A SCOPING REVIEW ON THE USE OF MRI TECHNIQUES TO ASSESS THE EFFECTS OF ADOLESCENT ALCOHOL CONSUMPTION AND HEAVY DRINKING

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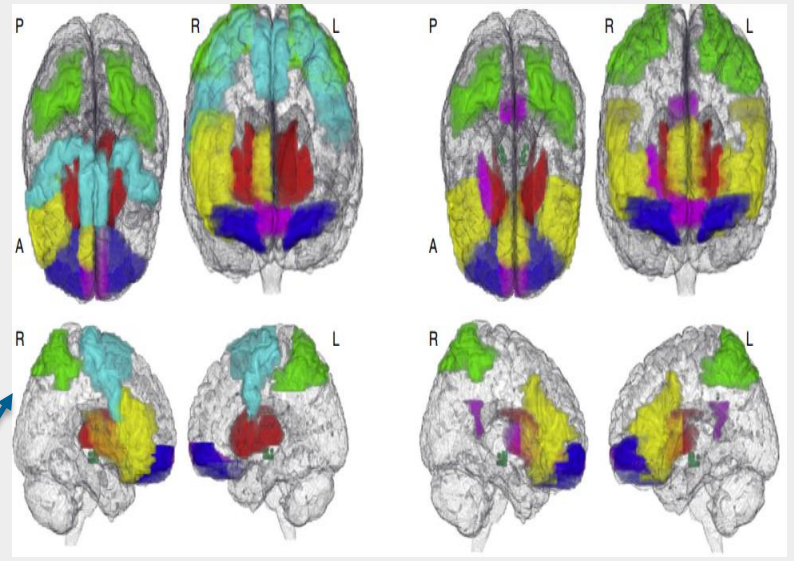
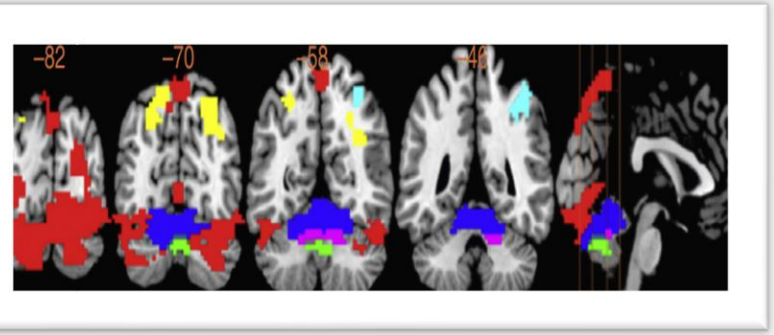
BACKGROUND

- Alcohol is the second leading risk factor, contributing to 2.6% (2.1-3.1) of DALYs among individuals aged 10 to 24 years (1)
- An estimated 26.5% (or 155 million) of adolescents aged 15-19 years report current use of alcohol use, 45.7% of whom engage in HED **=>** alcohol-related research has been identified as one of the top research priorities for the promotion of adolescent health (2)
- SA, adolescent alcohol consumption characterized by HED, with ⇧ levels attributed to adolescent males (4)
- Adolescence is a critical developmental period marked by differential maturation rates of cortical and subcortical brain structures. HED of particular concern during this period (4,5)
- Alcohol consumption, specifically HED, are accompanied by adverse structural brain changes in adolescent drinkers (6,7)





Images: Robert et al. Reinforcement related behaviors and adolescent alcohol abuse: from localized brain structures to coordinated networks. Behavioral Sciences. 2017, 13:106–116

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To quantify and evaluate the quality of studies using MRI techniques to assess the effects of heavy drinking during adolescence

- Protocol registered on Open Sciences Framework (OSF); published in the Brain Sciences Journal (publication year 2021)

brain sciences

MDPI

Study Protocol

The Use of Magnetic Resonance Imaging Techniques in Assessing the Effects of Alcohol Consumption and Heavy Drinking on the Adolescent Brain: A Scoping Review Protocol

