Comorbidity of Alcohol Use Disorders and Non-Communicable Diseases in Low- and Middle-Income Countries

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Abstract

Objective

The aim of this systematic review is to understand the relationship between alcohol use disorders (AUDs) and three non-communicable diseases [NCD] (cardiovascular diseases, respiratory diseases, and diabetes) in low and middle income countries (LMICs).

Methods

We searched the following databases using a systematic search strategy: Medline, EMBASE, PsycINFO, Global Health, LILACS (Latin American and Caribbean Health Sciences Literature), and AJOL (African Journal Online).

Results

We identified 1431 references through the database search and through a systematic screening process identified 13 studies that met our eligibility criteria. Amongst those with any kind of AUD, depending on the type of NCD, the prevalence ranged from 14% (diabetes) to 58% (hypertension). Amongst those with the selected NCDs, depending on the type of AUD, the prevalence ranged from 1.8% (diabetes) to 27.4% (ST-segment-elevation myocardial infarction). A range of AUDs were associated with hypertension in men, cardiovascular diseases, Left Ventricular Hypertrophy, and diabetes mellitus. In some studies, inverse associations were observed between AUD and two NCDs - hypertension and diabetes.

Conclusion

The burden of comorbid AUDs and NCDs in LMICs is high, and this should beeb countered through appropriate public health response such as policy interventions to control availability of alcohol, and through screening and brief interventions in primary care.

Key words: Alcohol use disorders, Non communicable diseases, Low- and middle- income countries

Introduction

Over the years, the Comparative Risk Assessments (CRAs) from the Global Burden of Disease (GBD) studies, and the World Health Organization (WHO) Global Status Reports on Alcohol and Health have provided overwhelming evidence identifying alcohol consumption and alcohol use disorders (AUDs) as major contributors to the global burden of disease and mortality (Ezzati et al., 2002; Ezzati et al., 2004; Forouzanfar et al., 2016a; Forouzanfar et al., 2016b; Lim et al., 2013; Murray & Lopez, 1997; Organization, 2018; Organization & Unit, 2014; Rehm et al., 2009). Similarly, non-communicable diseases (NCDs) too are a global public health concern with an estimated 41 million people dying from NCDs each year, equivalent to 71% of all deaths globally (WHO, 2018). There is a growing recognition of NCDs as a major threat to development in low- and middle- income countries (LMICs), with over 85% of global 'premature' (30-69 year olds) deaths occurring in such countries (WHO, 2018).

The global health discourse is gradually emphasising the social and environmental drivers of NCDs beyond unhealthy choices made by individuals (Alleyne et al., 2010). Alcohol use is one such individual-level risk factor, the consequences of which can be prevented through policy interventions impacting availability, affordability and marketing (Babor, 2010; Rehm et al., 2009; Rehm et al., 2003). Alcohol use is linked causally to many disease and injury categories, with more than 40 ICD-10 three-digit categories being fully attributable, and several more being partially attributable to alcohol (Rehm et al., 2017). For the four major NCDs (cardiovascular disease, cancers, chronic respiratory diseases and diabetes), AUDs are a key risk factor, which along with male sex, age, high blood pressure and body mass index (BMI) play a synergistic role in disease incidence (Lim et al., 2013; WHO, 2018).

As a result of increased economic growth, alcohol consumption is increasing in several LMICs e.g., Brazil and India (Cook et al., 2014). These countries account for a large chunk of the

world's population, and hence are important and influential stakeholders in global health development (Harmer & Fleck, 2014). Finally, some LMICs (e.g. Brazil, South Africa) have also reiterated their commitment to prevent and control NCDs and to reduce the impact of risk factors, such as harmful use of alcohol, on NCDs (*Communique of the IV Meeting of BRICS Health Ministers 2015*).

Extensive research has been done on the relationship between AUDs and NCDs across the globe. Reviews of this evidence has helped synthesise and elucidate the complexity of this relationship. Although this is useful, it is important to understand the nuances of this relationship in LMICs as they are contextually different from high income countries and the epidemiology of AUDs and NCDs is strongly influenced by societal factors, cultural norms, neighbourhoods, and social contexts. Hence, the aim of this review is to understand the relationship between AUDs and NCDs (cardiovascular diseases, respiratory diseases, and diabetes) in LMICs, and more specifically, the objectives are to examine the following (a) Prevalence of AUDs in those with selected NCDs, and (b) Prevalence of selected NCDs in those with AUDs.

