ensure the best possible support systems for the service users and their families. The concept of ‘shunting’ service users between mental health and substance disorder services is often apparent with a lack of clarity about case management responsibility. Furthermore, NICE (2016) guidance recommends that initial goals for alcohol and mental health comorbidities may be agreed on the basis of a harm reduction approach but that the ultimate goal for this specific service user grouping should be abstinence.

Three models of service delivery were identified from the literature:

> **Serial** - service users are treated separately by mental health or substance use disorder services at different times and locations;

Parallel - service users are treated simultaneously by separate treatment providers;

Integrated- service users are treated concurrently by both mental health and substance use service providers in one setting.

Whilst the integrated service model demonstrates more efficacious treatment outcomes (Mangrum et al., 2005; Muser et al., 2003; McCoy et al., 2003), it is not entirely clear how many treatment providers in the UK currently provide an integrated service for concomitant AuDs and mental health disorders. However, there is the suggestion that the majority of treatment models in the UK and the United States tend to work within the parameters of the serial and parallel models. In Europe there is substantial heterogeneity in the range of treatment models offered for co-existing disorders, although it is noted that the wide range of options may also act as barrier to treatment provision as some providers may lack the skills and expertise to address the needs incurred by both AuDs and mental health disorders.

Result from a rapid structured review of interventions for alcohol use problems/disorders and comorbid mental health conditions showed mixed results for both pharmacological and psychosocial intervention studies. Naltrexone (drug to combat alcohol craving), was the most commonly administered pharmacological intervention, however, mixed findings were reported when used in placebo-controlled trials (Brown et al., 2011; Di Nicola et al., 2017).

When combined with other drugs, Naltrexone demonstrated more positive outcomes for patients, than when used alone. Naltrexone combined with Disulfiram (produces an acute sensitivity to drinking alcohol) was successful at treating alcohol use and psychiatric symptoms compared to placebo (Petrakis et al., 2005). The use of Sertraline (anti-depressant) with Naltrexone was also successful at reducing alcohol use and depression (Pettinati et al., 2011). Another combination of drug treatments using Disulfiram and lorazepam (drug used to treat anxiety) also demonstrated promising outcomes with reductions in alcohol use and psychiatric symptoms. Similar to Naltrexone, when Sertraline was used alone it was less successful at treating comorbid conditions (Gual et al., 2003).

Quetiapine (anti–psychotic) also demonstrated mixed findings; Brown et al. (2014) found no reduction in alcohol cravings and an improvement in only one outcome measure for psychiatric symptoms whilst Marttinetti et al. (2008) reported reduction in both alcohol cravings and psychiatric symptom indicators. Another study combined an anti-psychotic with an anti-convulsant and reported a significant reduction in alcohol use and bipolar disorder. However, this was reported both within the treatment and placebo group (Salloum et al., 2005). Single application of anti-anxiety medication such as Acamprosate was reported to be the least effective in the treatment of comorbid conditions (Tolliver et al., 2012; Ralevski et al., 2011). Whilst the majority of studies were RCTs, a few demonstrated significant methodological issues including lack of appropriate control groups, small sample sizes and high attrition rates.

CBT was reported as an effective intervention in treating at least one aspect of comorbid problematic alcohol use and psychiatric conditions. Toneatto and Calderwood (2015) reported significant positive outcomes for reductions in both alcohol use and anxiety symptoms, Morely et al. (2016) highlighted a significant increase in days to relapse but no significant differences for depression and anxiety scores and Brown et al. (2011) reported no difference in alcohol scores for the intervention group but depression scores were significantly lower at the six-week follow up. A group based mixed modality study

(James et al., 2004) reported significant reductions in alcohol use and a range of psychiatric outcomes at three months follow up. Conversely, results from a study by Andrisano- Ruggieri et al. (2016) showed fewer positive results for the effectiveness of group counselling and results were hampered by a weak methodological design and poor presentation of findings.

Computer-based CBT outcomes were similar, if not more effective than therapist-based CBT for a reduction in depressive symptoms and alcohol use (Agyapong et al., 2013; Deady et al. 2016; Kay-Lambkin et al., 2008) and a non-significant reduction in alcohol-related problems only (Geisner et al., 2016). However, outcomes from MI based intervention were not significantly different when compared to a 'brief advice' intervention. However, both groups experienced improvements in comorbid conditions. Only one study reported a specific integrated intervention administrating a pharmacological agent and psychosocial support. Although a small sample and no control or comparison group, Lamotrigine and an individual relapse prevention programme demonstrated a significant reduction in problematic alcohol use and psychiatric symptoms.

