Growing Up
in New Zealand

Examining neurocognitive outcomes of children that have experienced prenatal alcohol exposure using data from the *Growing Up in New Zealand* cohort

Date: 11 August 2022

Prepared by

Raimond Jacquemard

Fiona Langridge

Denise Neumann

Stephane Janicot

Sinéad Miller

Joanna Chu

Chris Bullen

Table of Contents

List of Tables

List of Figures

Glossary of terms and acronyms

Term	Definition or translation
8Y	8 Year
ADHD	Attention Deficit Hyperactivity Disorder
ARND	Alcohol Related Neurodevelopmental Disorder
DCW	Data Collection Wave
GUiNZ	Growing Up in New Zealand
FAS	Fetal Alcohol Syndrome
FASD	Fetal Alcohol Spectrum Disorder
MOH	Ministry of Health
PAE	Prenatal Alcohol Exposure
SAP	Statistical Analysis Plan

Project Teams

Growing Up in New Zealand

Dr Fiona Langridge	Research Fellow, University of Auckland. Principal Co-investigator
Dr Denise Neumann	Research Fellow, University of Auckland
Avinesh Pillai	Biostatistician, University of Auckland
Stephane Janicot	Biostatistician, University of Auckland
Sinéad Miller	Biostatistician, University of Auckland

Ministry of Health

Dr Raimond Jacquemard	Paediatrician, Taranaki District Health Board. Project Lead
Harsh Vardhan	Programme manager, Child and Family Programmes

Scientific Advisory Group

Professor Chris Bullen	Professor of Public Health, Public Health Physician/Epidemiologist, NIHI, The University of Auckland
Dr Andi Crawford	Clinical Psychologist with Te Ara Manapou – Pregnancy and Parenting Support. Postdoctoral fellow with the University of Auckland
Sarah Goldsbury	Clinical Neuropsychologist, The FASD Centre Aotearoa, PhD candidate University of Otago
Dr Jin Russell	Developmental Paediatrician, PhD candidate University of Auckland
Sally Kedge	Director and founder of Talking Trouble Aotearoa NZ, Speech Language Therapist
Dr Braden Te Ao	Health Economist, The University of Auckland

Steering Group

Maria Ngawati	Hāpai te Hauora, Māori Public Health
Christine Rogan	Alcohol Healthwatch
Megan Tahere	Chief Māori Health and Equity Officer, Taranaki DHB. PhD candidate Massey University
Professor Anita Gibbs	Parent of a child with FASD, Professor of Social Work, University of Otago
A/Professor Vili Nosa	Associate Professor, Head of Pacific Health, University of Auckland
Pat Tuohy	Paediatrician Hutt Valley DHB. Past Chief Advisor Child and Youth Health, Ministry of Health

Acknowledgements

1. Executive summary

1.1 Background

Alcohol exposure during pregnancy is known to be associated with a range of neurocognitive difficulties which can affect people throughout their lifetime. Prevalence rates for Fetal Alcohol Spectrum disorder (FASD) of around 2-3% have been found in recent case ascertainment population studies in North America and the UK,[1–3] and systematic reviews found the global prevalence was 0.77 % with large differences between WHO regions.[4] Special subpopulations such as children and young people in care, correctional services, or special education have much higher rates.[5] Data on the prevalence of FASD in New Zealand are not yet available. However, various publications have consistently found that the level of antenatal alcohol exposure in New Zealand is high.[6–9] On this basis, it is likely that the true prevalence of FASD is similar to, or even higher than, that found in North America and the UK.

A definitive neurodevelopmental profile for FASD has not been established[10] and a recent systematic review has shown that the evidence base for screening tools for FASD is weak.[11,12] Consequently the gold standard for FASD prevalence studies is a case ascertainment method, but this is a complex and costly undertaking, and has not been prioritised by the Ministry of Health or other funding agencies in Aotearoa New Zealand. It is however being raised as a priority for key stakeholders including families impacted by FASD, clinicians and researchers. There have been mixed results with evaluating the impact of perinatal alcohol exposure on neurocognitive outcomes in longitudinal cohort studies.[13] However, McQuire et al.[14] was able to estimate the "screening prevalence" of FASD in a UK population-based cohort study.

In 2018, the Ministry commissioned a pilot study to investigate the feasibility of a case ascertainment study within the GUiNZ cohort at the 8-year Data Collection Wave. The outcome of this "Leading Lights" study was that determination of FASD prevalence in the GUiNZ cohort with case ascertainment methodology was not feasible.

The aim of the current study was to investigate the impact of antenatal alcohol exposure on neurocognitive outcomes in children in the GUiNZ cohort at 8 years and estimate the prevalence of children that might need assessment for FASD or other neurodevelopmental impairments.

1.2 Methods

A Steering Group and a Scientific Advisory Group were constituted to guide the direction of the study, oversee the development and implementation of the research, advise on strategic decisions, and ensure scientific rigour was applied. The groups had representation from a broad range of stakeholders, including people affected by FASD, health professionals and researchers.

This project was committed to being responsive to Māori and Pacific peoples, and to meet our responsibilities under Te Tiriti o Waitangi. Therefore, representation from Māori and Pacific members was a priority, both on the Scientific Advisory Group and on the Steering Group. There was a commitment to acknowledging the inequities in outcomes for Māori and Pacific peoples impacted by neurodevelopmental conditions,[15] and to incorporating approaches that both reflected Māori and Pacific lived realities, alongside acknowledging harm secondary to colonisation, stigmatisation and racism.[16] Processes were examined and adapted in alignment with the consolidated criteria for strengthening reporting of health research involving indigenous peoples (CONSIDER statement).[17] This set of principles provide a framework for assessing and adhering to cultural safety within research studies.

Initially it was proposed to estimate a FASD screening prevalence as was done in the McQuire et al. study.[14] At meetings with the Steering Group and the Scientific Advisory Group, reservations were expressed about validity of this approach within the GUiNZ longitudinal cohort. It was therefore agreed to focus on the prevalence of children in the GUiNZ cohort that present with neurocognitive difficulties, that may be related to FASD, and who might benefit from further assessment.

Measures from the GUiNZ data collection waves were selected to cover the neuropsychological domains of FASD as comprehensively as possible, alongside prenatal alcohol exposure. Preference was given to the NIH Toolbox Cognition Battery[18–20], Strengths and Difficulties Questionnaire (SDQ),[21,22] and Vineland Adaptive Behaviour Questionnaire,[23,24] social domain. The domain of neuroanatomy/ neurophysiology was not included because GUiNZ data do not include head circumference measurements. Thresholds were determined based on available norms; if not available they were set at the distribution of the participant data within GUiNZ. The prevalence of those children that might need assessment for FASD or other neurodevelopmental impairments was planned to be analysed by combining the number of children with neurocognitive impairments using the NIH Toolbox, Vineland Adaptive Behaviour Questionnaire and SDQ plus or minus alcohol exposure, based on Leading Lights screening criteria for inclusion in case ascertainment, divided by the total number of children in the cohort sample. A multivariate generalised logistic model was

developed of the primary outcomes, adjusting for key socio-demographic characteristics, and known confounders of FASD in children.

1.3   Key findings

- We identified a group of children with developmental difficulties irrespective of maternal alcohol consumption, with a higher burden in Māori and Pacific children.

- There was no association between prenatal alcohol exposure and neurocognitive outcomes in children at age 8 years in the GUiNZ longitudinal study cohort. This is unexpected and in contradiction to the evidence in the international literature which clearly documents adverse neurocognitive outcomes after prenatal alcohol exposure.

- The alcohol exposed groups did not have significantly greater odds of having more than one impairment compared to the non-exposed group.

- In several measures there was a trend towards less frequent impairment in the groups with 'exposure pre-pregnancy/before knowledge only' and 'up to 3 drinks per week'. However, the odds ratios for impairment across most of the measures of neurocognitive or behavioural impairment were not statistically significant, with the exception of the reading measure.

- Using a cut-off of 1.5 SD below the mean, 4.0% of the cohort had 3 or more impairments, and 10.7% had 2 or more impairments, irrespective of alcohol exposure. Using a cut-off of 2 SD below the mean, 1.2% had 3 or more impairments and 5% had 2 or more impairments irrespective of alcohol exposure.

- For Māori and Pacific participants:

    - A higher proportion of Māori (13%) and Pacific (10%) mothers reported having four or more drinks per week during pregnancy than European (7%) and Asian (2%) mothers.

    - A subgroup analysis of the distribution of alcohol exposure across outcome measures for Māori, Pacific, Asian and European participants found no consistent pattern.

    - In general, Māori and Pacific participants indicated a higher number of impairments, whether alcohol exposed or not. At a cut-off of 2 SD below the mean, 4.2% of European children and 3.7% of Asian children had 2 or more impairments, compared to 9.1% of Pacific, and 7.1% of Māori children.

- 8.1% of all respondents had one reported condition (ADHD, ASD, or learning difficulties), 1.3% had two of these conditions (ASD and ADHD or ASD and learning difficulties or ADHD and learning difficulties). None of the combinations reached a significant odds ratio when comparing the alcohol exposed groups to the non-exposed group.

- The odds ratios for prenatal alcohol exposure related to having experienced household challenges were significantly elevated for drug taking or alcoholism in the immediate family in the '4 drinks per week or more' group. Odds ratios were significantly elevated for prenatal alcohol exposure related to conflict between parents in all levels of alcohol exposure groups.

- Multiple logistic regression analysis on the interaction effect between alcohol exposure and household challenges on impairments showed that the effects of alcohol exposure and household challenges on impairment are independent from each other.

The use of these research findings to estimate the prevalence of FASD is limited by the inability of collected longitudinal research data to replicate the data gathered during clinical assessments, including a reliable alcohol use history. There are also gaps in data for key neurocognitive domains of FASD, as well as absence of facial dysmorphology measurements for the cohort.

Key strengths of this analysis include the involvement of the Steering Group and Scientific Advisory Group and alignment with the consolidated criteria for strengthening reporting of health research involving indigenous peoples (CONSIDER statement).

1.4   Recommendations

- Children with developmental difficulties, irrespective of maternal alcohol consumption, may present with complex developmental profiles but may not meet the criteria for disability services. However, they should be assessed to ascertain their neurodevelopmental strengths and vulnerabilities.

- More resources and better support are needed for children and families impacted by neurodevelopmental difficulties (whether due to alcohol exposure or not). This is particularly the case for Māori and Pacific families and children, who are disproportionately impacted.

- To estimate the prevalence of FASD in NZ a full population-based case ascertainment study following a protocol such as that of the WHO, is recommended.

- A smaller case ascertainment prevalence study (e.g. in schools) would be less costly and less complex to conduct than a full population-based prevalence study but would be limited in the generalisability of its findings by the sociodemographic characteristics of the school catchment area/population.

- It would be informative to determine prevalence in high-risk population groups, such as children in care, youth justice, alternative education, and other high-risk groups.

2. Introduction

Alcohol exposure during pregnancy is known to be associated with a range of neurocognitive difficulties which can affect people throughout their lifetime.

Fetal Alcohol Spectrum Disorder (FASD) is a prevalent disorder, outnumbering other common developmental disabilities such as autism spectrum disorder, which according to the World Health Organisation has a prevalence of about 1%. However, FASD comes with relatively little public recognition or understanding.[25] Older data suggested a global prevalence just below 1% for the FASD spectrum.[26] A meta-analysis on the global prevalence of FASD in 2017[4] found that the prevalence of FASD exceeded 1% in 76 countries. The highest rates were found in South Africa (11.1%), Croatia (5.3%) and Ireland (4.7%). More recent case ascertainment population studies confirm FASD prevalence rates above 1%. A study in Canada[1] found a population-based prevalence of FASD of 2-3% among elementary school students. Another study in the USA found a prevalence estimate of 1.1- 5%.[2] In a small-scale case ascertainment study in the UK the prevalence of FASD was 1.8 – 3.6%.[3] Special subpopulations such as children in care, correctional services, special education have much higher rates.[5]

Data on the prevalence of FASD in Aotearoa New Zealand are not yet available. Various publications however have consistently shown that the incidence of antenatal alcohol exposure in New Zealand is high.[6–9] About one in four women continue alcohol use after pregnancy recognition. This is higher than in the USA, where 10.2% of pregnant women report drinking in the last 30 days.[27] Therefore, it is safe to assume that the prevalence of FASD in Aotearoa New Zealand would be at least equal to the American or Canadian estimates, meaning more than 1%, and possibly up to 5% of the general population. In specific subpopulation groups one can expect this to be much higher.

The *Growing Up in New Zealand* (GUiNZ*)* longitudinal cohort study recruited 6822 pregnant women living within the Auckland, Counties Manukau or Waikato DHB regions who were due to have their babies between 25th April 2009 and 25th March 2010. The subsequent child cohort consisted of 6853 children, whose birth parameters closely aligned to all Aotearoa New Zealand births in 2007 – 2010 and who are broadly generalisable to Aotearoa New Zealand births in that same time period.[28,29] The recruited cohort provided adequate statistical power to undertake complex analyses of interlinked developmental trajectories over time across the whole cohort of children as well as within the Māori, Pacific and Asian subgroups of children (at least 1000 children in each of these subgroups). Since its inception, five major data collection waves (DCWs) have been completed for the *GUiNZ* cohort (late

pregnancy, 9 months, 2 years, 4.5 years, 8 years). A sixth major DCW is in process since 2021, with the children now being approximately 12 years of age.

There was greater attrition at the 8-year data collection wave for *GUiNZ* compared to previous DCWs with retention lowest for Pacific (59%), Māori (73%), Middle Eastern/Latin American/African (71%), Asian (76%) then European (93%).[30] Studies of alcohol use during pregnancy show that Māori and Pacific women have higher rates of drinking during pregnancy,[7] therefore high risk groups are likely under-represented in this cohort. Prevalence studies for FASD are typically conducted via a case ascertainment method. The World Health Organisation (WHO) has set up an excellent study protocol for this approach, and several countries have followed the protocol. However, the method is costly and funding in Aotearoa New Zealand has not been prioritised for this exercise.

In 2018, the Ministry of Health (MOH) commissioned *GUiNZ* and a group of clinicians to conduct a pilot study to investigate the feasibility of a case ascertainment study within the *GUiNZ* cohort. The pilot study was done with the Leading Lights (LL) group of children. This is a group of around 200 children recruited in the same way as the main GUiNZ cohort. Information from the LL group is used to ensure study methodologies for the main cohort are fit for purpose.

During the conception of the LL study a teleconference was held with international experts where a discussion occurred around what domains were most useful for screening of children who would subsequently be offered full FASD assessment. There was an agreement that the four most important domains were intelligence, adaptive function (particularly social communication), problem behaviour, and dysmorphology. Inclusion of more domains would lead to loss of sensitivity.

Following those discussions, the Vineland Adaptive Behaviour Scales (socialisation domain) was included within the child-proxy questionnaire at the 8-year Data Collection Wave. The National Institute of Health (NIH) Toolbox Cognition Battery and Strengths and Difficulties Questionnaire (SDQ; behaviour) were already part of the planned GUiNZ 8-year DCW and were retained. Screening criteria for children who would be offered full assessment were based on outcomes of these measures. Screening cut off was set at –1.5SD. This was deemed a reasonable cut-off to avoid having too many false negatives in the screening. It is also the cut-off for impairment in the Hoyme criteria for FASD diagnosis. The LL children also received facial photography to measure the facial features that can be associated with FASD.

The FASD project with the LL group showed several difficulties:

- Consent rates to re-contact families whose children met the screening criteria and

consent rates for full FASD assessment were low.

- The case ascertainment methodology was time consuming. Children spent up to 10 hours attending their appointments and clinicians and developmental coordinators spent around 16 hours per completing participant, including assessments, documentation and feedback time.

- At review only 12% of children had photos of sufficient quality to be able to quantify the three facial features associated with FASD. Therefore, the facial photography was not used in the LL analysis.

The outcome of the LL FASD pilot project was that in the environment of the *GUiNZ* cohort, face-to face FASD assessment for children who would meet screening criteria would not be feasible. Determination of FASD prevalence in the *GUiNZ* cohort with case ascertainment methodology was therefore not deemed possible.

The participants of the main *GUiNZ* cohort did go on to complete the NIH Toolbox Cognition Battery, Vineland Adaptive Behaviour Scales (socialisation domain) and SDQ at the 8-year DCW.

The MOH subsequently commissioned Dr Jacquemard and *GUiNZ* to complete the current study, which examines neurocognitive outcomes of children with prenatal alcohol exposure in the *GUiNZ* cohort. MOH has a FASD Action Plan in place. In the *Summary of progress on the FASD Action Plan* of March 2022 it reports that this study will estimate the prevalence of children in the *GUiNZ* cohort that present with neurocognitive difficulties that may be related to FASD and would benefit from further assessment.

This study focusses primarily on the relationship between neurocognitive outcomes and alcohol exposure perinatally in the *GUiNZ* cohort data. It cannot provide individualised diagnosis for FASD, nor an estimate of how many participants may meet neurocognitive criteria for FASD.