Materials and Methods

Study design

Systematic review.

Eligibility criteria

We did not set any limits to the year of publication, gender and age. We only included studies published in English. We included observational studies (cross sectional surveys, case control studies, and cohort studies), and excluded intervention studies, qualitative studies and case series. We included studies with participants having comorbid AUD and select NCDs. For the purpose of this review, we defined AUDs as any type of problem drinking (e.g. hazardous/risky drinking, harmful drinking, alcohol abuse, alcohol dependence) defined using standard

diagnostic criteria (e.g. ICD, DSM), clinical diagnosis, or any standardised questionnaire (e.g. AUDIT). We excluded general populations of NCD patients who do consume alcohol but do not have an AUD. The selected NCDs included cardiovascular diseases, respiratory diseases, and diabetes; three of the four NCDs that together account for more than 80% of all premature NCD deaths (Forouzanfar et al., 2016a). We excluded cancers, one of the four top killers amongst NCDs, as the relationship between alcohol use and cancers is relatively well established. We included studies conducted in LMICs which are defined by the World Bank as countries with Gross National Income (GNI) per capita below $3,995 (https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups)

Search strategy

We searched the following databases using a systematic search strategy: Medline, EMBASE, PsycINFO, Global Health, LILACS (Latin American and Caribbean Health Sciences Literature), and AJOL (African Journal Online). Additionally, we inspected the reference lists of all selected studies to identify additional relevant studies. Finally, we conducted a forward search on Web of Science to identify studies which might have been missed in the original electronic search and to identify studies which cited any of the included studies.

Our search strategy was organised under the following three 'search concepts': 1) Alcohol use disorders (e.g. hazardous drinking, risky drinking, alcohol dependence), 2) non-communicable diseases (e.g. angina, chronic obstructive pulmonary disease, diabetes mellitus), and 3) low- and middle-income countries (e.g. developing country, emerging nation, specific names of all LMICs). ~~The detailed search strategy that we used for the Medline database is provided in Appendix 1.~~ The protocol of the review was registered prospectively on PROSPERO (CRD42020191752).

Selection of studies and data extraction

The outputs of the search were extracted into the COVIDENCE online software (https://www.covidence.org/home) through which subsequent screening was conducted. Two reviewers independently inspected the titles and abstracts of the studies identified through the search strategy described above. In the case of any disagreement regarding inclusion, a third reviewer resolved the conflict. For the potentially eligible studies, the full paper was retrieved to ascertain whether it was eligible for inclusion and reviewed independently by the two reviewers. In the case of any disagreement regarding inclusion, a third reviewer resolved the conflict. A final list of eligible papers was thus generated and these proceeded to the next stage of data extraction. A formal data extraction form was designed to extract data relevant to the study aims. Following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, a record was made of the number of papers retrieved, the number of papers excluded and the reasons for their exclusion.

Results

We identified 1431 references through the database search. After removing 196 duplicates we screened the titles and abstracts of 1235 studies. 965 studies were excluded as they did not meet the eligibility criteria. Of the remaining 270 studies, 84 papers were either not accessible or not available in the English language. The full texts of the remaining 186 were assessed for eligibility. Subsequently, 173 studies were excluded as they did not meet the eligibility criteria and data was extracted from 13 studies (Figure 1).