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Abstract: *Introduction:* Alcohol consumption, specifically heavy drinking during adolescence, has been shown to be accompanied by adverse structural brain changes in adolescent drinkers. This scoping review will aim to quantify and evaluate the quality of studies in which magnetic resonance imaging (MRI) techniques are used to assess regional brain deficits among adolescents who consume alcohol. *Methods and analysis:* This scoping review will be conducted following the Arksey and O'Malley scoping review methodology framework and will be reported using Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) extension for Scoping Reviews (PRISMA-ScR) guidelines. Literature will be searched for the period January 1999 to March 2021. Two reviewers will independently screen titles/abstracts and full-texts in two consecutive screening stages. Eligible studies will be independently reviewed to ensure that inclusion criteria are met. Cohen's Kappa (κ) will be used to calculate inter-rater agreement. A third reviewer will resolve any disagreements. The Joanna Briggs Institute (JBI) Appraisal Tools will be used for quality appraisal of the included studies. Findings will be reported by means of a narrative overview, tabular presentation of study characteristics, and quality assessment, and a thematic analysis of major themes. This scoping review has been registered with the Open Science Framework. *Ethics and dissemination:* Scoping reviews do not require ethical approval, however, this review forms part of a larger study that has obtained approval from the Faculty of Health and Medical Sciences, Health Research Ethics Committee at Stellenbosch University (S20/04/086). Findings will be disseminated by means of peer-reviewed publications and conferences.

Keywords: scoping review protocol; adolescent alcohol use; magnetic resonance imaging

1. Strengths and Limitations of This Study

- This scoping review provides a critical review of the MRI techniques in identifying neuroanatomical brain deficits associated with adolescent alcohol consumption.
- In addition to the mapping of the evidence, this scoping review will provide a critical appraisal of the evidence using appropriate Joanna Briggs Appraisal Tools.
- A comprehensive search strategy was developed with the assistance of an information specialist and a public health systematic review expert. In addition, the technical aspects of the methodology was guided by the public health systematic review expert.
- The team consisted of experts in addiction research, neuroimaging techniques, and public health systematic reviews.

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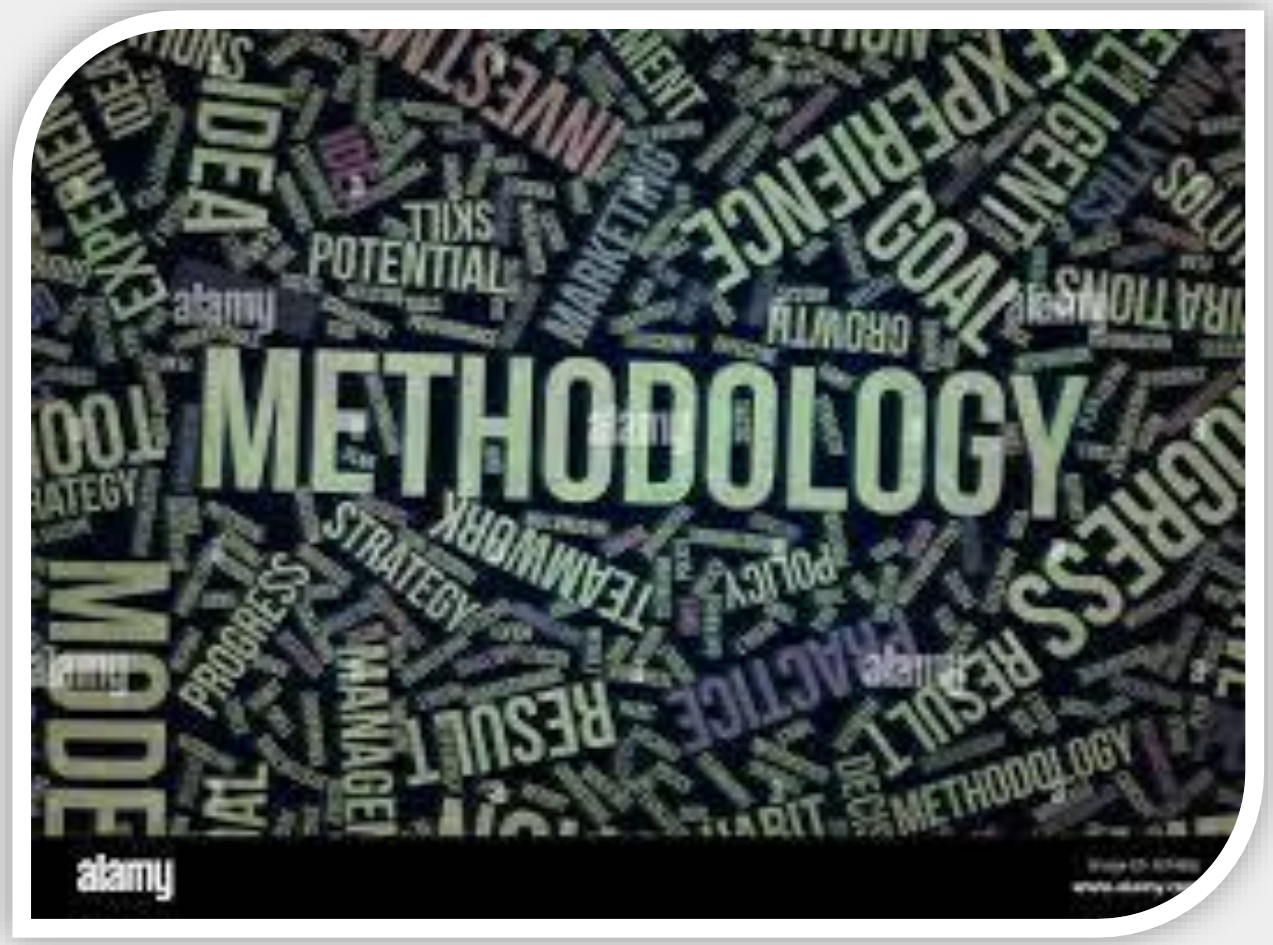