3. Behaviour and neurocognition

The behavioural and neurocognitive challenges that people with FASD face have been well described. These difficulties present from a young age, with a pervasive pattern of behavioural and neurocognitive disturbances, which become more and more complex as a child grows up. A definitive neurodevelopmental profile for FASD has however not been established.[10] The main difficulties are diminished intellectual functioning (though not necessarily in the disabled range), slow information processing, disturbances of attention, deficits in executive function and working memory, language, visual perception, memory, learning and adaptive functioning (particularly the social domain). Performance is increasingly impaired with increasing task complexity.[31] These neurocognitive issues are associated with behavioural disturbance and emotional dysregulation.

FASD also appears to be the leading cause of Attention Deficit Hyperactivity Disorder (ADHD). In clinical practice, many children with FASD will be managed for ADHD at the same time. A diagnosis of FASD is associated with increased risk for ADHD (relative risk = 7.6; attributable risk 86.8 %). Conversely, a diagnosis of ADHD predicts increased risk for FASD (relative risk 13.28; attributable risk 92.5 %).[32]

This multitude of behavioural and neurocognitive difficulties makes the diagnostic process for FASD complex. In clinical practice one often will see behavioural and neurocognitive difficulties gradually escalate as a child moves through the primary school years. In Aotearoa New Zealand, most clinicians follow the Canadian guidelines[33] for diagnosis of FASD. For a diagnosis of FASD, these guidelines require severe impairment (>2SD) in three or more of ten neurodevelopmental domains: neuroanatomy/neurophysiology; motor skills; cognition; language; academic achievement; memory; attention; executive function including impulse control and hyperactivity; affect regulation; adaptive behaviour, social skills or social communication. These diagnostic criteria are similar in the Australian guidelines for FASD.[34]

There is reasonable consensus among professionals about the battery of psychometric tools required to assess a child for FASD. This is not the case for screening for FASD. Proposed FASD screening tools have limited evidence base supporting their psychometric properties.[11,12] Recent studies have nevertheless attempted to use psychometric screening tools to screen populations for FASD,[14] or to compare neurocognitive outcomes of children exposed to alcohol with non-exposed children.[35]

4. Literature review

In this literature review we will summarise only the most relevant articles pertaining to the subject of the study. Where available, we have given preference to metanalyses and systematic reviews.

4.1 Drinking in pregnancy

Patterns of drinking during pregnancy in Aotearoa New Zealand have been documented in several studies. Across these studies there is a consistent pattern, with around 80% of women drinking before pregnancy and 25% continuing to drink during pregnancy (Table 1). Ten percent are at substantial risk, with either binge drinking during pregnancy, or drinking levels of more than 2 drinks per typical drinking day, or more than 7 drinks per week.

Table 1: Drinking during pregnancy in Aotearoa New Zealand

Publication year	Author	Drinking pattern
2006	Ho[6]	80% of women drank before pregnancy, 66% binge drank. 28% continued during pregnancy. 10% >2 per typical day, or >7 per week. 4% more than this.
2013	Mallard[7]	82% of women drank before pregnancy. 24% continue after pregnancy recognition. 12% at high risk in early pregnancy. Māori and Pacific women more at risk.
2018	Rossen[8]	23% exposed 1st trimester, 13% after 1st trimester.
2020	McDonald[9]	19% of women never drank. 29% continued to drink during pregnancy. 10% binge drank during pregnancy.

4.2 Prevalence of FASD worldwide

There were six articles reviewed on FASD prevalence worldwide. More recent case population-based ascertainment studies show a higher prevalence than reported previously and converge on a prevalence of between 1 and 5% in North America and the UK. Higher rates are reported in some countries with higher drinking levels (Table 2). Much higher rates are also reported in high-risk subpopulations. Terminology regarding FASD may differ in various publications about prevalence, depending on the guidelines that were used at the time of the studies. The various terms used are: FASD (fetal alcohol spectrum disorder), FAS (fetal alcohol syndrome), pFAS (partial fetal alcohol syndrome), ARND (alcohol related

neurodevelopmental disorder).

Table 2: Prevalence FASD worldwide

Publication year	Author	Study	Prevalence
1997	Sampson[26]	Critique	Combined rate of FAS and ARND of at least 9.1/1000 in Seattle for the period 1975 – 1981.
2017	Lange[4]	Systematic review	Global prevalence in children 7.7 per 1000. European region 19.9 per 1000. South Africa 111 per 1000.
2019	Popova[5]	Systematic review	Prevalence in children in care, correctional, special education, specialized clinical, and aboriginal populations 10 – 40x higher than in the general population.
2018	May[2]	Case ascertainment	Prevalence 3.3% children in 4 regions in USA. Range estimate 1.1-5%.
2019	Popova[1]	Case ascertainment	Prevalence 1.8% in students 7-9 years old in Ontario. Estimated range in this population 2-3%.
2021	McCarthy[3]	Case ascertainment	Prevalence 1.8% in students 8-9 years old in UK. Possible rate 3.6%.

4.3 FASD Diagnostic Guidelines

FASD guidelines have been developed in a few countries, including USA, Canada, Australia, and UK (Scottish Intercollegiate Guidelines network) (Table 3). Regarding diagnostic criteria the Australian and Scottish guidelines are by and large similar to the Canadian diagnostic guidelines of 2016.

Table 3: FASD Guidelines

Publication year	Author / Country	Comments
2005	Canada Chudley[36]	Harmonization of the 4-digit diagnostic codes of the University of Washington with the IOM (Institute of Medicine) terminology of FAS, partial FAS, ARND

Publication year	Author / Country	Comments
2005	USA Hoyme[37]	Terminology FAS, partial FAS, ARND.
2016	Canada Cook[33]	The diagnostic terminology is simplified into FASD with and without sentinel facial features. Growth is no longer a diagnostic criterion. Impairment (>2SD) in at least 3 of the 10 neurodevelopmental domains is required.
2016	USA Hoyme[38]	Maintain the terminology of the IOM (FAS, partial FASD, ARND), and the cut-off for developmental impairment is set at 1.5SD.
2017	Australia Bower[34]	Same diagnostic terminology and impairment cut-offs as the Canadian guideline
2019	UK SIGN[39]	Same diagnostic terminology and impairment cut-offs as the Canadian guideline

4.4   Neurocognitive and behavioural aspects of FASD

Numerous literature reports describe the neuropsychological and behavioural aspects of FASD. There is a pattern of pervasive neuropsychological difficulties with increasing difficulties with more complex tasks, deficits in executive function and in adaptive function (social domain) (Table 4). No definitive neuropsychological profile has been established.

Table 4: Neurocognition and behaviour in FASD

Publication year	Author	Type of study	Outcome
2009	Kodituwakku [40]	Review	Lower IQ, slow information processing, disturbances of attention, deficits in executive function, language, visual perception, memory, learning, and social functioning. Generalized deficit in processing and integration of information.
2011	Mattson[41]	Review	Diminished intellectual functioning, poor learning and memory, impaired executive and visual-spatial function, delayed motor and language development, and attention difficulties. Increased internalizing and

Publication year	Author	Type of study	Outcome
			eternalizing behaviour problems. High rate of comorbid psychiatric disorders. More impairment in complex tasks.
2013	Coriale[42]	Review	Majority does not have intellectual disability. They show executive function deficits, verbal memory deficits, language (comprehension), deficits on visual motor testing, and attention deficits. Secondary disabilities are legal problems, academic difficulties, dysfunctional behaviours, and emotional problems.
2014	Kodituwakku[31]	Review	Deficits in reflective orienting responses and associative learning. Performance decrements with increasing task complexity. Deficient adaptive skills, particularly social domain. Deficits in executive functioning. Behavioural and emotional regulatory problems.
2017	Lange[10]	Systematic review	Behavioural ratings by parents/caregivers have good sensitivity (63 to 98%) but varying specificity (42 to100%). Subtest scores from standardised test batteries have good specificity (72 to 96%) but varying sensitivity (60 to 88%). Definitive neurodevelopmental profile for FASD had not been established.
2020	Crawford[43]	Teacher rating, case control	Social cognition was the only independent predictor of teacher rated adaptive functioning even after including IQ, executive functioning, and adverse childhood experiences into the model.

4.5   Screening for FASD

Attempts have been made to investigate screening tools for FASD. There is however no universally accepted screening approach to FASD. We looked at two recent systematic reviews (Table 5).

Table 5: Screening for FASD

Publication year	Author	Study	Outcome
2021	Grubb[11]	Systematic review	Range of markers, dysmorphic facial features, and biomarkers. The evidence base is weak, with significant risk of bias. They caution against implementing FASD screening tools.
2022	Lim[12]	Systematic review	Screening tools performed well in the identification of individuals at risk for FAS, whilst the screening tools varied in the identification of individuals at risk of FASD.

4.6 Primary measures: Vineland Adaptive Behaviour Questionnaire, SDQ, NIH Toolbox cognition battery

Apart from the Vineland Adaptive Behaviour Questionnaire, all other measures in this study were part of the *GUiNZ* 8 Year Data Collection Wave protocol, and not specifically added for this study.

The Vineland Adaptive Behaviour Questionnaire is one of the psychometric tools that is routinely used in the diagnostic assessment of FASD. As such it is an accepted tool used in FASD assessment, for that reason it was added at the 8 year data collection wave, and is well justified for use in this study.

Lees[35] used the NIH Toolbox in their study, which we discuss in the section below on 'FASD in longitudinal cohort studies'. We have found no other studies that used the NIH Toolbox for FASD research. Important in the context of our study is that we have not used the NIH Toolbox Cognition Battery Global Cognition Composite score as it has been shown not to be a valid measure. Cognitive functions are more distinguished at age 8 years and it is recommended to look at the individual measures instead, especially for different ethnic subgroups.[19]

There are a number of cohort studies that have used the SDQ to assess children that have been exposed to alcohol (Table 6). Torshizian[44] looked at SDQ at 4.5 years of age in the *GUiNZ* cohort. Chu[13] did this again for the GUiNZ cohort at 8 years of age. A few other cohort studies have used the SDQ in their analysis. These studies are detailed in Chu's systematic review of longitudinal cohort studies that evaluated the impact of PAE on neurocognitive outcomes (submitted for publication).

Table 6: Strengths and Difficulties Questionnaire (SDQ)

SDQ			
Year	**Author**	**Type of study**	**Outcome**
2013	Alvik[45]	Retrospective Cohort study	Binge drinking up to 4 weeks after conception had a direct predictive effect on SDQ symptom scores in 5.5-year-olds.
2021	Torshizian[44]	Unpublished report. GUiNZ	Drinking during first trimester increases all SDQ subscales.
2022	Chu[13]	Unpublished report GUiNZ.	No significant differences in affect regulation. Association of PAE with a significantly increased risk of abnormal scores on two of the SDQ subscales among Māori mother (i.e., emotional and peer problems).

4.7   FASD in longitudinal cohort studies

The three studies below are reviewed in more detail, as they have relevance to the topic of this report.

McQuire[14] attempted to estimate a screening prevalence of FASD in the UK. Data were from a population-based cohort study (ALSPAC), which recruited pregnant women (total 14,541) with delivery dates between 1991 and 1992 from the Bristol area of the UK. They had 13,495 eligible participants. They used the Canadian guidelines for FASD (2005) to create FASD screening algorithms. They paired neurocognitive domains of the Canadian guidelines with behavioural and neurocognitive measure that were available for these children.

6.0% of children screened positive for FASD in the analysis that used the single imputation method (total N = 13,495), 7.2% in complete case analysis (total N = 223) and 17.0% in the analysis with multiple imputed data (total N = 13,495). They used a range of measures, including amongst others, WISC III short form, WOLD (Wechsler Objective Language Dimension), PALSC (pupil annual level school census), TEA-Ch (Test for Everyday Attention in Children)- sky search task, SDQ and SCDC (Social Communication Disorders Checklist). A positive FASD screen was more common among children of lower socioeconomic status and children from unplanned pregnancies. They concluded that their analyses showed that the complete case and single imputation methods that are commonly used in FASD prevalence studies are likely to underestimate FASD prevalence.

Lees[35] published a retrospective analysis testing for associations between reported maternal prenatal alcohol use and psychological, behavioural and neurodevelopmental outcomes in youth.[21] Participants were 9,719 youths (ages 9.0 to 10.9) from the ABCD (Adolescent Brain Cognitive Development) study, of which 25.9% were exposed to alcohol in utero. The ABCD study is a longitudinal study of a cohort of children (11,875 participants), born between 2005 and 2008. They used a variety of tools, including the CBCL (Child Behaviour Checklist), NIH Toolbox, and other measures for psychological and behavioural variables (mainly rating scales). They found that prenatal alcohol exposure of any severity was associated with greater psychopathology, attention deficits and impulsiveness, with some effects showing a dose-dependent response.

Chu[13] undertook a systematic review of longitudinal cohort studies that evaluated the impact of PAE on neurocognitive outcomes (submitted for publication). They identified 30 cohort studies (N=299,572) meeting criteria. The most common domains evaluated were affect regulation and cognition (i.e., IQ). Overall, the findings on the impact of PAE on neurocognitive outcomes were mixed across domains within the studies reviewed. None of the identified studies found evidence of the effect of PAE on executive function, but there were varied effects for motor skills (i.e. fine and gross motor movements), cognition, language, attention, affect regulation (i.e. expression of emotions) and adaptive behaviour (i.e. skills to function in everyday life). The most consistent adverse effect of PAE on a specific domain was the domain of affect regulation.

4.8   Antenatal alcohol exposure and *GUiNZ*

A few studies have looked at children that were alcohol exposed in pregnancy in the *GUiNZ* cohort. They are summarised in Table 7.

Table 7: *GUiNZ* Studies related to alcohol exposure

Publication year	Author	Topic	Outcome
2018	Rossen[8]	Alcohol consumption	23% exposed 1st trimester, 13% after 1st trimester. The odds of drinking alcohol during the first trimester were higher for women who were European or Māori with no secondary school qualification, in their first pregnancy, or with an unplanned pregnancy.

Publication year	Author	Topic	Outcome
2021 Unpublished	Torshizian[44]	SDQ at 54 months	Drinking in the first trimester negatively impacted on the child's development irrespective of the amount consumed. Drinking during the first trimester increased all SDQ subscales, indicating behavioural problems. The relationship between drinking in pregnancy and the child's developmental outcomes was confounded by many factors which were themselves heavily inter-related.
2022 Unpublished	Chu[13]	SDQ at 8 years	The authors found no significant differences in affect regulation at 8 years between exposure categories after controlling for confounders. No significant difference in affect regulation at 8 years with different levels and timing of exposure. Among Māori mothers they found an association of prenatal alcohol exposure with significantly increased risk of abnormal scores on two of the SDQ subscales. No significant associations among Pacific mothers were found.
2022 Submitted	Russell[46]	Developmental health profiles at 4.5 years	3.6% of children had developmental difficulties as their indicators of developmental health mean scores were low or lowest of any of the other developmental health profiles. No profile was statistically associated with maternal consumption of alcohol in first trimester, although trend was for slightly increased adjusted OR (~1.09) for children to have developmental difficulties, and slightly reduced adjusted OR (~0.89) for children to have a flourishing developmental profile.

5. Study aim and research questions

The overall aim of the study was to investigate the impact of antenatal alcohol exposure on neurocognitive outcomes in children and estimate prevalence of those children that might need assessment for FASD or other neurodevelopmental impairments, in the *GUiNZ* cohort at 8 years.

The research questions were:

1. What are the neurocognitive outcomes at 8 years for those children in the *GUiNZ* cohort exposed to alcohol antenatally compared with those not exposed?

2. What is the prevalence of children in the *GUiNZ* cohort that present with neurocognitive difficulties, that may be related to FASD and benefit from further assessment?

3. Are there any trends when comparing the data at 8 years of age to previous data collection points?

5.1 Study set-up

The study was commissioned by the Ministry of Health and set up as a collaboration between Dr Jacquemard, *GUiNZ*, and the University of Auckland. It was scheduled to run from 30 June 2021 to 30 June 2022.

A Steering Group and Scientific Advisory Group were constituted to guide the direction of the study. The groups met at key stages during the project via video conference.

The role of the Steering Group was to oversee the development and implementation of the research and advise on strategic decisions. The group had representation from a broad range of stakeholders, including people affected by FASD and health professionals.

The steering group consisted of:

- Principal investigator

- Co-investigators *GUiNZ*

- MOH representative

- Māori health expertise

- Pacific health expertise

- Consumer representative (families affected by FASD)

- Alcohol Healthwatch representative
- Clinician

The Steering group was tasked with the following:

1. Supporting the Research team in the development and direction of the study, in particular in relation to cultural safety and appropriate research activities.

2. Providing direction and oversight in the development and implementation of project deliverables.

3. Approving the project plan, delegations and associated timeline and maintain oversight of any subsequent amendments.

4. Ensure adequate audit, monitoring and evaluation of study progress in relation to Māori and Pacific participants and offer feedback and guidance on related issues, ensuring that adequate changes were made in relation to monitoring and evaluation, to improve responsiveness and cultural safety of the study for Māori and Pacific participants.