We included three studies each from India (Iyer & Omprakash, 2020; Nadkarni et al., 2017; Nebhinani et al., 2013) and South Africa (Peltzer, 2009; Peltzer & Phaswana-Mafuya, 2013; Pengpid et al., 2011), two each from Cameroon (Dzudie et al., 2018; Jingi et al., 2016) and Russia (Kashcheev et al., 2017; Malyutina et al., 2002) and one each from Brazil (Sandoval et al., 2020), China (Pan et al., 2016), and Sri Lanka (Medagama et al., 2015). The studies were situated in the community (Malyutina et al., 2002; Nadkarni et al., 2017; Peltzer, 2009;

Peltzer & Phaswana-Mafuya, 2013; Sandoval et al., 2020) or in hospitals (Medagama et al., 2015; Nebhinani et al., 2013; Pan et al., 2016; Pengpid et al., 2011) – sometimes in specialty units (Dzudie et al., 2018; Iyer & Omprakash, 2020; Jingi et al., 2016). One study specifically examined the adverse impacts on Russian emergency workers from the Chernobyl accident (Kashcheev et al., 2017). Most of the study samples included males and females from the general population. Some studies had only male participants (Iyer & Omprakash, 2020; Kashcheev et al., 2017; Malyutina et al., 2002; Nadkarni et al., 2017; Nebhinani et al., 2013), or participants defined by a particular NCD (Dzudie et al., 2018; Jingi et al., 2016; Medagama et al., 2015; Pan et al., 2016), substance use disorder (Nebhinani et al., 2013), or occupational exposure (Kashcheev et al., 2017). The mean age of the samples ranged from 32.8 years to 63.2 years; and the sample sizes ranged from 80 to 53,772. Table 1 summarises the characteristics of the studies included in this review.

Alcohol use disorder

The various types of drinking problems examined in the studies included heavy episodic drinkers (HED) or binge drinking (Malyutina et al., 2002; Peltzer & Phaswana-Mafuya, 2013; Sandoval et al., 2020), alcohol dependence (Iyer & Omprakash, 2020; Kashcheev et al., 2017; Nebhinani et al., 2013), alcohol abuse (Dzudie et al., 2018; Medagama et al., 2015; Pan et al., 2016), alcohol misuse (Jingi et al., 2016), hazardous or harmful use of alcohol (Nadkarni et al., 2017; Pengpid et al., 2011), and risky drinking (Peltzer, 2009). A few studies did not specify how AUD was defined while others defined it based on quantity/frequency of drinking (Iyer & Omprakash, 2020; Malyutina et al., 2002; Peltzer, 2009; Peltzer & Phaswana-Mafuya, 2013; Sandoval et al., 2020), ICD 10/DSM IV criteria (Iyer & Omprakash, 2020; Kashcheev et al., 2017; Nebhinani et al., 2013), or Alcohol Use Disorders Identification Test (AUDIT) score (Nadkarni et al., 2017; Pengpid et al., 2011).

Non-communicable diseases

The most commonly examined NCDs in the studies included hypertension (Iyer & Omprakash, 2020; Nadkarni et al., 2017; Nebhinani et al., 2013; Peltzer & Phaswana-Mafuya, 2013; Pengpid et al., 2011; Sandoval et al., 2020), and diabetes mellitus (Jingi et al., 2016; Nadkarni et al., 2017; Nebhinani et al., 2013; Pan et al., 2016; Peltzer, 2009; Peltzer & Phaswana-Mafuya, 2013; Pengpid et al., 2011; Sandoval et al., 2020), and other NCDs included Left Ventricular Hypertrophy (LVH) (Iyer & Omprakash, 2020), QTc prolongation (Iyer & Omprakash, 2020), pulmonary hypertension (Dzudie et al., 2018), 'Cardiovascular Diseases' (e.g. ischemic heart diseases) (Kashcheev et al., 2017; Malyutina et al., 2002), Acute Coronary Syndrome (unstable angina, myocardial infarction) (Medagama et al., 2015; Pengpid et al., 2011), asthma (Pengpid et al., 2011), bronchitis (Pengpid et al., 2011), and Coronary Heart Disease (Malyutina et al., 2002). While some studies relied on self-report of NCD (Nadkarni et al., 2017; Peltzer, 2009; Peltzer & Phaswana-Mafuya, 2013; Pengpid et al., 2011; Sandoval et al., 2020), the rest used objective measures such as tests (Dzudie et al.,

2018; Iyer & Omprakash, 2020; Medagama et al., 2015; Nadkarni et al., 2017; Nebhinani et al., 2013), clinical notes (Jingi et al., 2016), and standardised clinical criteria (Kashcheev et al., 2017; Malyutina et al., 2002; Pan et al., 2016).