Limitations

The review considered the policy frameworks and government guidelines for comorbid alcohol use disorders and a range of mental health disorders. This was a complex topic for a number of reasons, including the range of comorbid and multi-morbid conditions, the continuum of severity in mental health disorders and the wide variation in complex psychosocial modalities and pharmacological combinations used to address comorbid conditions. As regards the policy and service delivery review, a broad-based literature appraisal was undertaken to identify key documents for assessment, care planning and guidelines within the UK context together with a national and international review of the literature in relation to models of service delivery. This was not an exhaustive list and presented an overview of a number of the pertinent issues presented within a selection of the most relevant documents.

Similarly, whilst the studies included in the interventions review above demonstrate a range of positive outcomes the results must be interpreted with a level of caution. This is due to identified gaps in methodological rigour and study design. Despite the majority of studies reporting randomised controlled trials there were a number of design flaws in the methodologies, for example, small samples, missing data, high attrition rate at follow up and lack of control comparisons. Psychosocial studies were also more likely to report small sample sizes and showed a higher degree of heterogeneity primarily in relation to mixed alcohol and drug using comorbid samples.

Recommendations

Recommendations (Policy)

1. There should be a standard definition of co-existing mental health and alcohol use disorders which takes account of the myriad of complex issues associated with this multi-faceted diagnosis.
2. A UK national policy framework for working with comorbid mental health and substance use disorders should be developed and should house a specific section on addressing issues of morbidities related to AuDs.
3. It should also contain sections which are dedicated to specific assessment processes, care plans and a range of treatment models which are sufficiently amended to reflect the needs of patients/service users with complex comorbid, AuD needs.

Recommendations (Practice)

1. An individual who presents with a severe and enduring mental illness (SMI) should also be accurately assessed for the presence of a co-occurring AuD using a specific validated screening tool.
2. The shunting of service users between mental health substance use disorder services (including AuDs) should be avoided at all costs as this serves as a significant barrier to timely and adequate care and support for service users, carers and family members.
3. Combination drug treatments for AuDs and mental health comorbidities (specifically Naltrexone and Dilsulfiram within drug dyad modalities) showed positive indicators for alcohol and mental health outcomes; likewise psychosocial interventions which were largely CBT focused showed some benefits for practice. Therefore, it may be beneficial to include one or more of these drug combinations with CBT in future interventions.

Recommendations (Research)

1. A UK prevalence study should ascertain the number and category of service delivery models in the UK which address the needs of service users with concomitant AuDs and mental health disorders.
2. The studies did not always demonstrate a rigorous methodological approach or design standard. Therefore, it is recommended that high-quality random controlled trials of drug combinations are conducted with adequate sample sizes and robust control and comparison groups. It is also recommended that further methodologically rigorous intervention studies are funded to investigate integrated treatment modalities which include pharmacological and psychosocial interventions.

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Appendix A: Example search strategy

Search Strategy

"Substance use" OR "substance misuse" OR "substance abuse" OR "substance disorder*" OR
"alcohol use" OR "alcohol misuse" OR "alcohol abuse" OR "alcohol disorder*" OR "alcohol dependen*" OR alcoholi* OR korsakoffs OR "alcohol related brain disorder" OR "alcohol related brain injury"
AND
"Mental health disorder*" OR "mental illness*" OR "mental ill health" OR bipolar OR "personality disorder*" OR "complex need*" OR "social instability*" OR suicide* OR schizophrenia OR "psychiatric disorder*" OR "borderline personality disorder*" OR anxiety
AND
"Dual Diagnosis" OR "Co$morbid*"
AND
"Models of work*" OR "models of practice" OR "integrated model*" OR "parallel model*" OR "Methods of work*" OR Intervention OR "Group work" OR "Case management" OR "Psychosocial model*" OR "behavio* model*" OR "Motivational Interview*" OR "cognitive therap*" OR "cognitive behavio* therap*" OR CBT OR Naltrexone OR pabrinex OR vivitrol

Appendix B: Quality assessment using Cochrane Risk of Bias Tool (for RCTs)