The role of the Scientific Advisory Group was to ensure that scientific rigour was applied throughout the project. The group had representation from a range of persons with research experience.

The Scientific Advisory Group consisted of:

- Principal investigator
- Co-investigators *GUiNZ*
- Ministry of Health representative
- FASD clinicians and researchers (Māori and tauiwi)

The Scientific Advisory Group members were tasked with the following:

1. Reviewing and advising the research team on the study design and research methods;
   a. Guidance on research framework
   b. Review of analysis plan
   c. Consensus agreement on scales and cut offs matching FASD diagnostic criteria
   d. Review of analyses once completed

2. Ensuring research activities were culturally safe, ethical and appropriate

3. Responding to any issues that arose during the course of the study that related to

matters such as concerns about research quality, participant safety or data integrity and sovereignty.

4. Reviewing and advising on the outcomes of the study, including reports and publications that may result from it.

This project was committed to being responsive to Māori and Pacific peoples, and to meet our responsibilities under Te Tiriti o Waitangi (the Treaty of Waitangi). Therefore, representation from Māori and Pacific members was a priority, both on the scientific advisory group and on the steering group.

5.2   Responsiveness to Māori and Pacific peoples

In order to best address inequities in health outcomes for Māori and Pacific peoples,[15,47] and to avoid distrust,[48] researchers must consider how to incorporate approaches which reflect Māori and Pacific lived realities. This includes acknowledging harm secondary to colonisation, stigmatisation and racism, and consciously ensuring Māori and Pacific leadership, participation and priorities are central to research processes.[17]

When it comes to neurodevelopmental disorders, including those related to alcohol exposure, such as FASD in Aotearoa New Zealand, the inequities are stark, and have large implications for health, education, justice and social services.[16,43,49] The disproportionate impact on Māori is a breach of Te Tiriti o Waitangi and has wider ramifications due to the lack of health, education and social supports available for Māori children.[50] Additionally there is a history of stigmatising Indigenous communities based on FASD prevalence, rather than attributing this harm to the historical and generational trauma of colonisation.

In research investigating children impacted by neurocognitive outcomes related to alcohol there has been a little effort to incorporate Indigenous approaches, and these efforts are often in conflict with the academic system and its priorities.[49] In a recent global review of literature describing Indigenous experiences of people with prenatal alcohol exposure and FASD, there was only one study from Aotearoa New Zealand, which met criteria for inclusion.[49] This is in contrast with the priority placed on including cultural considerations/sensitivity/safety/inclusivity within research in FASD. One fifth of stakeholders interviewed about priorities for review of Australian assessment guidelines placed cultural consideration as important for reviewing content of assessment guidelines.[51]

6.   Consider statement

This study investigating neurocognitive outcomes related to prenatal alcohol exposure in the *GUiNZ* cohort, examined and adapted processes in alignment with the consolidated criteria for strengthening reporting of health research involving indigenous peoples (CONSIDER statement).[17] This set of principles provide a framework for assessing and adhering to cultural safety within research studies.

The CONSIDER statement contains eight research domains and 17 criteria for the reporting of research involving Indigenous Peoples. The CONSIDER statement aims to strengthen research practices and reporting to enhance research conduct and dissemination to support indigenous health equity. The checklist includes the research domains of (i) governance; (ii) relationships; (iii) prioritization; (iv) methodologies; (v) participation; (vi) capacity; (vii) analysis and findings; and (viii) dissemination.[17] The CONSIDER statement was used to reflect on key aspects of this study's alignment with reporting of research and are summarised in Appendix 1.

6.1   Domain One: Governance

Partnerships and governance were developed on the foundations of *GUiNZ's* Kaitiaki principles[48] which are a set of 12 high level principles developed by the Māori Kaitiaki group at the inception of the study[29] and the Māori and Pacific governance by way of advisory groups and GUiNZ theme leaders. GUiNZ endeavours to adhere to the principles of Te Mana Rauranga (Māori Data Sovereignty) and the emerging Pacific Data Sovereignty work through the Kaitiaki principles, including placing a kaitiaki section in the data access processes. For this study, investigating the relationship between prenatal alcohol use and neurocognitive outcomes, two advisory groups were set up: a scientific advisory and a steering group. It was a priority in both groups to ensure Māori and Pacific experts and community leaders were included in these groups. Part of the remit of these groups was to advise on research activities being culturally safe, ethical and appropriate. Advisors were included based on expertise, alongside relationship to the research team and other advisors. This ensured partnership was not symbolic, but rather operationalised through continued discussion, sharing and listening. Ideally there would have been Māori and Pacific researchers in the core team and more Māori and Pacific in the advisory groups to ensure there is a safe space for all Māori and Pacific researchers and advisors. This ability to ensure good representation of Māori and Pacific researchers and advisors is limited by structural and systems barriers due to lack of capacity and the system to build the capacity.

The research team was cognisant of the historical harms caused by researchers and their

organisations, due to lack of recognition of the impacts of colonisation and ensuring processes uphold the Te Tiriti o Waitangi.[17,48,49] Consideration of these harms was documented in the research analysis plan (Box 1) and discussed at length by the team and advisory groups. In response to concerns raised by key experts, analysis approaches and language were significantly adapted throughout the project timeline. A helpful adjustment may have been to have a mid-project review of terms of reference for advisors to ensure expectations were aligning.

6.2   Domain Two: Prioritisation

Although the research project was commissioned by the Ministry of Health, research aims were formed and then adapted by the steering and scientific advisory groups, which included Māori and Pacific experts. Before the start of the project, it would have been helpful to ensure greater consultation and input had occurred to confirm this was a wanted and needed study.

6.3   Domain Three: Research relationships

GUiNZ Kaitiaki principles focus on equity, Te Tiriti o Waitangi and Kaitiakitanga (guardianship) and these principles guide the appropriate and safe collection, storage, analysis and use of Māori data and knowledge.[48] The Kaitiaki and Pacific advisory groups, alongside the *GUiNZ* theme leads ensure that the approach of the *GUiNZ* study is consistent with the Kaitiaki principles, and that the collection, storage, analysis and use of knowledge is compatible with Māori and Pacific development goals and aspirations. For this study using *GUiNZ* data, consultation with the advisory groups including individual hui with experts was essential and this would have been enriched by more resource and time for Māori and Pacific guidance and advice in the formation of the study prior to study approval. The study team developed a positionality and commitment statement (Box 1). We acknowledge there is always more work to do for every Tangata Tiriti researcher to improve their approaches for Indigenous health and research.

> **Box 1: Team positionality and commitment statement**
>
> *The core study team consists of Tangata Tiriti who acknowledge their limitations in understanding and speaking for the lived experience of Tangata Whenua. We approach this project from our own worldviews and positionality, which includes clinical work and community-based interactions. We are committed to being responsive to Māori and Pacific and to meet our responsibilities under Te Tiriti o Waitangi in the study design, analysis, interpretation and reporting on examining neurocognitive outcomes related to alcohol exposure in Tamariki in Aotearoa New Zealand. We will do this by consulting with and listening to our Māori and Pacific experts throughout the project. Tangata Pākehā and Tauiwi working on this project are committed to implementing Māori and Pacific principles of health and health research under the guidance of our Māori and Pasifika experts.*
>
> *Ethnicity will not be used as an explanatory variable, but rather as the marker for socially constructed disadvantage that it represents. We recognise these data are precious and represent time and lived experience for these participants. In response we will treat the data with respect and care, with the aim that these findings will add to the considerable good done for wider communities and future generations. Privacy and protection of the participants will be upheld. Considering the anecdotal reports of burden of FASD prevalence in Māori we see it as our responsibility to expose inequities of resource for tamariki and rangatahi affected. We will be incorporating appropriate frameworks, based on the direction of our steering group and scientific advisory.*

6.4   Domain 4: Research methodology and methods

Methods for data analysis in this study were developed based on previous research in the neurocognitive outcomes related to prenatal alcohol exposure field.[14,35] These methods were adapted considerably in the course of the study based on concerns raised by experts, particularly related to validity, specifically cultural validity of tools used and representation within the data, alongside adapting wording to be more realistic regarding the ability of the study to describe prevalence of those that might require further assessment for FASD, rather than those that would have a definite diagnosis of FASD. This improved the trust and sense of safety in the project both for the research team and the advisory groups.

Careful consideration was made as to how to ensure Māori and Pacific data were visible in the study, but in a way which was not stigmatising. As such the selection of total response ethnicity variable for descriptive sub-group analysis of the different ethnic groups was used to ensure full inclusion of all those who identified with each ethnicity for sub-setting and descriptive analyses. For regression modelling analysis, externally prioritised ethnicity was used as a covariate. We recognise that ethnic identification is multi-dimensional and context

specific.[52] These variables were complimented by wider sociodemographic variables which could speak to the impact of environment including socioeconomic status and exposure to trauma. Consideration of including more indicators or proxies for inequity, racism and colonisation would have enriched the analyses if time and resources allowed.

6.5   Domain 5: Research participation

The research team recognised the need to ensure the burden on Māori and Pacific experts was as minimal as possible, while also ensuring maximum engagement and input, due to the "cultural double shift" that is commonplace.[53] This was outworked by limiting advisory meetings to four across the year of the study and by making time to dialogue outside of the meetings if required as well. The burden on Māori and Pacific advisors requires greater numbers on advisory boards and in research teams to spread the load, however structural and systems barriers further impede progress on this. Ideally a national research advisory for FASD/neurodevelopmental disorders would be worthwhile to ensure further efficiency for advisors being asked to be on multiple projects.

6.6   Domain 6: Research capacity

Time was made to process reflections and statistics with experts individually where required. These relational and responsive interactions between Tauiwi team members and indigenous team members provided for collaborative and mutual learning opportunities.

Individual team members sought learning opportunities to upskill in responsiveness to Te Tiriti o Waitangi, understanding of ethnicity variables and professional supervision with colleagues. Two of the team members were actively supporting the Culture & Identity, and Māori, Pacific and Asian themes of the *GUiNZ* study and had opportunities for continual learning via feedback from the experts within these domains and themes. It is important for tauiwi to acknowledge that there is no 'arrival' at cultural safety or competency and therefore there is a continual need for further upskilling on suitable frameworks, cultural safety and competency.

6.7   Domain 7: Research analysis and interpretation

A commitment was made pre-analysis, within the analysis plan, to avoid deficit and stigma-based approaches (Box 1). Before, during and after the analysis advisors were able to feedback on statistical plans and approaches. Experts were specifically consulted throughout the project including on the design, analysis plan and report write up. Emphasis was placed on reducing stigmatisation for whānau impacted by neurocognitive outcomes related to

alcohol harm, by acknowledging the historical trauma and breaches of Te Tiriti o Waitangi.

6.8   Domain 8: Research dissemination

The process of dissemination will be via government reports, research publications and presentations. Specific reach to Māori and Pacific stakeholders will be via experts in the advisory groups. Committing to write up the process by which this project included CONSIDER checklist items is a contribution to future research projects, wishing to integrate and thoughtfully adhere to methods which are led or are in partnership with Māori and Pacific and Tauiwi. Ideally dissemination would occur directly to the communities impacted by neurodisability in a way that is not stigmatising. In the future, building capacity and resourcing Māori research leadership and advisory for neurodisability is required to improve oversight and the ability to feedback research results.

The findings of this study are pointing towards the need for more investment into understanding the burden of neurodevelopmental disorders. They will be used to further advocate for more investment and policy to improve outcomes for people impacted. Ensuring the knowledge is in the right hands, and with those that can most advocate for and lobby for further resource and investment.

7. Methods

The initial discussions were about trying to estimate a FASD screening prevalence similar to the McQuire study.[14] At meetings with the steering group and the scientific advisory group reservations were expressed about this approach:

1. The scientific advisory expressed concern with the validity of some of the measures matched to domains, including the use of data from different developmental stages (Mcquire et al. used data scales from the same age group). It was also noted that previous research has found the developmental trajectories of the children aged 2-4.5 years are quite stable.[54] Children with low z-scores continue to stay in the same category, however before 2 years that position is unstable.

2. There were also concerns around the issue of discriminant validity particularly if using subscales from the same scale to measure different domains e.g. NIH Toolbox Cognition Battery across executive functioning, attention, and adaptive functioning.

3. The wording of prevalence and by proxy estimate screening was potentially overstating what the data is able to describe due to limitations in the datasets, such as limited coverage of all domains at age 8 years, no sentinel facial features data, no separate binge drinking variable and scales mainly being epidemiological rather than clinical.

Based on the feedback from advisory groups, reflections from the LL study and review of literature, the study team chose to develop and apply the analysis outlined below.

7.1   Participants

Children of the main cohort fulfilling the following criteria of selection were included in the study:

- Inclusions:
    - All singleton pregnancies
- Exclusions:
    - Children deceased at 1 year
    - Children with genetic conditions

7.2   Variables

Measures from the *GUiNZ* data collection waves were selected to cover the neuropsychological

domains of FASD as comprehensively as possible. Preference was given to the NIH Toolbox Cognition Battery, SDQ and Vineland Adaptive Behaviour Questionnaire (social domain). The domain of neuroanatomy/neurophysiology was not included as the *GUiNZ* data do not contain head circumference measurements. Motor skills are covered in the 4.5 year DCW, but not at the 8 year DCW. The other domains are all covered to a degree in the 8 year DCW. The measures used are summarised in Table 8.

Table 8: GUiNZ measures compared to Canadian FASD Guidelines (2016)

Neurocognitive domain	2-year DCW	4.5-year DCW	8-year DCW
Neuroanatomy/ Neurophysiology	No measure	No measure	No measure
Motor skills	Stack and topple task	Gross motor function scale	
Cognition			Pattern comparison processing speed test*
Language		Dynamic Indicators of Basic Early Literacy Skills (DIBELS) Parent Rating of Oral Language and Literacy (PROLL)	Oral reading recognition test*, Picture vocabulary test*
Academic achievement		Peabody picture vocabulary test (PPVT)	Harter scale, scholastic domain. Oral reading recognition*, Parental satisfaction with learning
Memory			Picture sequence memory test*, List sorting working memory*
Executive functioning, impulse control, hyperactivity			Dimensional change card sort test*, Hyperactivity subscale SDQ

Neurocognitive domain	2-year DCW	4.5-year DCW	8-year DCW
Attention			Flanker inhibitory control and attention test*, Mother report of ADHD at 8 years
Adaptive behaviour, social skills, social communication		Affective knowledge task total score, SDQ	SDQ conduct or peer problems, Vineland adaptive behaviour scales (social domain)
Affect regulation			SDQ emotional problems, Patient-Reported Outcomes Measurement Information System (PROMIS) T score for anxiety, Harter global self-worth scale

Footnote: Tests with * are part of the NIH Toolbox cognitive battery

Alcohol exposure

In the antenatal DCW of *GUiNZ* the questions asked were:

'On average how many drinks of alcohol did you drink per week: Before you were pregnant, in the first 3 months of pregnancy, after the first 3 months of pregnancy.'

The amounts were specified as: 'I did not drink alcohol', 'less than 1 drink per week', '2 drinks', '3 drinks', '4–6', '7–9', '10-14', '15-19', '20-39', '40 or more'.

A question regarding binge drinking was not asked.

The Canadian FASD guidelines (2016) specify that the threshold of alcohol exposure known to be associated with adverse neurodevelopmental effects is 7 or more (Canadian) standard drinks per week or any episode of drinking 4 or more drinks on the same occasion (binge). A Canadian standard drink is equivalent to 13.6g alcohol, which is found in 341ml 5% beer, 142ml 12% wine, or 43ml 40% alcohol. This corresponds well with what people in Aotearoa New Zealand would drink as a serving of alcoholic drink. We therefore set the cut-off for significant alcohol exposure at '4 drinks or more per week' as that would include any binge drinking. Sensitivity analysis was planned with a cut-off of 7 drinks or more to check if that would change the outcomes in comparison to 4 drinks or more.

The alcohol exposure groups were collapsed into the following four categories: 'No alcohol exposure', 'exposure pre-pregnancy or before knowledge of pregnancy only', 'up to 3 drinks per week' (any time during pregnancy), '4 drinks or more per week' (any time during pregnancy).

Vineland Adaptive Behaviour Questionnaire Socialisation domain (subscales relationships, play and leisure time and coping skills[12,13]

This standardised assessment tool was used to measure adaptive behaviour and support the diagnosis of neurodevelopmental conditions, administered in the *GUiNZ* 8-year DCW child proxy questionnaire. Included subdomains: Play and leisure time, Interpersonal relationships, Coping skills.