Table 2 summarises the information about prevalence and correlates/risk factors for comorbid NCD and AUDs. The following section organises that information by the type of NCD.

Hypertension

More than half of those with frequent heavy episodic drinking have hypertension (53%)(Sandoval et al., 2020). A relatively lower proportion of those with non-frequent heavy episodic drinking have hypertension (40.4%)(Sandoval et al., 2020). At the more severe end of the AUD spectrum i.e. alcohol dependence, 41.1% have hypertension(Nebhinani et al., 2013). In a study that compared those who had alcohol dependence for less than 10 years with those who had it for more than 10 years, in the former, the prevalence of hypertension reduced significantly after inpatient treatment (55% vs 25%; p<0.01~~=0.001~~). In the latter group, the reduction in prevalence was not statistically significantly (58% vs 50%; ~~p=0.5~~NS) (Iyer & Omprakash, 2020).

Both heavy episodic drinking (OR 1.32; 95% CI 1.09-1.59) and frequent heavy episodic drinking (OR 1.95; 95% CI 1.43-2.66) were associated with hypertension in men(Sandoval et al., 2020). Compared with men who had no AUD at baseline and follow-up, those with incident AUD were more likely to have self-reported hypertension (OR 2.5; 95% CI 1.5–4.4) (Nadkarni et al., 2017). Compared to men who had recovered, those with persistent AUD were less likely to have objectively measured hypertension (OR 0.3; 95% CI 0.1–0.8) (Nadkarni et al., 2017). Finally, binge drinking was not associated with hypertension (Peltzer & Phaswana-Mafuya, 2013), and heavy episodic drinking was not associated with hypertension in women(Sandoval et al., 2020).

Diabetes

More than half of those with frequent heavy episodic drinking have diabetes (52.4%) (Sandoval et al., 2020). A relatively lower proportion of those non-frequent heavy episodic drinking have diabetes (28.9%)(Sandoval et al., 2020). Of those with alcohol dependence, 14% have diabetes(Nebhinani et al., 2013). There was no significant difference ~~(p=0.462)~~ in prevalence of alcohol misuse amongst those with diabetes and on treatment with oral hypoglycemics 1.8% (95% CI 0.2–6.4) compared to those who were on treatment with insulin 4.3% (95% CI 0.1–21.9) (Jingi et al., 2016).

Alcohol abuse is an independent risk factor for development of diabetes mellitus (HR, 2.00; 95% CI, 1.43–2.79; P < 0.001) (Pan et al., 2016). Compared to men who have recovered, those with persistent AUD were more likely to have self-reported diabetes (OR 2.8; 95% CI 1.1–7.0) (Nadkarni et al., 2017). Compared to men with no AUD at baseline and follow-up, incident AUD were more likely to have self-reported diabetes (OR 2.2; 95% CI 1.1–4.5) (Nadkarni et al., 2017). Among men, diabetes was inversely associated with hazardous/harmful drinking (OR 0.56; 95% CI 0.31–0.99) and heavy episodic drinking (OR 0.52; 95% CI 0.32-0.85) (Pengpid et al., 2011; Sandoval et al., 2020). Finally, risky drinking and binge drinking was not associated with diabetes (Peltzer, 2009; Peltzer & Phaswana-Mafuya, 2013); and heavy episodic drinking was not associated with diabetes in women (Sandoval et al., 2020).

Other cardiovascular diseases

21.3% of those with pulmonary hypertension(Dzudie et al., 2018) and 18% of those with ACS (Medagama et al., 2015) had “alcohol abuse”. There was a significant difference (p=0.035) in the prevalence of alcohol abuse in those with ST-segment-elevation myocardial infarction (STEMI) (27.4%) compared to those with unstable angina or non-STEMI (14.5%) (Medagama et al., 2015).

Risk of cardiovascular diseases is greater in those with alcohol dependence compared to those with no alcohol dependence (RR 1.36; 95% 1.18-1.55; p < 0.001) (Kashcheev et al.,

2017). Left Ventricular Hypertrophy was significantly greater in those who had alcohol dependence for more than 10 years as compared to those who had it for less than 10 years (Iyer & Omprakash, 2020). Finally, binge drinking was not a significant risk factor for cardiovascular mortality (Malyutina et al., 2002).