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- Arksey & O'Malley scoping review framework; reported using PRISMA & PRISMA-ScR guidelines
- *A priori* eligibility criteria
- Search strategy developed in consultation with experts and IS (Cochrane Centre)
- Search period: January 1999 to March 2021 (updated to March 2022)
- Cochrane Library, PubMed, and Scopus, English-only search [conducted by IS (Cochrane Centre)]
- Two reviewers independently screened titles/abstracts and full-texts in two consecutive screening stages
- Disagreements resolved by third reviewer
- JBI Critical Appraisal Checklists for:
  - ✓ Analytical Cross-Sectional Studies (8 domains);
  - ✓ Cohort Studies (11 domains) and;
  - ✓ Systematic Reviews (11 domains)
- Data extracted using self-developed data collection tool (13 domains)

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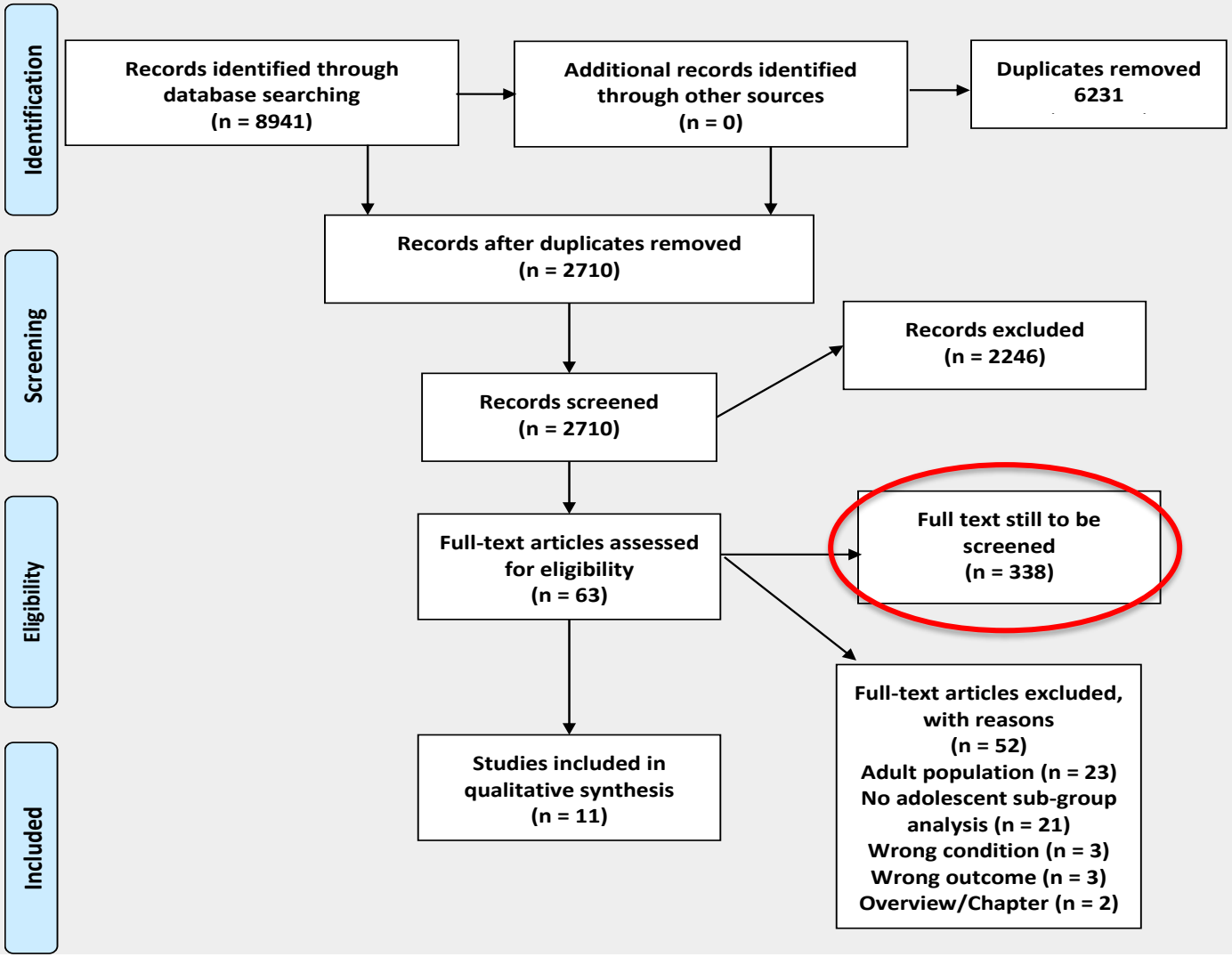
PRISMA flow diagram



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RESULTS

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Study details	Study design	MRI /Outcome assessment	Main findings
1. Aloi et al. 2018, USA	Cross-sectional; convenience sampling (n=82, 14-18yrs)	fMRI, aST (emotional stimuli)	Regions affected: amygdala ($p < 0.001$), dlPFC, aCC, precuneus (p's < 0.05) (as functions of executive function and response control task performance)
2. Banz et al. 2019, USA	Cross-sectional; convenience sampling (n=170, mean age=18.42, sd=0.7)	fMRI; vMWT (spatial working memory)	Reduced SWM-related activity in the dorsolateral prefrontal cortex (p=0.04) and hippocampus (p-0.039)