National Institute of Health (NIH) Toolbox for Assessment of Neurological and Behavioral Function Cognition Battery[14–16]

This is a standard set of cognitive measures as a brief assessment tool for large-scale epidemiologic and longitudinal studies and to allow for international cross-study comparisons.[18] The tool was used at 8 years, assessing six subdomains: executive function (with tests of cognitive flexibility and inhibitory control/attention), episodic memory, language, reading, working memory, and processing speed.[18] An evaluation of the psychometric properties of the NIH Toolbox Cognition Battery with the *GUiNZ* data suggests that it is preferable in the Aotearoa New Zealand context to use the individual raw/computed measures rather than composites and adjusted measures because the adjusted scales are normed to USA.[19]

Strengths and Difficulties Questionnaire (SDQ)

The SDQ is a tool used worldwide to screen children's psychosocial attributes. This scale measures emotional symptoms, conduct problems, hyperactivity/inattention, peer relationship problems and pro-social behaviour.[21,22] Additionally, an internalising subscale can be formed by combining the peer and emotional subscales and an externalising subscale can be formed by combining the hyperactivity and behavioural subscales.[55] The SDQ was used in the 2 year DCW and the 54 month DCW and was found to have good structural validity and internal consistency.[56]

Cognitive and language functioning at four and a half years

Cognitive abilities of the children were assessed using a range of different measures. To capture receptive language, a short adapted version of the Peabody Picture Vocabulary Test (PPVT) was used.[57,58] Furthermore, inhibitory control using the Luria hand clap task, a

modified version of Luria's Pencil Tapping task from the Luria-Nebraska Neuropsychological Battery was used.[59] To assess early literacy ability, the letter naming fluency task of the Dynamic Indicators of Basic Early Literacy Skills (DIBELS).[60] was administered as a standardized test of children's phonological awareness and early reading ability. Further, pragmatic language ability (communication over and above vocabulary) was assessed with the Parent Rating of Oral Language and Literacy (PROLL) which is an adapted version of Teacher Rating of Oral Language and Literacy (TROLL), a reliable and valid instrument measuring skills critical for speaking and listening.[61] To get a quick indicator of early academic skills at preschool age, the children's writing, numeracy and symbols ability was assessed with the Name and Numbers tasks from the Who Am I? Developmental Assessment.[62] The child is asked to write their name as well as to write down some numbers. Additionally, a Count up and Count down task as administered (the interviewer asking the child to count up from 1 to 10 as well as to count down from 10 to 1). It is noted that language is not considered a highly accurate or sensitive screening domain.

Stack and Topple task[63]

This task measures key aspects of a child's attention, inhibitory (self) control, motor control and social engagement. It was administered at age two years as part of the child observations.

Affective Knowledge Task[64]

This is a widely used emotional knowledge test. At 4.5 years a modified receptive/expressive task was used. Six faces portraying emotions were presented in random order and asked 'how does HE/SHE feel?'. 2 points were given for each correct emotion or acceptable synonym. 1 point was given for an incorrect emotion within similar emotional valence. 0 points were given for incorrect emotion within opposite emotional valence. Crawford (2018)[65] found that *'although IQ, executive functioning, social cognition and ACES were significantly correlated with teacher-rated adaptive function in an FASD group, when a multiple linear regression analyses was performed, social cognition, especially recognizing emotion on adults' faces, was the only significant independent predictor of teacher-rated adaptive functioning. This is important from a Te Ao Māori perspective as Māori society is built upon whakapapa and whanaungatanga which requires highly developed social and emotional skills.'*

Child Behaviour Questionnaire

GUiNZ used the Infant Behavior Questionnaire-Very Short form (IBQ-VSF) at 9 months. The CBQ-VSF30 used at 54 months is an age-appropriate continuation of the IBQ- VSF measuring

Gross Motor Function Scale

This is a selection of 11 items from the World Health Motor Development measure gross motor function at the age of 4.5 years.

Pre-existing diagnosed neuro-developmental conditions

Pre-existing diagnosed-neuro-developmental conditions were screened using questions asked at 9 months, 2 years, 3.5 years, 4.5 years and 8 years for conditions such as genetic disorders and neurodevelopmental conditions such as Autistic Spectrum Disorder and learning difficulties.

Self-concept and perceived competency – Harter Scale[31]

This full instrument taps five specific self-concept domains: Scholastic Competence, Athletic Competence, Social Competence*, Physical Appearance and Behavioral Conduct. In addition, a separate, sixth subscale, captures Global Self-Worth (or self-esteem). There are a total of 36 items, six for each subscale. Marsh found that students' self-concept in specific learning areas has a higher correlation with their performance in those learning areas than other self-concept measures, including general measures of academic self-concept.[66] Scholastic competence and global self-worth scales are available in the 8 year datasets.

7.3   Sociodemographic factors and co-variates

Sex at birth

Boy or girl as assigned at birth, based on data from the 6-week DCW.

Age

Calculated using the child's date of birth (as recorded at the 6-week DCW) and the date each child participated in the the eight-year data collection wave (as per the date stamp within the online survey).

Preterm delivery

Linked data to perinatal datasets.

Maternal age

Date of birth as reported by the mother antenatally and the date the mother participated in the 8 year DCW.

Child's ethnicity

As reported by the mother at the 54-month DCW. Total ethnicity was used for descriptive analyses. For inference statistical modelling, ethnicity was externally prioritised based on StatsNZ Level 1 ethnicity groupings, in the following order of priority: Māori, Pacific, Asian, Middle Eastern/Latin American/African, Other, European or Residual categories.[67,68] To ensure adequate cell size, participants were grouped according to categories for the current study: European; Māori; Pacific; Asian; Other

Socio-economic status

Determined based on the NZ deprivation index (NZDep) as an area-based measure of socioeconomic deprivation in Aotearoa New Zealand at 8 years.

Maternal education

Calculated using the mother's report of their education level at the antenatal DCW. Participants were grouped into one of the five categories: 'no secondary school qualifications'; 'secondary school/NCEA 1-4'; 'Diploma/Trade Certificate/NCEA 5-6'; 'Bachelor's degree'; 'Higher degree').

History of trauma

At 8 years the mothers were asked: Has {NAME} ever experienced any of the following? With answer options including: Death of a parent; Death of a close family member; Death of a close friend; Divorce/ separation of parents; Moving house; Moving country; Stay in foster home/residential care; Serious physical illness/ injury; Serious physical illness/ injury of a family member; Drug taking/ alcoholism in the immediate family; Mental illness in the immediate family; Conflict between parents; Parent in prison; Christchurch Earthquake; Natural disaster (other than Christchurch Earthquake); Other disturbing event, please specify. A *household challenges* variable was created based on the same categories in the Adverse Childhood Experiences study[69] which included 6 of the life event variables (Divorce/ separation of parents, Drug taking/ alcoholism in the immediate family, Mental illness in the immediate family, Conflict between parents, Parent in prison, Stay in foster home/ residential care).

7.3.1 Leading Lights (LL) inclusion criteria

The screening criteria for significant neurodevelopment/cognitive impairment for LL children were:

- Score of 1.5 SD below the normative score on at least two NIH Toolbox Cognition Battery domain tasks **or** on the NIH Toolbox Global Cognition composite score;

- **or** score of 1.5 SD below the normative score on the Vineland Adaptive Behaviour Scales socialisation domain

- **or** score in the abnormal range on the SDQ total difficulties score.

7.4   Preparation of scales and variables

Threshold levels

The threshold levels were determined based on discussions with the Scientific Advisory Group. They were based on 1) available norms for standardised tests or 2) norms in the research literature. If neither of those sources were available, we used the distribution of the participant data within *GUiNZ* (1.5 and 2 standard deviations (SD) below the mean for data that were normally distributed, and/or ≤ 3rd percentile for data with a skewed distribution as per McQuire.[21] Diagnostic guidelines specify 2 SD from the mean or below 3rd percentile, depending on the measure. However, when looking at screening for difficulties, we used 1.5 SD from the mean for the threshold of referring children for further assessment, as in the LL project (see Table 9 for thresholds used for screening for difficulties).

Table 9: Thresholds for screening for difficulties

Data collection wave	Outcome	Values	Cut-off
8-year	Vineland adaptative behaviour questionnaire	Range 51 - 127	Mean - 1.5 SD, Mean - 2SD
	NIH - Cognitive Flexibility	Range 1.5 - 9.88	Mean - 1.5 SD, Mean - 2SD
	NIH - Picture Vocabulary Test	Range -9.91 - 6.19	Mean - 1.5 SD, Mean - 2SD
	NIH - Flanker Inhibitory Control and Attention Test	Range 3.3 - 9.58	Mean - 1.5 SD, Mean - 2SD
	NIH - Oral Reading Recognition Test	Range -11.2 - 10.6	Mean - 1.5 SD, Mean - 2SD
	NIH - List Sorting Working Memory Test	Range 0 - 26	Mean - 1.5 SD, Mean - 2SD
	NIH - Picture Sequence Memory Test	Range -2.2 - 1.55	Mean - 1.5 SD, Mean - 2SD

Data collection wave	Outcome	Values	Cut-off
	SDQ - Emotional problems subscale	Range 0 - 10	>= 5
	SDQ - Peer problems subscale	Range 0 - 10	>= 5
	SDQ - Hyperactivity subscale	Range 0 - 10	>= 8
	SDQ - Conduct problems subscale	Range 0 - 8	>= 4
	SDQ - Prosocial behaviour subscale	Range 0 - 10	<= 6
	SDQ - Total difficulties scale	Range 0 - 31	>= 17
	Harter Scale - Global self-worth sub-domain score	Range 6 - 24	Mean - 1.5 SD, Mean - 2SD
	Harter Scale - Scholastic sub-domain score	Range 6 - 24	Mean - 1.5 SD, Mean - 2SD
	Satisfaction with child's processing in learning	1 - Very satisfied -> 9 -Completely dissatisfied	Low level of satisfaction – Fairly dissatisfied – completely dissatisfied
	PROMIS anxiety score	Range 32 - 84	Mean + 1.5 SD, Mean + 2SD
4.5-year	PPVT		Mean - 1.5 SD, Mean - 2SD
	DIBELS	Range 0 - 69	Children who could not name a single letter (score 0) vs all other children
	PROLL		25th Percentile
	Affective knowledge task	Range 0 - 12	<= 5 (standard norm)[56].
	Handclap task		Mean - 1.5 SD, Mean - 2SD
	Gross Motor Function Scale	Range 1 -5, 62 different values	Mean - 1.5 SD, Mean - 2SD

Data collection wave	Outcome	Values	Cut-off
	Child behaviour questionnaire		Mean - 1.5 SD, Mean - 2SD
2-year	Stack and Topple task		Score <= 2

Denominator

All mother-children dyads who completed the 8-year DCW.

Missing data

Imputation was considered for missing data based on McQuire et al.[14] Multiple imputation and single imputation methods were considered based on missingness. Imputation would have been very complex due to the number of measures being used at the 8-year DCW where there is greatest attrition. In this dataset there was a limited number of variables that could have been imputed as most had >50% missingness. Previous research[48] has looked at all cognitive outcomes from 9-months to 54-months in the *GUiNZ* study. Missing data in the cognitive outcomes were multiple imputed via multivariate Imputation by chained Equations and the findings for factor analysis of cognitive outcomes with the imputed dataset was compared with the complete cases. While the numbers were different, results were similar in the sense of how cognitive outcomes grouped together, suggesting comparable findings.

7.5 Analyses

Analyses were undertaken using R (version 4.0 and 4.0.2), R studio and Excel (version 2002 and 2016).

7.5.1 Summary statistics

Univariate descriptive statistics

Frequencies, percentages, means and standard deviations, medians and interquartile ranges were used to explore the data:

- Univariate distribution of neurocognitive and prenatal alcohol exposure variables
- Univariate distribution of socio-demographic factors and known confounders of FASD in children

Bivariate descriptive statistics

Depending on the format of the variables, the following metrics and statistical tests were used: Chi Square tests, risk ratios and contingency tables were used if both variables are categorical. Means, standard deviations, t-tests and One-way ANOVA were used to explore the association between a categorical and a continuous variable. The following bivariate descriptive statistics were undertaken:

- Neurocognitive outcomes and prenatal alcohol exposure variables

- Neurocognitive outcomes by the socio-demographic factors

- Prenatal alcohol exposure and diagnosed developmental conditions

- Prenatal alcohol exposure and household trauma

- Associations between the prenatal alcohol exposure and the neurocognitive outcomes variables

7.5.2 Estimated prevalence of those children that might meet criteria for assessment for FASD

The prevalence of those children that might need assessment for FASD or other neurodevelopmental impairments was planned to be analysed by combining the numbers of children with prenatal alcohol exposure plus the number of neurocognitive impairments using NIH Toolbox Cognition Battery, Vineland Adaptive Behaviour Scales (socialisation domain) and SDQ based on LL screening criteria for inclusion in case ascertainment, divided by the total number of children in the cohort sample. This was adapted as per below:

7.5.3 Current study inclusion criteria

The screening criteria for significant neurodevelopmental/cognitive impairment for children in the main cohort at 8 years was a range of children based on both:

- Children who had 2 or more impairments based on a cut-off of 2 SD below the normative score

- Children that had 2 or more impairments based on a cut-off of 1.5 SD below the normative score

Alcohol exposure was not included in the screening criteria at LL- therefore we planned to measure the numbers and proportions with and without alcohol exposure.

7.5.4 Sensitivity analysis

Bias in the sample was checked by comparing the sample in this study at the original cohort using chi square for known co-existing factors related to FASD and sociodemographic factors: ethnicity; maternal alcohol consumption; maternal education.

7.5.5 Multivariate Models

A multivariate generalised logistic model was developed of the primary outcomes, adjusting for key socio-demographic characteristics, and known confounders of FASD in children.

7.5.6 Procedure

For each outcome, a univariate regression model was fitted for each potential covariate separately. The univariate model was considered as significant if the p-value of the covariate was < 0.1.

For each outcome, a final multivariate model was fitted, with the significant covariates from each univariate model. Variables in this final multivariate model were considered significant at level p < 0.05. Continuous outcomes were modelled using linear regression models. Other general linear models were considered for non-continuous outcomes, such as logistic regression models or ordinal models (cumulative link model).

Alcohol exposure variables predicting neurocognitive and behavioural outcomes:

1. At 8 years:
    (i) Highest accuracy outcomes:
        (a) NIH Toolbox Cognition Battery
        (b) Vineland Adaptive Behaviour Scales socialisation domain
        (c) SDQ
    (ii) Lower accuracy/priority outcomes:
        (a) Harter scale
        (b) Parental satisfaction with learning
        (c) Mother report of ADHD at 8 years,
        (d) Learning difficulties
        (e) Autistic Spectrum Disorder at 2 to 8 years
        (f) PROMIS anxiety scale
2. At 4.5 years lower accuracy/priority outcomes:
        (a) DIBELS

    (b)   PROLL

    (c)   PPVT

    (d)   Handclap task

    (e)   Affective knowledge task

    (f)   Child Behaviour Questionnaire

    (g)   Gross Motor Function Scale

3.   At 2 years lower accuracy/priority outcome:

    (a)   Stack and Topple task

4.   Outcomes both continuous and dichotomised 1,5, 2.0 SD below mean, 3rd percentile

5.   Controlling for covariates:

    (a)   age

    (b)   sex at birth

    (c)   maternal education

    (d)   preterm delivery

    (e)   NZDep

    (f)   history of trauma

    (g)   Planned pregnancy y/n

6.   For total cohort and subset for each main ethnic group: Māori; Pacific; Asian; New Zealand European (total response mother reported child ethnicity at 54-months, if sample size allowed)

8. Results

8.1 Description of sample

There were 6670 mother-child dyads antenatally. These dyads were not all used for every analysis because of missing values of included variables. Most mothers were in the 25–40-year-old age group (5086, 76%) and had received at least an NCEA secondary school qualification or higher (6173, 93%). Only 5% (324) children were born preterm and there were slightly more boys (3442, 52%) than girls (3212, 48.2%). The externally prioritised ethnicity distribution of the children (at 54 months) was European (2634, 40%), Māori (1478, 22%), Pacific (844, 12.7%) Asian (890, 13.4%) and Other (142, 2.1). Almost one third of the sample (1775, 27%) lived in low deprivation areas. During the first trimester of pregnancy 440 (7%) reported drinking four or more drinks of alcohol a week, and during the second and third trimester of pregnancy 56 (1%) reported drinking four or more drinks of alcohol a week (Table 10).