Table 3 cross tabulates the various types of AUDs and NCDs to summarise the association or risk relationship between the two.

Discussion

AUDs are an important driver of poorer health and higher healthcare costs; and behavioural conditions, such as AUDs, comorbid with medical conditions, incur much higher healthcare costs than those without such comorbidities (Freeman et al., 2014; Hayes et al., 2016; Laderman, 2015). However, despite substantial health risks from such comorbidities, they are under-researched, under-recognized and under-treated (Walter et al., 2017).

This review is the first synthesis of the evidence examining the relationship between AUDs and a select set of the commonest NCDs in LMICs. The prevalence of AUDs amongst those with the select NCDs, and vice versa, is higher than in the general population. The association between AUDs and some of the select NCDs (viz diabetes, cardiovascular conditions) is less clear. The evidence is mixed, with some studies showing a clear association between the two conditions, others showing no association, while still others suggesting a protective effect (in diabetes) and a differential effect in some cases based on gender (i.e. association in men but not in women).

Considering the high prevalence of NCDs in those with AUDs, and vice versa, identification of these conditions through proactive screening and treatment is especially critical. Timely and relevant care for those with comorbid AUD and NCDs can be sub-optimal because of a lack of clarity about clinical responsibility for the care for each of these conditions. Hence, establishing shared care pathways which focus on integrated care for both AUDs and NCDs is of critical importance.

NCDs and AUDs are a major threat to development in LMICs and need to be reframed within broader discussions around social determinants and not just as outcomes of unhealthy choices made by individuals. Screening and intervention for drinking problems should be integrated into routine healthcare as a broader lifestyle intervention, especially since alcohol is a behavioural risk factor shared across several NCDs. Finally, while AUDs are individual-

level risk factors for NCDs, prevention efforts should also focus on public health interventions designed to reduce availability, affordability, and marketing of alcohol.

Despite considerable research in the past, the mechanisms underlying the association between AUDs and NCDs is not well understood, and findings have been inconsistent. For example, the much reported “J-shaped relationship” between alcohol and metabolic health has been criticised for being affected by misclassification and confounding (Chikritzhs et al., 2015). Future research, particularly in LMICs, needs to focus on longitudinal studies which compare the risk with appropriately matched healthy controls. Finally, the overall research examining the comorbidity of AUDs and NCDs in LMICs is very limited. Considering the burden associated with both AUDs and NCDs, it is paramount that there is a concerted effort to enhance research efforts to explore the complex relationships between in AUDs and NCDs in LMICs.

Our review is not without its limitations, some related to the source studies and others related to our methodology. Of particular importance is the lack of consistency between the studies in in how the range of AUDs are defined. This is a larger problem that plagues AUD research and precludes the effective synthesis of the evidence. Additionally, the self-report of NCDs in some of the studies has implications on the validity of the findings. Finally, the cross-sectional design of many of the included studies limits the conclusions that we can draw about causal relationships between AUD and the selected NCDs. Our review is limited by our inclusion criterion related to language, especially since some studies from LMICs might be published in vernacular languages in national or regional journals. Our review’s major strength lies in its use of robust and systematic processes (e.g., double screening) to identify eligible studies.

To conclude, the burden of comorbid AUDs and NCDs in LMICs is high, but there is a lack of an appropriate public health response in such countries. This is of particular concern in LMICs where alcohol availability is increasing, prices are low, enforcement of appropriate laws is often minimal, and the promotion of alcohol consumption is poorly regulated. To counter the

harmful effects of alcohol use in NCDs early intervention through screening and brief interventions in primary care is crucial. Additionally, at the population level, policy actions such as restrictions on alcohol availability and marketing and higher alcohol taxes can help reduce the alcohol consumption and it's adverse impact in at-risk populations.