Cochrane Risk of Bias Tool (for RCTs)							
Type of bias	***Selection***		***Performance***	***Detection***	***Attrition***	***Reporting***	
Author Year	***Random sequence generation***	***Allocation concealment***	***Blinding of participants and personnel***	***Blinding of outcome assessment***	***Incomplete outcome data***	***Selective reporting***	***Other biases***
Agyapong et al., 2013	Low	Low	Moderate	Low	Moderate	Low	Low
Baker et al., 2002	High	High	?	Low	High	?	High
Brady et al., 2005	Low	Low	Low	High	High	Low	High
Brown et al., 2009	Low	Low	High	High	High	Low	High
Brown et al., 2011	High	High	High	High	High	Low	High
Brown et al., 2014	Low	Low	Low	Low	High	Low	High
Deady et al., 2016	High	High	Low	Low	high	Low	High
Geisner et al., 2016	High	High	?	?	?	Low	High
Gual et al., 2003	High	High	Low	High	High	High	High
Hernandez-Avila et al., 2004	Low	Low	High	High	High	Low	High
James et al., 2004	Moderate	Moderate	High	High	High	?	High
Kay-Lambkin et al., 2009	High	High	?	Low	Moderate	?	High
Morley et al., 2016	Moderate	Moderate	?	Low	Low	?	Low
Toneatto & Calderwood 2015	High	High	?	?	High	?	High
Petrakis et al., 2005	High	High	High	High	High	Low	High
Pettinati et al., 2005	Low	Low	?	?	High	?	High
Ralevski et al., 2011	High	High	High	High	High	?	High
Tolliver et al., 2012	High	High	High	?	High	?	High
Salloum et al., 2005	Low	Low	Low	Low	Low	Low	High

Quality assessment using Evidence Project Study Risk of Bias Tool (for non-RCTs)

Evidence project Study Risk of Bias Tool (for non-RCTs)									
	Study design includes			***Comparison groups equivalent at baseline on***		***Sampling bias***			
Author Year	***Pre-post intervention***	***Control or comparison group No***	***Cohort***	***Socio demographics***	***Outcome measures***	***Random assignment (group or individual) to the intervention***	***Participants randomly selected for assessment***	***Control for potential confounders***	***Follow up rate >80%***
Andrisano-Ruggieri et al., 2016	Yes	Yes	Yes	N/a	N/a	No	No	No	?
Bogenshutz et al 2016	Yes	No	No	N/a	N/a	No	No	No	No
Di Nicola et al., 2017	Yes	Yes	Yes	Yes	Yes	No	No	No	?
Martinotti et al., 2008	Yes	No	Yes	N/a	N/a	No	No	No	No
Rubio et al., 2006	Yes	No	Yes	N/a	N/a	No	No	No	Yes

Appendix C: Abbreviations used in Table 2

ADIS-IV: Anxiety disorders interview schedule
AIMS: Abnormal Involuntary Movement Scale
ALT/AST: Alanine aminotransferase test
ASI: Addiction Severity Index
AUDIT: Alcohol Use Disorders Identification Test
BAI: Brief alcohol Intervention
BARS: Barnes Akathisia Scale
BDI-II: Becks depression Inventory-II
BPRS: Brief psychiatric rating scale
BRMS: Bech-Rafaelsen Mania Scale
BSI: Brief Symptom Inventory
CAD: Cumulative Abstinence Duration
CAPS: Clinician Administrated PTSD Symptom Scale
CDT: Carbohydrate-deficient transferrin test
CG: Control group
CGI-S: Clinical Global Impression-severity scale
CIWA-Ar: Clinical Institute Withdrawal Assessment
CPZ: chlorpromazine equivalent dose
DASS-2: Depression, Anxiety and Stress Scale
DAST: Drug abuse screening test
DD: Drinking days
DDQ: Daily drinking questionnaire
ECG: Electrocardiogram test
EuropASI: European Addiction Severity index
EG: Experimental group
GGT: Gamma-glutamyl Transferase test
HAM-A: Hamilton Anxiety Rating Scale
HDDs: heavy drinking days
HRSD/HAM-D: Hamilton Rating Scale for Depression
HSCL: Hopkins Symptom checklist
MADRS: Montgomery-Asberg Depression Rating Scale
MALT: Munich Alcoholism Test
MHRSD: Modified Hamilton Rating Scale for Depression
MINI: International Neuropsychiatric Interview questionnaire
PACS: Penn Alcohol Craving Scale
PANSS: Positive and negative syndrome
PHQ-9: Patient Health Questionnaire
POLYTOT: number of substances used
PRD-III: Psychobiology of Recovery in Depression III Somatic Symptom Scale
PSQI: Pittsburgh Sleep Quality Index
OTI: Opiate Treatment Index
RAPI: Rutgers alcohol problem index
TAC: transdermal alcohol concentration
TLFB: Timeline Feedback score
TOT-AL: Total alcohol drinking test
SADS; Severity of Alcohol Dependence Scale
SAI: State Anxiety Inventory
SAS: Simpson-Angus Scale
SCID-RV: Structured clinical interview for DSM
SCL-90: Symptom checklist 90 revised
UDS: Urine drug screening test

VASC: Visual Analogue Scale for Craving severity
YMRS: Youth Mania Rating Scale