Table 10: Description of Sample

Variable	Levels	N	(%)
Mother age (antenatal)	19 or less	323	(4.8)
	20 to 24	971	(14.6)
	25 to 29	1627	(24.4)
	30 to 34	2077	(31.2)
	35 to 39	1382	(20.7)
	40 or more	282	(4.2)
	Missing	<10	(0)
Mother education (antenatal)	No secondary school qualification	470	(7.1)
	Secondary school/NCEA 1-4	1589	(23.8)
	Diploma/Trade cert/NCEA 5-6	2036	(30.6)
	Bachelor's degree	1502	(22.5)
	Higher degree	1046	(15.7)
	Missing	20	(0.3)
Gender - 6 weeks	Boy	3442	(51.7)
	Girl	3212	(48.2)

Variable	Levels	N	(%)
	Missing	<10	(0.1)
Term (Derived from gestation age in weeks)	Pre-term (<37 GW)	324	(4.9)
	Term (37-41 GW)	6156	(92.4)
	Post-term (>41 GW)	166	(2.5)
	Missing	17	(0.3)
Externally prioritised ethnicity (54 months)	European	2634	(39.5)
	Māori	1478	(22.2)
	Pacific	844	(12.7)
	Asian	890	(13.4)
	Other	142	(2.1)
	Missing	675	(10.1)
NZ deprivation index - 8 years	1	588	(8.8)
	2	651	(9.8)
	3	536	(8)
	4	519	(7.8)
	5	497	(7.5)
	6	460	(6.9)
	7	417	(6.3)
	8	402	(6)
	9	433	(6.5)
	10	550	(8.3)
	Missing	1610	(24.2)
Number of drinks of alcohol during the first three months of pregnancy	Did not drink	5136	(77.1)
	Less than 1 drink	602	(9)
	1 to 3 drinks	466	(7)
	4 to 19 drinks	388	(5.8)
	20 drinks or more	52	(0.8)
	Missing	19	(0.3)
	Did not drink	5750	(86.3)

Variable	Levels	N	(%)
Number of drinks of alcohol after the first three months of pregnancy	Less than 1 drink	629	(9.4)
	1 to 3 drinks	215	(3.2)
	4 to 19 drinks	46	(0.7)
	20 drinks or more	10	(0.2)
	Missing	13	(0.2)

8.2 Prenatal alcohol exposure

Prenatally, almost 7% (n=449) of the cohort drank four or more alcoholic drinks per week, and 22% (n=1440) drank up to three drinks per week. There were 43% (n=2850) who had exposure to alcohol either before they were pregnant or before they knew they were pregnant, and 29% (n=1904) were not exposed either pre pregnancy/knowledge of pregnancy or during the pregnancy (Table 11). These exposure levels varied by ethnicity, with a higher number of Māori (13%) and Pacific (10%) mothers being exposed to four or more drinks per week during pregnancy than European (7%) and Asian (2%) (Figure 1).

Table 11: Univariate distribution of the overall alcohol consumption variable

Variable	Levels	N	(%)
Overall alcohol consumption	No exposure	1904	(28.6)
	Exposure pre-pregnancy / before knowledge only	2850	(42.8)
	Up to 3 drinks per week during the pregnancy (highest level)	1440	(21.6)
	4 drinks per week or more during the pregnancy (highest level)	449	(6.7)
	Missing	20	(0.3)
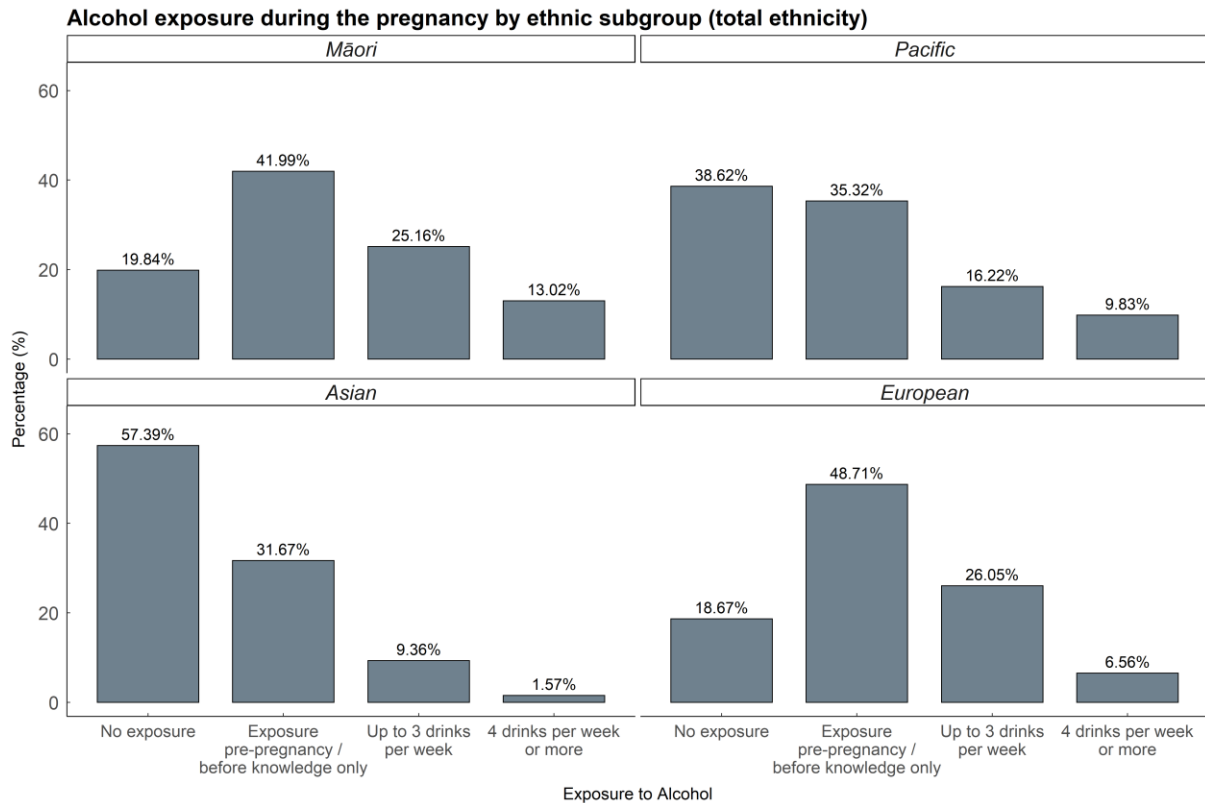
Figure 1: Alcohol exposure during pregnancy by ethnic subgroup (total ethnicity)

8.3 Neurocognitive outcomes related to prenatal alcohol exposure

The odds ratios for impairment across most of the measures of neurocognitive or behavioural impairment were not statistically significant when comparing the alcohol exposed groups to the reference group (not exposed). This was the same whether the cut-off for impairment was set at 1.5 SD or 2 SD below the mean. Odds ratios for the working memory test appeared significant when looking at conditional distribution, but this was no longer the case when controlling for sex, externally prioritized ethnicity, NZDep, mothers' education and planned pregnancy.

Table 12 - Table 14 present a summary of odds ratios for the NIH Toolbox Cognitive Battery, SDQ and Vineland Adaptive Behaviour Scales socialisation domain. Sensitivity analysis showed that when using ≥ 7 drinks per week as cut-off instead of ≥ 4 drinks per week, this did not affect the results (results for ≥ 7 drinks per week not shown). In several measures there was a trend towards less frequent impairment in the groups with 'exposure pre-pregnancy/before knowledge only' and 'up to 3 drinks per week'.

The reading measure showed a significant difference (Oral Reading Recognition Test): Exposure '4 drinks per week or more' was more likely to be impaired compared to 'No exposure' (OR=2.03, p<0.05). The association remained significant after controlling for sex,

externally prioritised ethnicity, NZDep, mothers' education, mothers' age, planned pregnancy and number of adverse events.

Table 12: Results NIH Toolbox Cognition Battery logistic models, dichotomised outcomes, odds ratios

Measure	SD	OR level1	OR level 2	OR level 3
Dimensional change card sort test	1.5	0.832	0.795	1.2
	2	0.793	0.662	1.21
Picture vocabulary test	1.5	0.781	0.636	0.943
	2	0.703	0.679	0.967
Flanker inhibitory control and attention test	1.5	0.847	0.752	0.821
	2	0.821	0.7	0.59
Oral reading recognition test	1.5	1.13	0.903	1.18
	2	1.17	0.779	2.03*
List sorting working memory	1.5	0.92	0.459*	0.786
	2	0.904	0.583*	0.81
Picture sequence memory test	1.5	1.23	0.803	0.865
	2	1.29	0.532	1.09
Pattern comparison PST	1.5	1.39	1.34	1.07
	2	1.52	0.892	1.22

Note. Note. Odds ratios are the odds of having an impairment for a particular subgroup in comparison with the reference group 'No exposure' ; Level 1: Exposure pre-pregnancy/before knowledge only, Level 2: Up to 3 drinks per week, Level 3: 4 drinks per week or more; PST = processing speed test.

Table 13: SDQ, logistic models, dichotomised outcomes, odds ratios

SDQ DCW8	Emotional problems OR	Conduct problems	Hyperactivity Inattention OR	Peer problems OR	Total difficulties OR	Prosocial behaviours
Pre-preg	0.94	0.84	1.18	0.71	0.93	0.99
≤3 drinks	0.76	0.87	1.29	0.64	0.78	0.92
≥4 drinks	0.84	1.21	1.36	1.08	1.25	1.02

Note. Odds ratios are the odds of having a difficulty in comparison with the reference group. The reference group is 'No exposure' (OR = 1).; Other covariates included in the model: Sex, Externally prioritised ethnicity, NZDEP2013, Mother education and Mother age.; Cut-offs for

the SDQ: Emotional problems: ≥5, Conduct problems: ≥4, Hyperactivity-inattention: ≥8, Peer problems: ≥4, Total difficulties: ≥17.; None of the odds ratios had a p-value <0.05 for the Fisher's Exact Test.

Table 14: Vineland Adaptive Behaviour Questionnaire, social domain-logistic models: dichotomised outcomes, odds ratios

SDQ DCW8	OR -2SD	P-value	OR -1.5 SD	P-value
Pre-preg	0.716	0.174	0.822	0.203
≤3 drinks	0.601	0.093	0.575	0.004
≥4 drinks	0.933	0.852	1.05	0.872

Note. Reference group: no exposure. Other covariates included in the model: Externally prioritised ethnicity, NZDEP2013, Mothers' education, Mothers' age and Planned pregnancy.

8.3.1 Subgroup analysis

A subgroup analysis of the distribution of alcohol exposure across outcome measures for Māori, Pacific, Asian and European participants was conducted, suggesting no consistent pattern. In general, Māori and Pacific participants indicated a higher number of impairments, whether alcohol exposed or not (Figure 2 and Figure 3).
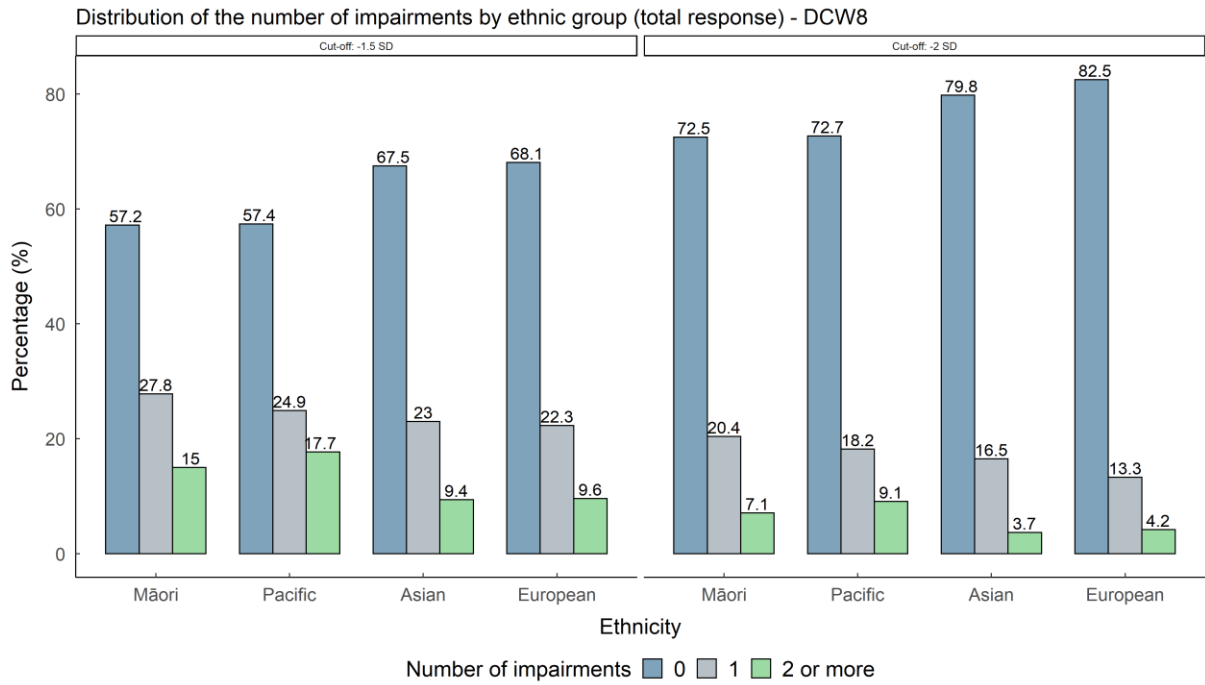
Figure 2: Distribution of the number of impairments by main ethnic groups (total response)
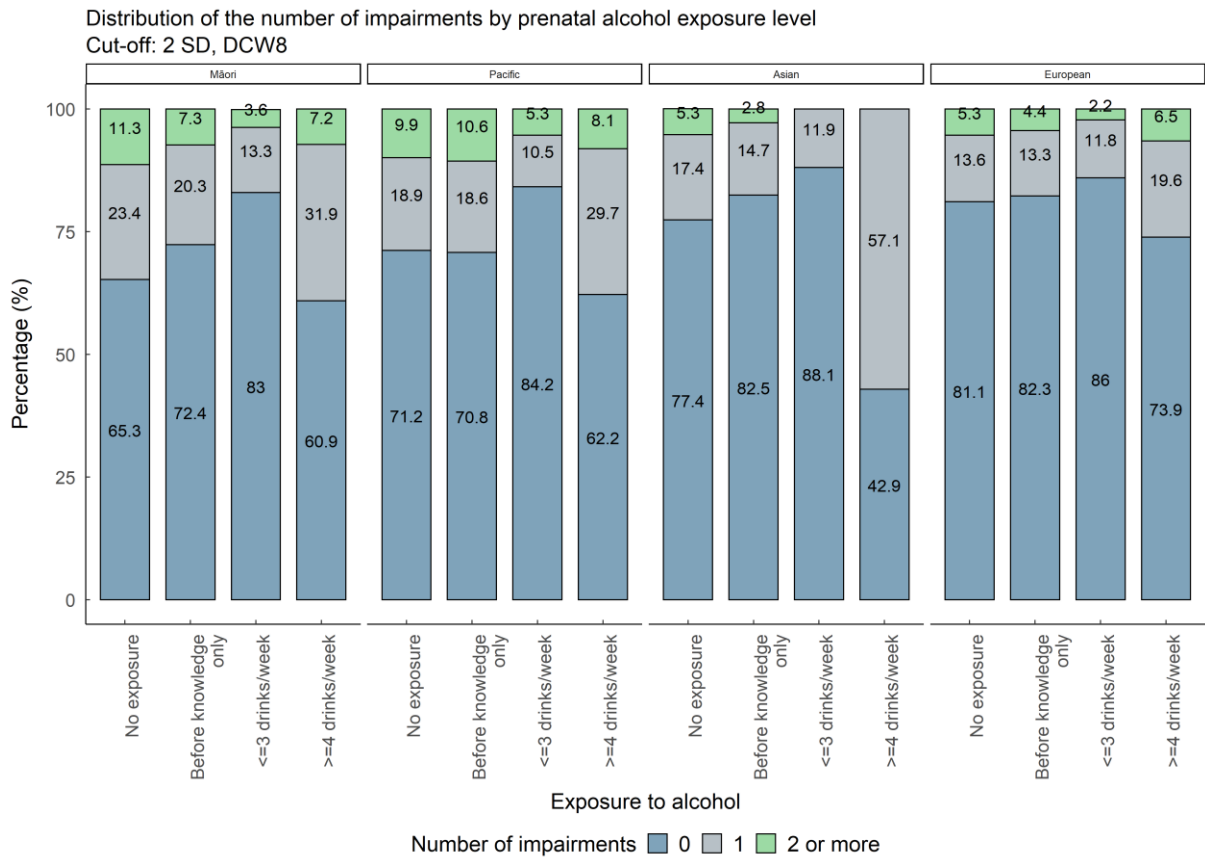
Figure 3: Distribution of the number of impairments (cut-off 2 SD below mean) by prenatal alcohol exposure level for main ethnic groups (total response)

8.3.2 Number of impairments

We assessed how many children had multiple impairments in the main measures, comprising NIH Toolbox Cognition battery, Vineland adaptive behaviour scales (social scale) and SDQ. Children with a diagnosis of ASD were not excluded. The number of children with known ASD in the *GUiNZ* cohort at the 8-year DCW is 120.

Using a cut-off for impairment at 1.5 SD below the mean, 4.01% of the cohort had 3 or more impairments, and 10.68% had 2 or more impairments irrespective of alcohol exposure. Using a cut-off of 2 SD below the mean, 1.23% had 3 or more impairments and 4.99% had 2 or more impairments irrespective of alcohol exposure (Figure 4).