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Table 1: Description of studies included in the review

Author, Year	Country	Setting	Sampling strategy	Sample	Mean age (SD)	N	Study design
Sandoval, 2020	Brazil	Community	Random	Male (M), Female (F)	42.4 (16.7)	53034	Cross-sectional survey
Iyer, 2019	India	Psychiatry ward in general hospital	Convenience	M	'Group 1 alcoholics' 39 (9.1) 'Group 2 alcoholics' 48.8 (8.8)	80	Cross-sectional survey
Dzudie, 2018	Cameroon	Rural cardiac centre	Consecutive patients	M, F Newly diagnosed pulmonary hypertension	62.7 (18.7)	150	Prospective cohort study
Kascheev, 2017	Russia	Occupational	Convenience	M, liquidators from the Chernobyl zone	Not specified	53772	Cohort study
Nadkarni, 2017	India	Community	Random	M	32.8 (8.6)	1899	Retrospective cohort study
Jingi, 2016	Cameroon	Ophthalmology ward in general hospital	Convenience	M, F Type 2 Diabetes Mellitus	59.3 (7.9)	134	Cross-sectional survey
Pan, 2016	China	Hospital	Convenience	M, F	43.3 (15.5)	2011	Cohort study

				Patients with chronic pancreatitis			
Medagama, 2015	Sri Lanka	Hospital	Consecutive patients	M, F Patients with Acute Coronary Syndrome (ACS)	63.2 (11.2)	256	Cohort study
Nebhinani, 2013	India	Hospital	Convenience	Men admitted to the inpatient unit of Drug De-addiction and Treatment Centre	34.24 (10.25)	256	Cross-sectional survey
Peltzer, 2013	South Africa	Community	Systematic random	M, F >60 years	Not specified	2144	Cross-sectional survey
Pengpid, 2011	South Africa	Hospital	Consecutive patients	M, F Outpatients from following clinics - family practice, general out-patient department, cardiology, diabetes and ear nose and throat department and from a dispensary	36.1 (11.6)	1532	Cross-sectional survey
Peltzer, 2009	South Africa	Community	Systematic random	M, F	Not specified	2314	Cross-sectional survey
Malyutina, 2002	Russia	Community	Random	M	Not specified	6502	Prospective cohort study

Table 2: The relationship between alcohol use disorder and selected non-communicable diseases

Author, Year	Alcohol use disorder	Definition	Non-communicable disease	Definition	Prevalence	Correlates/Risk factors
Sandoval, 2020	Heavy episodic drinkers (HED) Frequent HED	≥5 drinks (men) or ≥4 drinks (women) on one occasion in the last 30 days. HED occurred ≥4 days in the last 30 days.	Hypertension Diabetes	Self-report	53% with frequent HED and 40.4% with HED had hypertension. 52.4% with frequent HED and 28.9% with HED had diabetes	HED (OR 1.32; 95% CI 1.09-1.59) and frequent HED (OR 1.95; 95% CI 1.43-2.66) associated positively with hypertension and HED was inversely associated with diabetes (OR 0.52; 95% CI 0.32-0.85) in men.

						HED and frequent HED not associated with hypertension or diabetes in women.
Iyer, 2019	Alcohol dependence 'Group 1 alcoholic' 'Group 2 alcoholic'	Daily ethanol consumption >90 mL, >4 days/week, and fulfilled DSM IV criteria. 'Alcoholic' for ≤10 years. 'Alcoholic' for >10 years.	Hypertension Left Ventricular hypertrophy (LVH) QTc prolongation	Systolic blood pressure ≥130 mm Hg and diastolic blood pressure ≥80 mm Hg. Solokow Lyon Voltage criteria and Cornell criteria. >450 ms	Group 1: 55% had hypertension at admission and 25% ($p<0.01$) after two weeks of admission. Group 2: 58% had hypertension at admission and 50% (NS) after two weeks of admission.	LVH was significantly greater in Group 2 compared to Group 1.
Dzudie, 2018	Alcohol abuse	Not specified	Pulmonary hypertension	Right ventricular systolic pressure ≥35 mmHg in the absence of pulmonary	21.3% of those with pulmonary hypertension had alcohol abuse.	