3. Bava et al. 2009, USA	Cross-sectional; convenience sampling (n=72, 16-19yrs, mean age=17.9, sd=0.8)	DTI (FA; MD)	Lower FA for users vs. controls: (i) right inferior frontal gyrus (p=0.04); (ii) left occipito-frontal tract (p=0.02) Lower MD for users vs. controls: left inferior longitudinal fasciculus (p=0.03)
4. Bava et al. 2013, USA	Retrospective, longitudinal; convenience sampling (n=92, mean age=18.1, sd: 1.2)	DTI (FA; MD; AD; RD)	More alcohol use during the interscan interval predicted higher mean diffusivity (i.e., worsened integrity) in right ($p < .05$) and left (p=.06) superior longitudinal fasciculi, above and beyond baseline values in these bundles.
5. Cservenka et al. 2015, USA	Prospective, longitudinal; convenience sampling (n=34, 12-18yrs)	fMRI; WOF (reward processing)	No effects in the VS; left cerebellum (reward response) negatively correlated with mean number of drinks consumed/drinking day in the last 90 days ($p<0.05$)
6. Gan et al. 2014, Germany	Single-blind placebo-controlled cross-over design (longitudinal); randomised sampling (n=50; 18-19yrs)	fMRI; SST (inhibition-executive function)	Impaired inhibitory control associated with attenuated brain responses in the right ronto-temporal portion of the inhibition network ($p<0.001$)
7. Jones et al. 2016, USA	Retrospective, longitudinal; convenience sampling (n=26, 13-16yrs)	fMRI (WOF) task (executive function- decision making)	Region of interest (ROI) analysis: during decision making, significant binge-drinking related reduction in brain activation in the left dorsal caudate in the DLPFC (p=0.05). Whole brain analysis: decrease in fronto-parietal brain activation prior to initiation of alcohol use, in adolescents who went on to binge drink ($p<0.01$).