The alcohol exposed groups did not have significant odds ratios of having more than one impairment as compared to the non-exposed group (Table 16).

The group of ≥20 drinks per week had a high percentage of children with at least one impairment (53.84%), but numbers were small (<10) (Table 17).
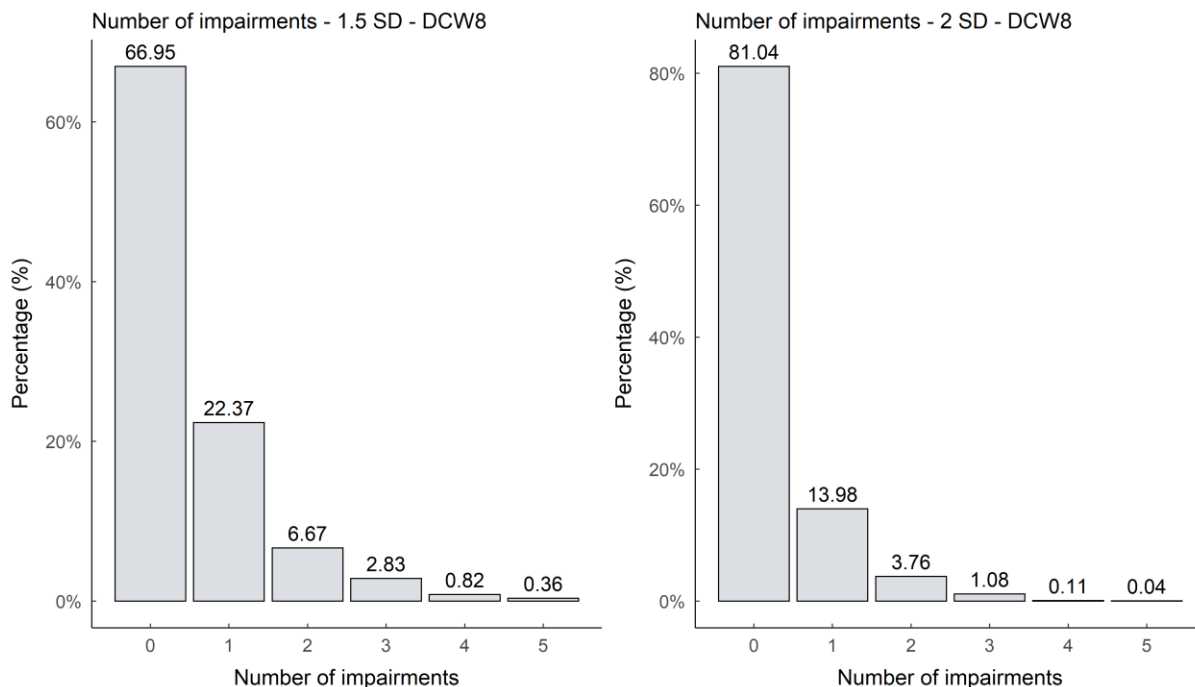
Figure 4: Number of impairments at 1.5 SD and at 2SD below the mean

Table 15: Number of impairments by alcohol exposure level, cut-off -2SD

	0		1		2 or more	
	N	(%)	N	(%)	N	(%)
No exposure	465	(78)	91	(15.3)	40	(6.7)
Exposure pre-pregnancy / before knowledge only	1115	(81.6)	186	(13.6)	65	(4.8)
Up to 3 drinks per week	562	(85.6)	76	(11.6)	18	(2.7)
4 drinks per week or more	116	(70.3)	36	(21.8)	13	(7.9)

Table 16: Ordinal model - number of impairments (cut-off -2SD)

		OR	95% CI	P-value
Alcohol exposure	No exposure	(Reference group)		
	Exposure pre-pregnancy / before knowledge only	0.91	[0.706; 1.18]	0.467
	Up to 3 drinks per week	0.644	[0.471; 0.878]	0.0056
	4 drinks per week or more	1.18	[0.782; 1.77]	0.419

Note. Odds ratios are the odds of having impairments in comparison with the reference group 'No exposure'. Covariates included in the model: Sex, externally prioritised ethnicity, Mothers' age, Planned pregnancy and Number of adverse events.

Table 17: Number of impairments by alcohol exposure level of 20 drinks: - cut-off -2SD

	0		1		2 or more	
	N	(%)	N	(%)	N	(%)
< 20 drinks per week	2252	(81.3)	384	(13.9)	134	(4.8)
>= 20 drinks per week	<10	(46.2)	<10	(38.5)	<10	(15.4)

8.3.3 Developmental diagnosis (ADHD, ASD, learning difficulties)

The odds ratios for the presence of ADHD appear elevated in the alcohol exposed groups compared to the non-exposed groups. However, when corrected for covariates, this did not achieve statistical significance (Table 18). One explanation for this may be the issue that the number of children reported with a diagnosis of ADHD is far lower than expected. The total number of children with diagnosed ADHD is only 0.67% of the sample, whereas according to the National Health Survey 2017-2020, the rate in the geographical recruitment area of GUiNZ is 1.7 –2.2%.

Table 18: Total number of ADHD respondents by alcohol exposure level

	N	(%)	N	(%)	OR[1]	P-Value	N	(%)
No exposure	1058	23.0	<10	0.04	(Reference)		1060	(5.6)
Exposure pre-pregnancy / before knowledge only	2150	46.7	21	0.5	5.22	0.05	2171	(6.8)
Up to 3 drinks per week	1069	23.2	<10	0.1	2.43	0.67	1074	(5.4)
4 drinks per week or more	291	6.3	<10	0.07	5.50	0.19	294	(7.1)
Total	4568	99.3	31	0.7			4599	100

Note. [1]Odds ratios are the odds of having a Developmental condition for a particular subgroup in comparison with the reference group 'No exposure'. Other covariates included in the model: Sex.

The odds ratios for having ASD as well as for having reported learning difficulties was not in the significant range when comparing alcohol exposed groups to the reference group (not exposed).

8.1% of total respondents had one reported condition (ADHD, ASD, or learning difficulties), 1.33% had two of these conditions (ASD and ADHD or ASD and learning difficulties or ADHD and learning difficulties). None of the combinations reached a significant odds ratio when comparing the alcohol exposed groups to the non-exposed group.

8.3.4 Household challenges

The odds ratios for prenatal alcohol exposure related to having experienced household challenges were significantly elevated for drug taking/alcoholism in the immediate family in

the '4 drinks per week or more' group (OR 2.15, p<0.05); covariates included in the model were Externally prioritised ethnicity, NZDEP2013, Mothers' education and Mothers' age. Odds ratios were further significantly elevated for prenatal alcohol exposure related to conflict between parents in the '4 drinks per week or more' group (OR 1.53, p<0.05) as well as in the 'Exposure pre-pregnancy/before knowledge only' (OR 1.31, p<0.05) and 'Up to 3 drinks per week (OR 1.47, p<0.05) groups; covariates included in the model were Externally prioritised ethnicity, NZDEP2013, Mothers' education and Mothers' age.

The odds ratios for the other household challenges were not significantly elevated. These included death of a parent, mental illness in the immediate family, parent in prison, death of a close family member, separation or divorce of parent, stay in a foster home/residential care, moving house, experience of family conflict and experience of other conflict.

Looking at total number of traumatic life events, odds ratios were elevated but not significantly when examining the impact of prenatal alcohol exposure once covariates were included (Table 19).

Table 19: Total number of traumatic life events by absolute alcohol exposure

	0		1		2		3		4		Total	
	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
No alcohol Exposure	330	6.86	342	7.1	225	4.7	144	3	91	1.9	1132	23.5
Alcohol Exposure	765	15.9	1019	21.2	927	19.3	556	11.6	412	8.6	3679	76.5
OR[1]	Reference		1.11		1.21		1.20		1.29			
Total	1095	22.8	1361	28.3	1152	23.9	700	14.6	503	10.5	4811	100

Note. [1]Odds ratios are the odds of having a life event occur for a particular subgroup in comparison with the reference group 'No alcohol exposure'. Other covariates included in the model: Externally prioritised ethnicity, NZDEP2013, Mothers' education, Age

8.3.5   The combined trauma/impairments/alcohol analysis.

Interaction effect between alcohol exposure and household challenges on impairment

To test if there is an underlying interaction effect between alcohol exposure and household challenges on impairments, multiple logistic regression analysis was conducted and compared to the above models. The Wald chi-squared tests from both models with and without interaction were compared to see if a model with an interaction fits better. The following models included covariates: Sex, externally prioritised ethnicity, NZDEP2013, Mothers' education and Planned pregnancy. These models showed no significant interaction effect, indicating the effects of alcohol exposure and household challenges on impairment are independent from each other (Table 20 - Table 23).

Table 20: Wald Chi-square multiple regression model for independent variables, alcohol exposure and household challenges effect on impairment (cut-off level 1.5 SD below mean)

Effect	Wald Chi-Square	Pr > ChiSq
Alcohol Exposure	11.43	0.076
Household challenges	3.30	0.192

Table 21: Wald Chi-Square multiple regression model fit for independent variables, alcohol exposure and household challenges with interaction effect on impairment (cut-off level 1.5 SD below mean)

Effect	Wald Chi-Square	Pr > ChiSq
Alcohol Exposure	7.92	0.244
Household challenge	0.57	0.752
Alcohol Exposure X Household challenges	7.84	0.250

Table 22: Wald Chi-Square Multiple regression model fit for independent variables Alcohol Exposure and Household challenges effect on impairment (cut-off level 2 SD below mean)

Effect	Wald Chi-Square	Pr > ChiSq
Alcohol Exposure	14.80	0.022
Household challenges	6.86	0.032

Table 23: Wald Chi-Square Multiple regression model fit for independent variables Alcohol Exposure and Household challenges with interaction effect on impairment (cut-off level 2 SD below mean)

Effect	Wald Chi-Square	Pr > ChiSq
Alcohol Exposure	11.23	0.082
Household challenge	1.40	0.497
Alcohol Exposure X Household challenge	5.38	0.497

8.4 Cohort comparison Antenatal vs 8 Years

A comparison between the cohort samples at the antenatal DCW and the 8-year DCW showed some significant differences. Particularly, there were significantly less Māori (69.9%), Pacific (51.7%) and Asian (65.9%) of the original cohort participating at 8 years compared to European (88%). Furthermore, the 'Pre-pregnancy/before knowledge only' (78.5%) and the '4 drinks per week or more' (67.9%) alcohol exposure groups participated significantly more in the 8Y DCW compared to the 'No exposure' group (59.5%). Participation of the original cohort at the 8Y DCW was also significantly higher if mothers had a bachelor's degree (83.5%) or higher degree (85.0%) as compared to mother with no secondary school qualification (48.9%) (Table 24).

Table 24: Difference between the original cohort and the cohort at 8 years

Variable		Percentage of original cohort in 8 years subsample (%)	OR
Alcohol exposure	No exposure	59.5	(Reference)
	Pre-pregnancy/before knowledge only	78.5	1.42*
	Up to 3 drinks per week	77.5	1.34
	4 drinks per week or more	67.9	1.58*
Externally prioritised ethnicity	European	88	(Reference)
	Māori	69.9	0.63**
	Pacific	51.7	0.39***
	Asian	65.9	0.36***
Maternal Education	No sec school qualification	48.9	(Reference)
	Sec school/NCEA-4	63	1.37
	Diploma/Trade cert/NCEA-6,5	69.8	1.40
	Bachelor's degree*	83.5	2.00**
	Higher degree*	85	1.89**

Note. Participation in the 8-year DCW (*=p<0.05; **=p<0.01; ***=p<0.001).

9. Discussion

This study found no evidence of an association between prenatal alcohol exposure and neurocognitive outcomes in children assessed at 8 years in the *GUiNZ* longitudinal study. The only measure that showed a significant difference between alcohol exposed groups and the non-exposed group was the oral reading recognition test. Language is often impaired in children with FASD, but there is no plausible reason why language should be the only difficulty. The alcohol exposed groups did not show significantly increased odds of having more than one impairment as compared to the non-exposed group.

However, there is a group of children with broad neurodevelopmental impairment, irrespective of alcohol exposure. These are the children that have impairments across multiple domains of neurocognition. Even at a cut-off level of 2 SD below the mean, 5% of children have 2 or more impairments, and 1.2% of children had 3 or more impairments. This is in line with what Russell et al[46] found in their study of the *GUiNZ* cohort at 54 months of age, where 3.6% of the cohort children showed a profile of developmental difficulties. This profile was not associated with maternal alcohol consumption. These children need to be seen by Child Development Services.

Subgroup analysis for the Māori, Pacific and Asian cohorts found no clear associations between alcohol exposure and neurocognitive measures. However, we found higher rates of impairments in Pacific and Māori children, irrespective of alcohol exposure. For instance, at a cut-off of 2 SD below the mean, 8.2% of Pacific and 6.8% of Māori children had 2 or more impairments as compared to 4.1% of European children. Furthermore, Māori and Pacific had higher rates of exposure to alcohol prenatally, further increasing risk of FASD and inequities for these groups.

There was no observed association between prenatal alcohol exposure and diagnosed ADHD, ASD or Learning difficulties. In clinical practice the relationship between FASD and ADHD however is very strong. One possible explanation contributing to this finding might be the issue that at the *GUiNZ* 8-year DCW, ADHD was not specifically mentioned as a response option for the question if there was a diagnosis of pre-existing -neuro-developmental conditions, but it was possible to indicate this as free text under the 'Other' open response option. This methodological set up has possibly contributed to the reporting of far fewer cases of ADHD than what one would expect from the National Health Survey.[70]

We found no correlation between antenatal alcohol exposure and SDQ at 8 years of age. Torshizian[44] looked at the SDQ at age 54 months for children in the GUiNZ study. They found lower levels of drinking were associated with lower SDQ scores, however drinking during the first trimester increased the SDQ summary score. [44]

9.1 Limitations

The study has several limitations. We were not able to obtain facial measurements for the cohort, as is routinely done in diagnostic assessment of FASD. There are no strong data on differential diagnosis either as this was only available as by-proxy report from the mother. The measures used do not cover the neurocognitive domains of FASD with the same strength as a clinical assessment. Apart from the Vineland Adaptive Behaviour Questionnaire none of the measures are used in clinical practice for assessment of FASD. There is also the question of cultural validity and cultural bias of the neurocognitive measures with respect to their content and administration procedure, especially measures related to language assessment.[71,72] Additionally, a proportion of the children in our sample are bilingual, with some having another language as English as their primary language which might have affected the test results. A further limitation might be the assessment of neurocognitive tools by non-experts even though standard administration procedures were applied and the interviewers were trained to administer the tests.

There may be attrition bias because of the retention rates at the 8-year DCW, i.e. ethnicity and maternal education level were strong factors in attrition. This may limit the overall generalisability of the findings. One potential solution would have been to apply multiple imputation procedures to account for missing data, however there was only a limited number of variables suitable for imputation as most measures had more than 50% missingness.

Our study population may also be biased as it may not include children presenting with complex psycho-social histories such as those in Oranga Tamariki care.

The nature of questions around alcohol use during pregnancy is sensitive, and there is a risk of response bias. In the clinical context it requires considerable effort to obtain the correct alcohol history. The size of the group that reports any alcohol use during pregnancy in this study is consistent with other studies. However, the group of mothers that reported high drinking levels is smaller than reported in other New Zealand studies.[6,7,9] Hence, it is very possible that alcohol use is under-reported by mothers in *GUiNZ*, and this could be the case in other cohort studies too.

For this study, there were concerns around the categories of alcohol use in pregnancy as asked in *GUiNZ*. Particularly, 'drinking prior to pregnancy' was combined as one question with 'before knowledge of pregnancy'. This category therefore may include children who were heavily alcohol exposed in early pregnancy. No question about binge drinking was asked. Binge drinking is however a risk factor for FASD and commonly reported during pregnancy in Aotearoa New Zealand.[7,9]

We noted a J-shaped curve for some of the measures, with a reversed association of alcohol

exposure being protective at lower drinking levels. This is counter-intuitive, but a common finding in health research. Torshizian[44] found the same pattern when looking at the SDQ data in *GUiNZ* at 54 months, as well Chu[13] at 8 years.

In a similar study, Lees[35] compared neurocognitive and behavioural outcomes in children with PAE with non-exposed children and found significant differences between the groups. Their initial cohort however is significantly larger than the *GUiNZ* cohort (11,875 versus 6,822). Their longitudinal cohort was also specifically designed to measure adolescent brain cognitive development. This may have placed them in a better position to measure behavioural and cognitive outcomes from the beginning. McQuire[14] attempted to estimate a screening prevalence for FASD in the UK. They also used a longitudinal regional cohort study as basis and their cohort was twice the size of the *GUiNZ* cohort. Their battery of behavioural and neurocognitive screening measures appears to be more comprehensive than those available at the *GUiNZ* 8-year DCW, with better coverage of the neuropsychological domains for FASD diagnosis.