				stenosis and right heart failure.		
Kascheev, 2017	Alcohol dependence	ICD 10 criteria	"Cardiovascular diseases," including acute rheumatic fever and chronic rheumatic heart diseases; ischemic heart diseases; diseases of arteries, arterioles and capillaries; deep vein thrombosis; and pulmonary embolism	ICD 10 criteria		Relative Risk of cardiovascular diseases in the presence of alcohol dependence 1.36 (95% 1.18; 1.55); $p < 0.001$
Nadkarni, 2017	Alcohol use disorder	Alcohol Use Disorders Identification Test (AUDIT) score of ≥ 8	Hypertension Diabetes Mellitus	Self-reported and objective measurement Self-reported		Compared to recovered men with AUD, persistent AUD more likely to have self-reported diabetes (OR 2.8; 95% CI 1.1–7.0). Compared no AUD at baseline and follow-up, incident AUD more likely to have self-reported

						diabetes (OR 2.2; 95% CI 1.1–4.5). Compared with no AUD at baseline and follow-up, incident AUD more likely to have self-reported hypertension (OR 2.5; 95% CI 1.5–4.4). Compared to recovered AUD, persistent AUD less likely to have objectively measured hypertension (OR 0.3; 95% CI 0.1–0.8).
Jingi, 2016	Alcohol misuse	Not specified	Diabetes Mellitus (DM)	As per clinical notes	Prevalence of alcohol misuse amongst those with DM and on treatment with oral hypoglycemics 1.8% (95% CI 0.2–6.4) and on treatment with insulin 4.3% (95% CI 0.1–21.9), NS	

Pan, 2016	Alcohol abuse	Not specified	Diabetes Mellitus	As per criteria of the American Diabetes Association.		Alcohol abuse (HR, 2.00; 95% CI, 1.43–2.79; P < 0.001) is an independent risk factor for development of diabetes mellitus
Medagama, 2015	Alcohol abuse	Not specified	ACS including unstable angina (UA), ST-segment-elevation myocardial infarction (STEMI), and non-STEMI (NSTEMI)	STEMI- ECG criteria for the diagnosis of acute STEMI or new-onset left bundle-branch block, and increased serum concentrations of biochemical markers of myocardial necrosis (if available). UA and NSTEMI- ischemic type chest pain and ST segment	18% of those with ACS had alcohol abuse. Prevalence of alcohol abuse in STEMI (27.4 %) vs UA/NSTEMI (14.5 %) (p<0.05)	

				depression more than 1 mm and T wave inversion greater than 1 mm in contiguous ECG leads.		
Nebhinani, 2013	Alcohol dependence	ICD 10 criteria	Hypertension Diabetes	BP ≥130/≥85 or diagnosed as hypertensive Fasting blood Glucose ≥100 mg or diagnosed as diabetes	41.1% of those with alcohol dependence had hypertension. 14% of those with alcohol dependence had diabetes	
Peltzer, 2013	Binge drinking	>3 drinks/one occasion/week	Hypertension Diabetes	Self-reported		Binge drinking was not independently associated with diabetes and hypertension
Pengpid, 2011	Hazardous or harmful use of alcohol	AUDIT score ≥8	Heart attack/Angina, Hypertension, Asthma, Bronchitis, Diabetes	Self-reported		Among men, diabetes was inversely associated with hazardous/harmful drinking OR 0.56 (95% CI 0.31–0.99)

Peltzer, 2009	Risky drinking	Consumed 15 or more units in the past week	Diabetes Mellitus	Self-reported		Risky drinking was not associated with diabetes
Malyutina, 2002	Binge drinking	Consumption of ≥160g alcohol on a typical occasion	Cardiovascular Disease, Coronary Heart Disease	ICD-9		Binge drinking was not a significant risk factor for cardiovascular mortality

NS=Non-significant

Table 3: The association or risk relationship between AUD and NCDs

	Hypertension (HT)	HT in men	HT in women	Diabetes Mellitus (DM)	DM in men	DM in women	Cardiovascular disease	Cardiovascular mortality
Heavy Episodic Drinking (HED)		↑	-		↓	-		
Frequent HED		↑						
New alcohol use disorder (AUD)		↑			↑			
Persistent AUD		↓	↑		↑			
Binge drinking	-			-				-
Alcohol abuse				↑				
Hazardous/harmful drinking					↓			
Risky drinking				-				
Alcohol dependence							↑	