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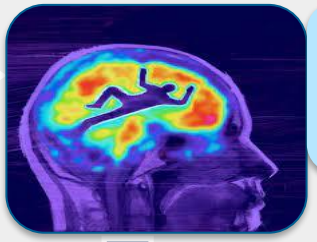
Study details	Study design	MRI/ Outcome assessment	Main findings
8. **Robert et al. 2017 (settings of included studies not reported)**	Review; N=19 studies, samples sizes of included studies range: n=24-3489, age range=12-19yrs	fMRI; sMRI; MID (reward); SSRTT (inhibition- executive function); G/NG (inhibition- executive function); Verbal learning	Life experiences, personality, and neurobiological differences, including neuroimaging and genetic features, are the most important binge drinking antecedents. Among neuroimaging phenotypes, when combining both structural and functional data, the vmPFC and left IFG classify binge drinkers and non-drinkers at age 14; right middle and precentral gyri and bilateral sFG predict future drinkers.
9. **Squeglia et al. 2012, USA**	Cross-sectional; convenience sampling (n=59, 16-19yrs)	sMRI	Binge × gender interactions ($p<0.05$) for cortical thickness in four left frontal regions: frontal pole, pars orbitalis, medial orbital frontal, and rostral anterior cingulate. Female bingers v female controls: thicker cortices; male bingers vs male controls: thinner cortices.
10. **Wetherill et al. 2013a, USA**	Prospective, longitudinal; convenience sampling (n=60, 12-14yrs)	fMRI; G/N-G (inhibition- executive function)	Blackout+ youth greater activation during inhibitory processing than nondrinkers and blackout− youth in frontal and cerebellar brain regions.
11. **Wetherill et al 2013b, USA**	Prospective, longitudinal; convenience sampling (n=40, 11.7-16.7yrs)	fMRI; G/N-G (inhibition- executive function)	Responses common to inhibitory circuitry: frontal, temporal, and parietal regions. Less fMRI response contrast for heavy drinking vs no-drinking at baseline: parietal, subcortical, and cerebellar (($p < .01$, clusters > 756 microliters), then increased activation after the onset of heavy drinking in frontal, parietal, and cerebellar areas.

MAIN FINDINGS

- Total 11; 4 cross-sec; 3 prosp long; 2 retro long; 1 single-blind cross-over; 1 review

- 10 Primary research: n=34-170, 11.7-19yrs
- 1 Review: n=19, 12-19yrs



- Primary research: 7 fMRI; 1 sMRI; 2 DTI
- Review: fMRI and sMRI

- ⬇PFC and ⬇cerebellar region activation
- Thinner cortices (L. frontal) for fem. binge vs. contr; thicker cortices for male binge vs. contr.
- ⬇subcortical wm structures
- Two studies showed ⬆activation during inhibition tasks (neural effort) for blackout+ youth vs. blackout- youth and contr.