Chu et al.,[13] in their systematic review of longitudinal cohort studies that evaluated the impact of PAE on neurocognitive outcomes found mixed neurocognitive outcomes, with no effect on executive function.

In summary, cohort studies don't seem to show a consistent pattern of neurodevelopmental difficulties in children with antenatal alcohol exposure. This is not what one would expect. It may be that cohort studies are not the ideal environment to conduct studies looking at neurodevelopmental outcomes of children who were exposed to alcohol antenatally. Contributing to that could be the alcohol exposure question not being asked in sufficient detail, or that the questions about alcohol use are not answered in a reliable way in the set-up of a cohort study. Self-reported alcohol consumption during pregnancy is likely to under-estimate the total population alcohol consumption.[73–75]

9.2   Strengths

Though there was attrition at the 8-year DCW, there still is general representation of Aotearoa New Zealand's population within the dataset with respect to ethnicity and socioeconomic status. Irrespective of the outcomes of the current study, *GUiNZ* data can be used in future analysis for longitudinal trends of neurocognitive development including previous data collection points and their association with outcomes at later ages.

The involvement of the steering group and the scientific advisory groups are strengths of this study. These groups offered valuable advice in guiding the direction of the study. We have shown that it is feasible to involve a broad group of stake holders in a study like this. We also adapted processes in alignment with the consolidated criteria for strengthening reporting of health research involving indigenous peoples (CONSIDER statement).

The ability to iterate and modify in response to expert feedback and oversight, has been described as important for cultural congruence.[76] It has also been deemed important to facilitate national research advisory groups to progress research in a way which addresses community priorities, and aligns with agreed values.[77]

It is not common for research projects to explicitly state their process and adherence to cultural safety, including engagement/relationship with community, governance and positionality of researchers. This needs to become more commonplace in order to address the power imbalances,[78] and to facilitate research which is connected directly with the communities with the most need. For FASD in Aotearoa New Zealand, there are barriers to access to both diagnostic and support services.[49] In regards to prevalence, rates of FASD are most likely higher for Indigenous people. This is also shown by the number of impairments for Māori and Pacific children in this study. Therefore, services in Aotearoa New Zealand must be designed to respond in a meaningful way to the needs of Māori and Pacific families. In a study by Crawford et al [43]only 39% of children with FASD met Aotearoa New Zealand's criteria to access Disability Support Services, 46% had received specialist support from the Ministry of Education and very few met criteria for Child and Adolescent Mental Health Services. Western models of service provision do not factor in historical trauma, inequity and disadvantage experienced by Māori and Pacific peoples, and therefore are not adequate to address the challenges and barriers.

There is a need to reframe research in the neurodisability sector to avoid stigmatising families further. Cultural appropriateness of psychometric tools needs to be taken into account when planning and interpreting research involving neurodevelopmental conditions.[50] Historically families impacted by FASD have been stigmatised, however this must be replaced with consideration of the impact of colonisation and generational trauma, alongside the longstanding and persistent health injustices and inequities. Research which takes these factors into account and destigmatises, is an important step towards responding to these inequities.[43]

10. Conclusions / Recommendations

This study shows a group of children with developmental difficulties irrespective of maternal alcohol consumption, with a higher burden in Māori and Pacific children. These are children that need to be seen in developmental services for neurodevelopmental assessment. Irrespective of exposure to alcohol prenatally, these children present with complex developmental profiles and currently may not meet the criteria for disability services.

The current study does not answer questions regarding prevalence of FASD in Aotearoa New Zealand. A population-based case ascertainment study following a protocol such as the WHO is recommended. Separate from this, it is important to determine prevalence in high-risk population groups, such as children in care, youth justice, alternative education and other high-risk groups.

Attempts to set up a population-based prevalence study should continue. Health economics research on FASD in Aotearoa New Zealand could be conducted in tandem with that. If funding and complexity of a larger scale prevalence study remain problematic, one could consider a smaller scale case ascertainment prevalence study. This could be conducted in schools and would answer some questions about prevalence. It should however be approached with caution, as there will be limits in generalisability by the sociodemographic characteristics of the school catchment area/population.

In absence of prevalence data for New Zealand, there are good data about the prevalence of FASD internationally. Most recent data converge around a prevalence of 2-3% (USA, Canada, UK), with outliers in some countries with higher alcohol exposure. Data also consistently show that alcohol exposure in pregnancy in Aotearoa New Zealand is high[6–9] and at least at the American or Canadian rate. Therefore, services in Aotearoa New Zealand regarding diagnosis and management of FASD should be geared towards a prevalence of at least 2-3%.

Regardless of accurate prevalence data, there is a need to provide further resource, support and funding for those who are impacted by neurodevelopmental difficulties both due to alcohol exposure, and not due to alcohol exposure. Priority must be placed on this, particularly for Māori and Pacific who are disproportionately impacted, and this must be done in the context of acknowledging historical failings, trauma and environmental factors, rather than placing individualised blame and stigmatising. The findings from this study suggest the need for greater resourcing of assessment, intervention and support post diagnosis for these children.

References

1. Popova S, Lange S, Poznyak V, et al. Population-based prevalence of fetal alcohol spectrum disorder in Canada. *BMC Public Health*. 2019;19(1):845. doi:10.1186/s12889-019-7213-3

2. May PA, Chambers CD, Kalberg WO, et al. Prevalence of Fetal Alcohol Spectrum Disorders in 4 US Communities. *JAMA*. 2018;319(5):474-482. doi:10.1001/jama.2017.21896

3. McCarthy R, Mukherjee RAS, Fleming KM, et al. Prevalence of fetal alcohol spectrum disorder in Greater Manchester, UK: An active case ascertainment study. *Alcoholism: Clinical and Experimental Research*. 2021;45(11):2271-2281. doi:10.1111/acer.14705

4. Lange S, Probst C, Gmel G, Rehm J, Burd L, Popova S. Global Prevalence of Fetal Alcohol Spectrum Disorder Among Children and Youth. *JAMA Pediatr*. 2017;171(10):948-956. doi:10.1001/jamapediatrics.2017.1919

5. Popova S, Lange S, Shield K, Burd L, Rehm J. Prevalence of fetal alcohol spectrum disorder among special subpopulations: a systematic review and meta-analysis. *Addiction*. 2019;114(7):1150-1172. doi:10.1111/add.14598

6. Ho R, Jacquemard R. Maternal alcohol use before and during pregnancy among women in Taranaki, New Zealand. *N Z Med J*. 2009;122(1306):20-32.

7. Mallard SR, Connor JL, Houghton LA. Maternal factors associated with heavy periconceptional alcohol intake and drinking following pregnancy recognition: A post-partum survey of New Zealand women. *Drug and Alcohol Review*. 2013;32(4):389-397. doi:10.1111/dar.12024

8. Rossen F, Newcombe D, Parag V, et al. Alcohol consumption in New Zealand women before and during pregnancy: findings from the Growing Up in New Zealand study. *N Z Med J*. 2018;131(1479):24-34.

9. McDonald BW, Watson PE. Maternal alcohol intakes before and during pregnancy: Impact on the mother and infant outcome to 18 months. *Nordic Studies on Alcohol and Drugs*. 2020;37(2):153-171. doi:10.1177/1455072520905404

10. Lange S, Rovet J, Rehm J, Popova S. Neurodevelopmental profile of Fetal Alcohol Spectrum Disorder: A systematic review. *BMC Psychol*. 2017;5(1):22. doi:10.1186/s40359-017-0191-2

11. Grubb M, Golden A, Withers A, Vellone D, Young A, McLachlan K. Screening approaches for identifying fetal alcohol spectrum disorder in children, adolescents, and adults: A systematic review. *Alcohol Clin Exp Res*. 2021;45(8):1527-1547. doi:10.1111/acer.14657

12. Lim YH, Watkins RE, Jones H, Kippin NR, Finlay-Jones A. Fetal alcohol spectrum disorders screening tools: A systematic review. *Res Dev Disabil*. 2022;122:104168. doi:10.1016/j.ridd.2021.104168

13. Chu, J.T.W., McCormack, J., Marsh, S., Wells, A., Bullen, C. Impact of Prenatal Alcohol Exposure on Neurodevelopmental Outcomes: A Systematic Review. Manuscript submitted for publication. Published online 2022.

14. McQuire C, Mukherjee R, Hurt L, et al. Screening prevalence of fetal alcohol spectrum disorders in a region of the United Kingdom: A population-based birth-cohort study. *Prev Med*. 2019;118:344-351. doi:10.1016/j.ypmed.2018.10.013

15. Goodyear-Smith F, Ashton T. New Zealand health system: universalism struggles with persisting inequities. *Lancet*. 2019;394(10196):432-442. doi:10.1016/S0140-6736(19)31238-3

16. Came H, O'Sullivan D, Kidd J, McCreanor T. The Waitangi Tribunal's WAI 2575 Report. *Health Hum Rights*. 2020;22(1):209-220.

17. Huria T, Palmer S, Pitama S, et al. Consolidated criteria for strengthening reporting of health research involving indigenous peoples: The CONSIDER statement. *BMC Medical Research Methodology*. 2019;19. doi:10.1186/s12874-019-0815-8

18. Weintraub S, Bauer PJ, Zelazo PD, et al. I. NIH Toolbox Cognition Battery (CB): introduction and pediatric data. *Monogr Soc Res Child Dev*. 2013;78(4):1-15. doi:10.1111/mono.12031

19. Neumann D, Peterson ER, Underwood L, Morton S, Waldie K. Exploring the Factor Structure of the NIH Toolbox Cognition Battery in a Large Sample of 8-Year-Old Children in Aotearoa New Zealand. *Journal of the International Neuropsychological Society*. Published online 2021. doi:10.1017/S1355617720001265

20. Gershon RC, Wagster MV, Hendrie HC, Fox NA, Cook KF, Nowinski CJ. NIH toolbox for assessment of neurological and behavioral function. *Neurology*. 2013;80(11 Suppl 3):S2-6. doi:10.1212/WNL.0b013e3182872e5f

21. Goodman R. The Strengths and Difficulties Questionnaire: a research note. *J Child Psychol Psychiatry*. 1997;38(5):581-586. doi:10.1111/j.1469-7610.1997.tb01545.x

22. Goodman R. Psychometric Properties of the Strengths and Difficulties Questionnaire. *Journal of the American Academy of Child & Adolescent Psychiatry*. 2001;40(11):1337-1345. doi:10.1097/00004583-200111000-00015

23. Sparrow S, Cicchetti D. Diagnostic uses of the Vineland Adaptive Behavior Scales. *Journal of pediatric psychology*. Published online 1985. doi:10.1093/JPEPSY/10.2.215

24. Sparrow SS, Balla DA, Cicchetti D V., Harrison PL. Vineland adaptive behavior scales: Interview edition, survey form. Circle Pines, MN: American Guidance Service. In: ; 1984.

25. Flannigan K, Unsworth K, Harding K. *CanFASD Issue Paper: The Prevalence of Fetal Alcohol Spectrum Disorder*.; 2018.

26. Sampson PD, Streissguth AP, Bookstein FL, et al. Incidence of fetal alcohol syndrome and prevalence of alcohol-related neurodevelopmental disorder. *Teratology*. 1997;56(5):317-326. doi:10.1002/(SICI)1096-9926(199711)56:5<317::AID-TERA5>3.0.CO;2-U

27. DEJONG K, OLYAEI A, LO JO. Alcohol Use in Pregnancy. *Clin Obstet Gynecol*. 2019;62(1):142-155. doi:10.1097/GRF.0000000000000414

28. Morton S, Ramke J, Kinloch J, et al. Growing Up in New Zealand cohort alignment with all New Zealand births. *Australian and New Zealand Journal of Public Health*. 2014;39. doi:10.1111/1753-6405.12220

29. Morton SMB, Grant CC, Carr PEA, et al. How do you recruit and retain a prebirth cohort? Lessons learnt from growing up in New Zealand. *Eval Health Prof*. 2014;37(4):411-433. doi:10.1177/0163278712462717

30. Morton, S.M.B., Walker, C.G., Gerritsen, S., Smith, A., Cha, J., Atatoa Carr, P., Chen, R., Exeter, D.J., Fa'alili-Fidow, J., Fenaughty, J., Grant, C. Kim, H., Kingi, T., Lai, H., Langridge, F., Marks, E.J., Meissel, K., Napier, C., Paine, S., Peterson, E.R., Pilai, A., Reese, E., Underwood, L., Waldie, K.E, Wall, C. Growing Up in New Zealand: A longitudinal study of New Zealand children and their families. Now We Are Eight. Auckland: Growing Up in New Zealand.

31. Kodituwakku P, Kodituwakku E. Cognitive and Behavioral Profiles of Children with Fetal Alcohol Spectrum Disorders. *Curr Dev Disord Rep*. 2014;1(3):149-160. doi:10.1007/s40474-014-0022-6

32. Burd L. FASD and ADHD: Are they related and How? *BMC Psychiatry*. 2016;16:325. doi:10.1186/s12888-016-1028-x

33. Cook JL, Green CR, Lilley CM, et al. Fetal alcohol spectrum disorder: a guideline for diagnosis across the lifespan. *CMAJ*. 2016;188(3):191-197. doi:10.1503/cmaj.141593

34. Bower C, Elliott E, Zimmet M, et al. Australian guide to the diagnosis of foetal alcohol spectrum disorder: A summary. *Journal of paediatrics and child health*. Published online 2017. doi:10.1111/jpc.13625

35. Lees B, Mewton L, Jacobus J, et al. Association of Prenatal Alcohol Exposure With Psychological, Behavioral, and Neurodevelopmental Outcomes in Children From the Adolescent Brain Cognitive Development Study. *Am J Psychiatry*. 2020;177(11):1060-1072. doi:10.1176/appi.ajp.2020.20010086

36. Chudley AE. Fetal alcohol spectrum disorder: Canadian guidelines for diagnosis. *Canadian Medical Association Journal*. 2005;172(5_suppl):S1-S21. doi:10.1503/cmaj.1040302

37. Eugene Hoyme H, May PA, Kalberg WO, et al. A Practical Clinical Approach to Diagnosis of Fetal Alcohol Spectrum Disorders: Clarification of the 1996 Institute of Medicine Criteria. *Pediatrics*. 2005;115(1):39-47. doi:10.1542/peds.2004-0259

38. Hoyme HE, Kalberg WO, Elliott AJ, et al. Updated Clinical Guidelines for Diagnosing Fetal Alcohol Spectrum Disorders. *Pediatrics*. 2016;138(2):e20154256. doi:10.1542/peds.2015-4256

39. sign156.pdf. Accessed June 21, 2022. https://www.sign.ac.uk/media/1092/sign156.pdf

40. Kodituwakku PW. Neurocognitive Profile In Children With Fetal Alcohol Spectrum Disorders. *Dev Disabil Res Rev*. 2009;15(3):218-224. doi:10.1002/ddrr.73

41. Mattson SN, Crocker N, Nguyen TT. Fetal alcohol spectrum disorders: neuropsychological and behavioral features. *Neuropsychol Rev*. 2011;21(2):81-101. doi:10.1007/s11065-011-9167-9

42. Coriale G, Fiorentino D, Di Lauro F, et al. Fetal Alcohol Spectrum Disorder (FASD): neurobehavioral profile, indications for diagnosis and treatment. *Riv Psichiatr*. 2013;48(5):359-369. doi:10.1708/1356.15062

43. Crawford A, Kahungunu LTHTNRRK, Peterson ER, McGinn V, Robertshaw K, Tippett L. Cognitive and social/emotional influences on adaptive functioning in children with FASD: Clinical and cultural considerations. *Child neuropsychology : a journal on normal and abnormal development in childhood and adolescence*. Published online 2020. doi:10.1080/09297049.2020.1771296

44. Torshizian, E., Kelly, G., & Cheung, J. The impact of drinking in pregnancy on child development. Unpublished report. Published online 2021.

45. Alvik A, Aalen OO, Lindemann R. Early fetal binge alcohol exposure predicts high behavioral symptom scores in 5.5-year-old children. *Alcohol Clin Exp Res*. 2013;37(11):1954-1962. doi:10.1111/acer.12182

46. Russel J, Grant C, Morton S, Denny S, Paine SJ,. Prevalence and predictors of developmental health difficulties within New Zealand preschool-aged children: A latent profile analysis, In press.

47. Curtis E, Jones R, Tipene-Leach D, et al. Why cultural safety rather than cultural competency is required to achieve health equity: a literature review and recommended definition. *Int J Equity Health*. 2019;18:174. doi:10.1186/s12939-019-1082-3

48. Paine SJ, Neumann D, Langridge F, Peters A, Kingi T. Kaitiakitanga – principles for protecting and promoting tamariki and rangatahi wellbeing in Growing Up in New Zealand. *Journal of the Royal Society of New Zealand*. Published online May 22, 2022:1-11. doi:10.1080/03036758.2022.2066142

49. Espiner E, Apou F, Strickett E, Crawford A, Ngawati M. Describing the experience of Indigenous peoples with prenatal alcohol exposure and FASD: a global review of the literature to inform a Kaupapa Māori study into the experiences of Māori with FASD. *New Zealand Medical Journal*. Published online 2022:14.