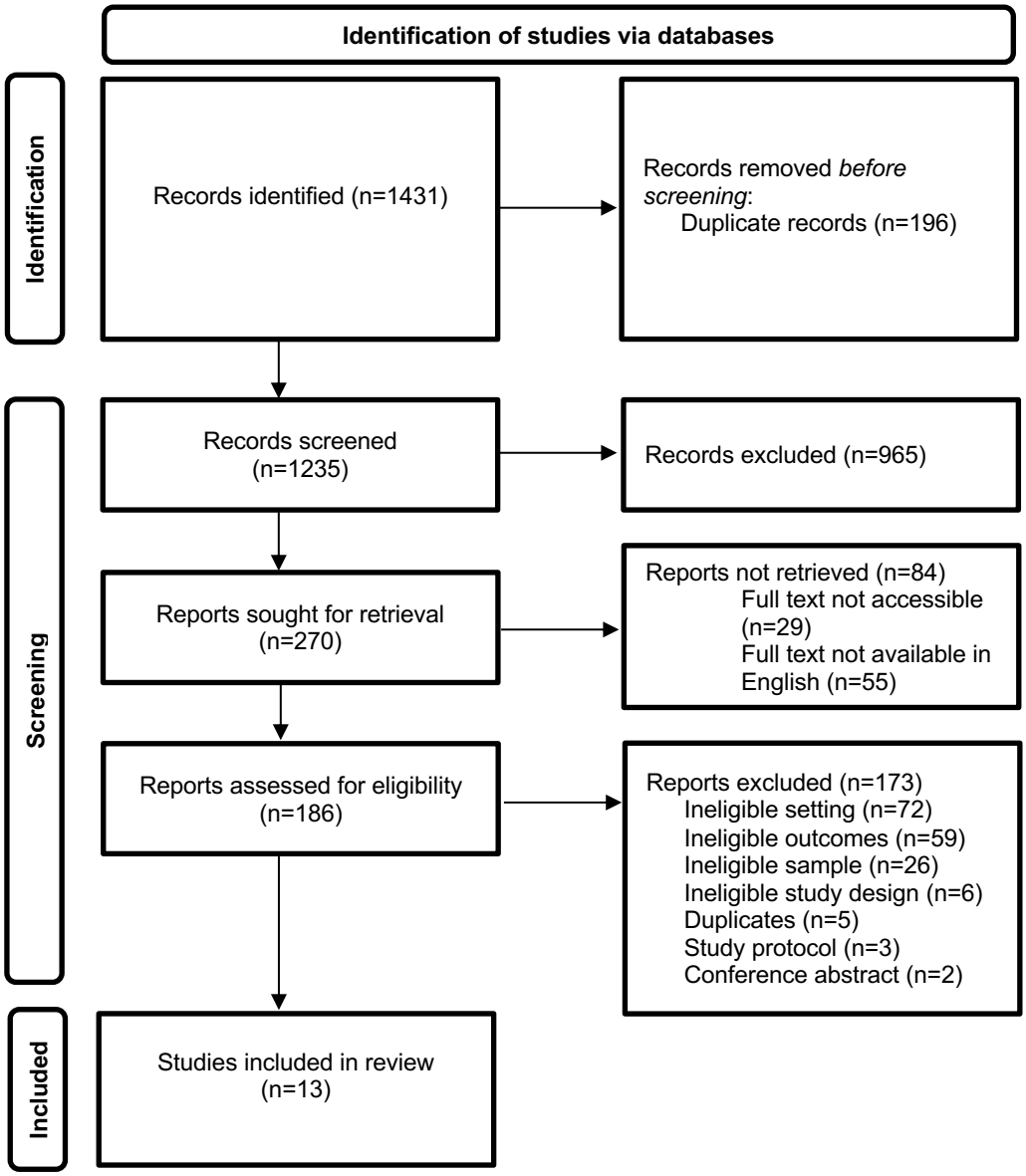

Figure 1: Flow of information through the different phases of the review.