Figure 1. Quality Appraisal for Cross-Sectional Studies

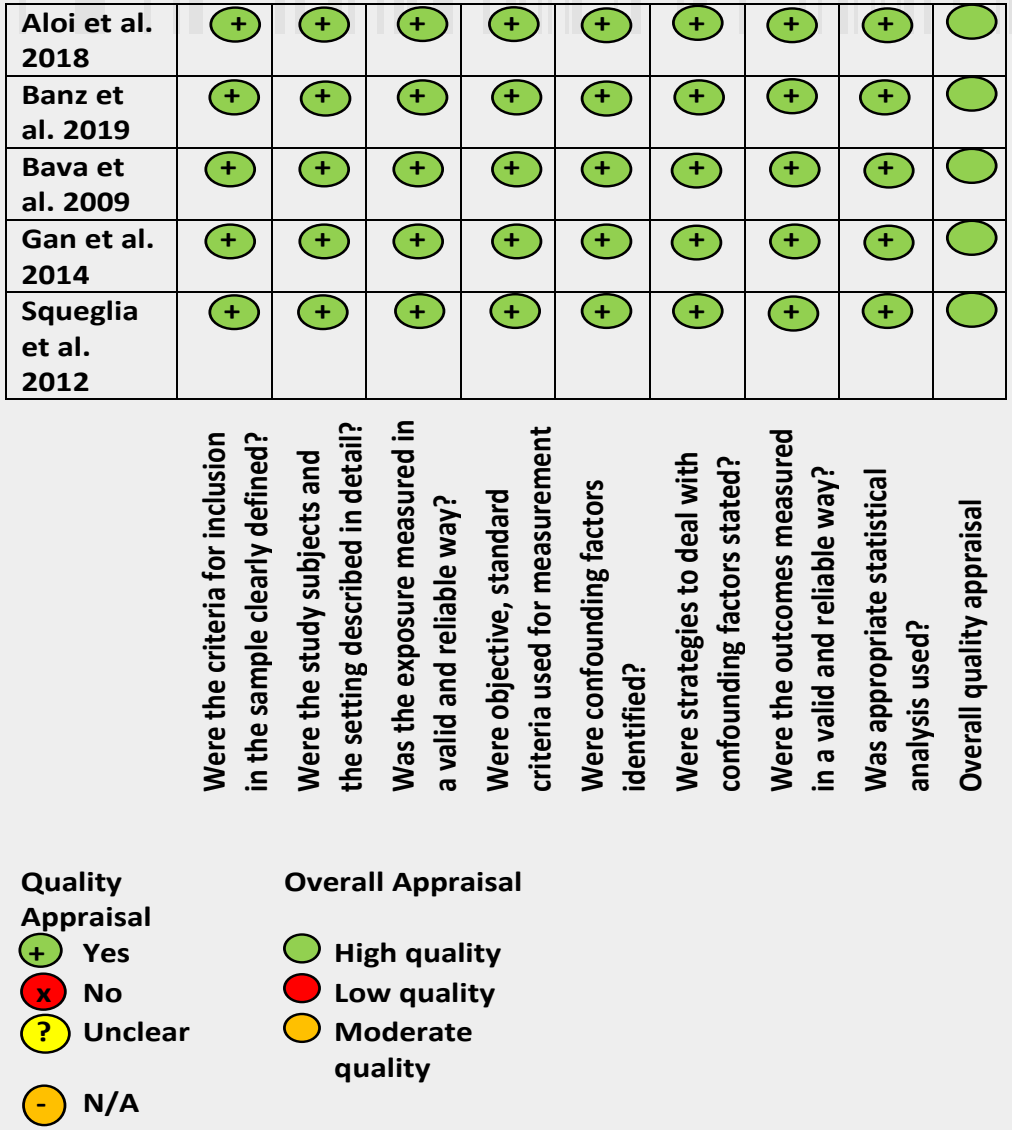


Figure 2. Quality Appraisal for Cohort Studies

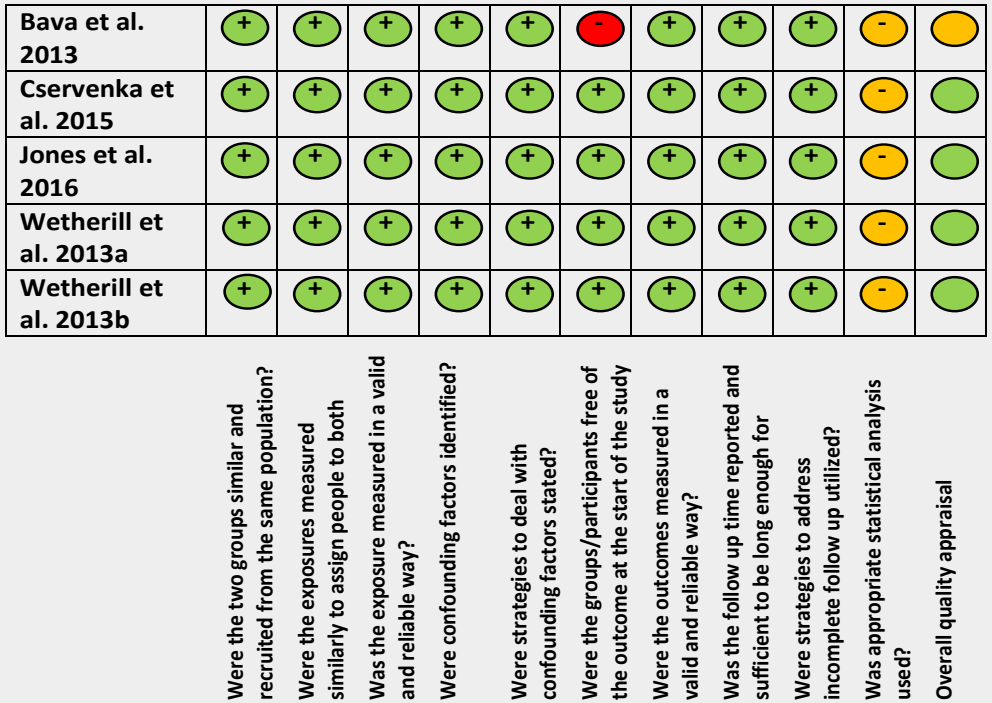
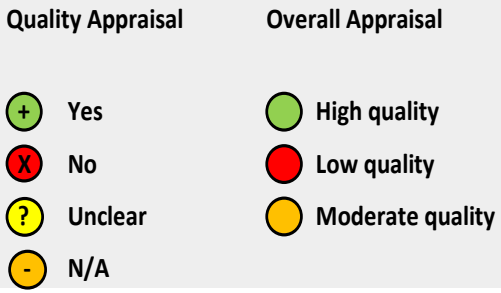


Figure 3. Quality Appraisal for Systematic Reviews

	Is the review question clearly and explicitly stated?	Were the inclusion criteria appropriate for the review question?	Was the search strategy appropriate?	Were the sources and resources used to search for studies adequate?	Were the criteria for appraising studies appropriate?	Was critical appraisal conducted by two or more reviewers	Were there methods to minimize errors in data extraction?	Were the methods used to combine studies appropriate?	Was the likelihood of publication bias assessed?	Were recommendations for policy and/or practice supported by the	Were the specific directives for new research appropriate?	Overall quality appraisal
Robert et al. 2017	X	?	?	?	-	-	-	-	X	?	+	



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CONCLUSIONS

- Generally high methodological quality of studies using MRI techniques, however, the review lacked methodological rigour;
- Sample sizes tend to be small;
- Deficits in brain regions involved in reward (cerebellar regions etc.) and inhibition/executive function (PFC) found for adolescents with heavy drinking, but process is complicated;
- MRI techniques present novel, non-invasive ways of assessing the neurobiology of adolescent alcohol intake;
- MRI allows the opportunity for gaining insights into the mechanisms of the brain-behaviour axis in substance use research.

NEXT STEPS:

- Conduct a diagnostic test accuracy (DTA) review with meta-analysis

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THANK YOU

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