50. Hunting G, Browne A. Decolonizing Policy Discourse: Reframing the 'Problem' of Fetal Alcohol Spectrum Disorder. *undefined*. Published online 2012. Accessed June 21, 2022. https://www.semanticscholar.org/paper/Decolonizing-Policy-Discourse%3A-Reframing-the-of-Hunting-Browne/a7b8e821ccabbb7633b90ea7ed8d3162b5a2fac2

51. Hayes N, Akison L, Goldsbury S, et al. Key Stakeholder Priorities for the Review and Update of the Australian Guide to Diagnosis of Fetal Alcohol Spectrum Disorder: A Qualitative Descriptive Study. *International journal of environmental research and public health*. Published online 2022. doi:10.3390/ijerph19105823

52. Atatoa Carr P, Langridge F, Neumann D, et al. 'Seeing' our tamariki in longitudinal studies: exploring the complexity of ethnic identification trajectories within Growing Up in New

Zealand. *Journal of the Royal Society of New Zealand*. 2022;0(0):1-17. doi:10.1080/03036758.2022.2064518

53. Haar J, Martin WJ. He aronga takirua: Cultural double-shift of Māori scientists. *Human Relations*. 2022;75(6):1001-1027. doi:10.1177/00187267211003955

54. Prevalence and predictors of developmental health difficulties within New Zealand preschool-aged children A latent profile analysis.pdf.

55. Goodman A, Lamping D, Ploubidis G. When to Use Broader Internalising and Externalising Subscales Instead of the Hypothesised Five Subscales on the Strengths and Difficulties Questionnaire (SDQ): Data from British Parents, Teachers and Children. *Journal of abnormal child psychology*. Published online 2010. doi:10.1007/s10802-010-9434-x

56. D'Souza S, Waldie KE, Peterson ER, Underwood L, Morton SMB. Psychometric Properties and Normative Data for the Preschool Strengths and Difficulties Questionnaire in Two-Year-Old Children. *J Abnorm Child Psychol*. 2017;45(2):345-357. doi:10.1007/s10802-016-0176-2

57. Report on Adapted PPVT-III and Who Am I? studylib.net. Accessed June 29, 2022. https://studylib.net/doc/7823074/report-on-adapted-ppvt-iii-and-who-am-i?

58. Dunn LMDLM. *Examiner's Manual for the PPVT-III, Peabody Picture Vocabulary Test, Third Edition - Form IIIA and Form IIIB*. American Guidance Service; 1997.

59. Golden CJ, Purisch AD, Hammeke TA. *The Luria-Nebraska Neuropsychological Battery: A Manual for Clinical and Experimental Uses*. University of Nebraska Press; 1979.

60. Good RH, Kaminski RA. Dynamic Indicators of Basic Early Literacy Skills TM 6 th Edition. *undefined*. Published online 2002. Accessed April 21, 2022. https://www.semanticscholar.org/paper/Dynamic-Indicators-of-Basic-Early-Literacy-Skills-6-Good-Kaminski/84dbb8fa9f7631c0565d0afcac13beebe3dd1b92

61. Dickinson DK, McCabe A, Sprague K. Teacher Rating of Oral Language and Literacy (TROLL): A Research-Based Tool. CIERA Report. Published online September 20, 2001. Accessed June 29, 2022. https://eric.ed.gov/?id=ED468087

62. De Lemos MM, Doig BA. *Who Am I?* Australian Council for Educational Research; 1999.

63. Ross H. Establishment of social games among toddlers. Published online 1982. doi:10.1037/0012-1649.18.4.509

64. Denham S. Social Cognition, Prosocial Behavior and Emotion in Preschoolers: Contextual Validation. Published online 1986. doi:10.2307/1130651

65. Crawford A. *Social Cognition, Executive Functioning and IQ. What Are the Important Influences on Adaptive Functioning in Children with Fetal Alcohol Spectrum Disorder?* 2018.

66. Marsh HW. Content Specificity of Relations between Academic Achievement and Academic Self-Concept. *Journal of Educational Psychology*. 1992;84(1):35-42.

67. Ariā - Classifications. Accessed June 29, 2022.
   http://aria.stats.govt.nz/aria/?_ga=2.22759995.1425463559.1634760053-
   853545396.1619642325#ClassificationView:uri=http://stats.govt.nz/cms/ClassificationVers
   ion/l36xYpbxsRh7IW1p

68. Devlin M, Mason K, Yeh LC, New Zealand, Ministry of Health. *Presenting Ethnicity:
   Comparing Prioritised and Total Response Ethnicity in Descriptive Analyses of New Zealand
   Health Monitor Surveys*. Ministry of Health; 2008. Accessed June 29, 2022.
   http://www.moh.govt.nz/moh.nsf/pagesmh/7681/$File/presenting-ethnicity-2008.pdf

69. Felitti VJ, Anda RF, Nordenberg D, et al. Relationship of childhood abuse and household
   dysfunction to many of the leading causes of death in adults. The Adverse Childhood
   Experiences (ACE) Study. *Am J Prev Med*. 1998;14(4):245-258. doi:10.1016/s0749-
   3797(98)00017-8

70. Regional Results 2017–2020: New Zealand Health Survey. Ministry of Health NZ. Accessed
   June 29, 2022. https://www.health.govt.nz/publication/regional-results-2017-2020-new-
   zealand-health-survey

71. Haitana, T., Pitama, S., & Rucklidge, J.J. Cultural biases in the peabody picture vocabulary
   test-III: Testing tamariki in a New Zealand sample. *New Zealand Journal of Psychology*.
   39(3):24-34.

72. Ogden, J.A., & McFarlane-Nathan, G.J.N. Cultural bias in the neuropsychological
   assessment of young Maori men. *New Zealand Journal of Psychology*. 1997;26:2-12.

73. Jacobson SW, Jacobson JL, Sokol RJ, Martier SS, Ager JW, Kaplan MG. Maternal recall of
   alcohol, cocaine, and marijuana use during pregnancy. *Neurotoxicol Teratol*.
   1991;13(5):535-540. doi:10.1016/0892-0362(91)90062-2

74. Ernhart CB, Morrow-Tlucak M, Sokol RJ, Martier S. Underreporting of alcohol use in
   pregnancy. *Alcohol Clin Exp Res*. 1988;12(4):506-511. doi:10.1111/j.1530-
   0277.1988.tb00233.x

75. Morrow-Tlucak M, Ernhart C, Sokol R, Martier S, Ager J. Underreporting of alcohol use in
   pregnancy: relationship to alcohol problem history. *Alcoholism, clinical and experimental
   research*. Published online 1989. doi:10.1111/J.1530-0277.1989.TB00343.X

76. Montag AC, Dusek ML, Ortega ML, Camp-Mazzetti A, Calac DJ, Chambers CD. Tailoring an
   Alcohol Intervention for American Indian Alaska Native Women of Childbearing Age:
   Listening to the Community. *Alcohol Clin Exp Res*. 2017;41(11):1938-1945.
   doi:10.1111/acer.13485

77. Finlay-Jones A, Elliott EJ, Mayers D, et al. Community Priority setting for Fetal Alcohol
   Spectrum Disorder Research in Australia. *IJPDS*. 2020;5(3). doi:10.23889/ijpds.v5i3.1359

78. Johnston S, Boyle JS. Northern British Columbian Aboriginal mothers: raising adolescents
   with fetal alcohol spectrum disorder. *J Transcult Nurs*. 2013;24(1):60-67.
   doi:10.1177/1043659612452006

Appendix 1

Table 25: Alignment with Consider Statement

	CONSIDER STATEMENT		NEUROCOGNITIVE OUTCOMES STUDY	
	Domains and checklist items	Description	Strengths	Reflections
Research Governance				
1.	Partnership agreements	Describe partnerships between research institution and Indigenous-governing organization for research.	Original were partnerships between GUiNZ and Iwi, but also Māori theme leads/Kaitiaki group. This study included setting up advisory group including Māori and Pacific experts/advisors with clear terms of reference. Effort made to ensure partnership was not symbolic but operationalised through continued discussion, sharing, listening.	Would have been helpful to have Māori and Pacific researchers in the core team More Māori and Pacific in the advisory groups to ensure there is a safe space for all Māori and Pacific researchers and advisors.
2.	Accountability	Describe accountability and review mechanisms within the partnership agreement that addresses harm minimization	Inclusion of Māori and Pacific clinical and research expertise on the advisory groups. Harm was considered and included from outset – documented in analysis plan. Advisory group and	It may have been helpful to have a mid-project review of terms of reference. More time and resource invested into relationship development would have

	CONSIDER STATEMENT		NEUROCOGNITIVE OUTCOMES STUDY	
	Domains and checklist items	Description	Strengths	Reflections
			steering group meetings included robust discussions on harm minimisation and forward thinking for potential of findings to provide benefit vs harm. Project team adjusted analyses and processes based on feedback from Māori and Pacific experts on advisory groups. Consideration of how FASD is framed for Māori and Pacific – removing stigma and racist stereotypes.	potentially improved engagement with the project.
3.	Protection of Indigenous intellectual property	Specify methods to protect Indigenous intellectual property and knowledge arising from the research including financial and intellectual benefits	GUiNZ has a data access process which includes consideration of Kaitiakitanga of data. For this study the intent was to ensure equity is central to recommendations – as this is an important disorder impacting on Māori and Pacific therefore higher resources are needed for these groups.	Would have been helpful to double check and review high level arrangements around protection of Māori and Pacific intellectual property – at the organisational level.
Prioritisation				

	CONSIDER STATEMENT		NEUROCOGNITIVE OUTCOMES STUDY	
	Domains and checklist items	**Description**	**Strengths**	**Reflections**
4.	Indigenous input in research aims	Explain how the research aims emerged from priorities identified by either Indigenous stakeholder, governing bodies, funders, non-government organization(s), stakeholders, consumers, and empirical evidence	The research project was commissioned by the government, but research aims were formed and adapted with the steering and scientific advisory groups – including Māori and Pacific experts, NGOs, stakeholders.	Further consultation and input before the start of the project towards confirmation that this is a needed and wanted study.
Relationships				
5.	Adherence to indigenous ethical guidelines	Specify measures that adhere and honour Indigenous ethical guidelines, processes, and approvals for all relevant Indigenous stakeholders, recognizing that multiple Indigenous partners may be involved, e.g., Indigenous ethics committee approval, regional/national ethics approval processes	GUiNZ continues to adapt ethical amendments for each data collection wave to consider responsiveness to Māori and Pacific. Consultation with Steering and Advisory Group was throughout the project.	More resource and time for Māori and Pacific guidance and advice in the formation of the study prior to approval.

	CONSIDER STATEMENT		NEUROCOGNITIVE OUTCOMES STUDY	
	Domains and checklist items	**Description**	**Strengths**	**Reflections**
6.	Indigenous stakeholder involvement	Report how Indigenous stakeholders were involved in the research processes (i.e., research design, funding, implementation, analysis, dissemination/recruitment).	GUiNZ partnership with Māori stakeholders are described elsewhere.(Paine et al., 2022) For this project there were four Māori experts and one Pacific expert. Effort made to meet with experts individually if they couldn't make meetings or had extra questions.	Ideally it would have been helpful to have more Māori and Pacific community representatives involved.
7.	Expertise of research team in indigenous health and research	Describe the expertise of the research team in Indigenous health and research.	The core research team had some experience in Māori and Pacific health research and were clear on their positionality from the outset – in meetings, the analysis plan and in the report. The advisors on the advisory groups were a combination of clinical and research experts in the fields of alcohol, neurodisability and FASD.	It would have been more ideal to have Māori and Pacific researchers in the core team. We acknowledge there is always work to do for every tangata Tiriti researcher to improve their approaches for Indigenous health and research.
Methodologies				

	CONSIDER STATEMENT		NEUROCOGNITIVE OUTCOMES STUDY	
	Domains and checklist items	**Description**	**Strengths**	**Reflections**
8.	Methodological approach	Describe the methodological approach of the research including a rationale of methods used and implication for Indigenous stakeholders, e.g., privacy and confidentiality (individual and collective)	Methods were developed based on previous research in this field from overseas, however adapted during the course of development based on feedback from Māori and Pacific experts. Use of ethnicity variables Total response and external prioritisation variables were informed by previous work in GUiNZ.(Atatoa Carr et al., 2022) Consideration of cultural validity of the tools.	More Māori and Pacific specific analyses would have been helpful if time and resource allowed. Further consideration of cultural validity of tools including what other measures should be included in the analysis.
9.	Consideration of environment and Indigenous worldviews	Describe how the research methodology incorporated consideration of the physical, social, economic and cultural environment of the participants and prospective participants. (e.g., impacts of colonization, racism, and social justice). As well as Indigenous worldviews.	Inclusion of sociodemographic variables Ethnicity approach – total response variable for ethnic sub-group descriptive analysis Consideration of colonisation/racism/indigenous worldviews in report write up.	Ideally more inclusion of indicators or proxies for inequity, racism and colonisation could have been further woven into analyses if time and resource allowed.

CONSIDER STATEMENT		NEUROCOGNITIVE OUTCOMES STUDY	
Domains and checklist items	**Description**	**Strengths**	**Reflections**
Participation			
10. Individual and collective consensus	Specify how individual and collective consent was sought to conduct future analysis on collected samples and data (e.g., additional secondary analyses; third-parties accessing samples (genetic, tissue, blood) for further analyses).	The process of study set up and consent in GUiNZ is described elsewhere.(Morton et al., 2014; Paine et al., 2022)	Not applicable
11. Resourcing	Described how the resource demands (current and future) placed on Indigenous participants and communities involved in the research were identified and agreed upon including any resourcing for participation, knowledge, and expertise	It was decided to have four meetings to ensure efficient use of time for experts. Aspired to morph into a national group to ensure better cohesion in this space. Ensured individual responsive discussion with Māori/Pacific experts when needed.	Burden on Māori and Pacific advisors was more than non-Māori/non-Pacific. This can only be rectified with greater numbers involved to spread the load and more resourcing however structural and systems barriers further impede progress on this.
12. Biological tissue	Specify how biological tissue and other samples including data	Not applicable	Not applicable

	CONSIDER STATEMENT		NEUROCOGNITIVE OUTCOMES STUDY	
	Domains and checklist items	Description	Strengths	Reflections
		were stored, explaining the processes of removal from traditional lands, if done, and of disposal.		
Capacity				
13.	Indigenous research capacity	Explain how the research supported the development and maintenance of Indigenous research capacity (e.g., specific funding of Indigenous researchers).	Relational and responsive interactions between tau iwi team members and indigenous team members provided for collaborative and mutual learning opportunities.	Māori and Pacific researchers in the core team would have allowed for greater knowledge transaction and capacity building between team members.
14.	Professional Development	Discuss how the research team undertook professional development opportunities to develop the capacity to partner with Indigenous stakeholders?	Individual team members have sought learning opportunities to upskill in workshops on responsiveness to Māori and Pacific, use of ethnicity variables and te Tiriti o Waitangi training.	The core team could have done further upskilling on suitable frameworks, cultural safety and competency.
Analysis and Interpretation				

	CONSIDER STATEMENT		NEUROCOGNITIVE OUTCOMES STUDY	
	Domains and checklist items	Description	Strengths	Reflections
15.	Inclusion of Indigenous values	Specify how the research analysis and reporting supported critical inquiry and a strength-based approach that was inclusive of Indigenous values.	Māori experts on the advisory group were specifically consulted throughout the project, including design, analysis plan, interpretation of findings and report write up. Emphasis was placed on reducing stigmatisation for whānau impacted by neurocognitive outcomes related to alcohol harm, by acknowledging the historical trauma and breaches of Te Tiriti o Waitangi.	Indigenous values could have been more incorporated into the core outputs at study set up.
Dissemination				
16.	To relevant Indigenous governing bodies and peoples	Describe the dissemination of the research findings to relevant Indigenous governing bodies and peoples	The process of dissemination is via government reports, research publications and presentations. Specific reach to Māori and Pacific stakeholders will is in partnership with experts in the advisory groups. Writing an article up on this will contribute to this and checklist number 17.	Ideally dissemination would occur directly to the communities impacted by neurodisability in a way that is not stigmatising. In the future building capacity and resourcing Māori research leadership and advisory for neurodisability to improve oversight and the ability to feedback research results.

	CONSIDER STATEMENT		NEUROCOGNITIVE OUTCOMES STUDY	
	Domains and checklist items	**Description**	**Strengths**	**Reflections**
17.	Knowledge translation and implementation	Discuss the process for knowledge translation and implementation to support Indigenous advancement (e.g., research capacity, policy, investment).	The findings of this study are pointing towards the need for more investment into understanding the burden of neurodevelopmental disorders. They will be used to further advocate for more investment and policy to improve outcomes for whānau impacted.	Ensuring the knowledge is in the right hands, and with those that can most advocate for and lobby for further resource and investment.