

# Is the occasional drink harmful in pregnancy? Evidence from a cohort study: AQUA

Jane Halliday  
Reproductive Epidemiology, Genetics

on behalf of the AQUA team



21.11.18.

# Asking questions about alcohol in pregnancy (AQUA): a cohort study of the fetal effects of alcohol use in pregnancy

Jane Halliday,<sup>1</sup> Colleen O'Leary,<sup>2</sup> Susan Donath,<sup>1</sup> Della Forster,<sup>3</sup> Peter Anderson,<sup>1</sup> Sharon Lewis,<sup>1</sup> Cate Nagle,<sup>4</sup> Jeffrey Craig,<sup>1</sup> Elizabeth Elliott<sup>5</sup> and Evi Muggli<sup>1</sup>  
with Harry Matthews,<sup>1</sup> Tony Penington,<sup>1</sup> Sue White,<sup>1</sup> Peter Claes,<sup>6</sup>

<sup>1</sup> Murdoch Children Research Institute

<sup>4</sup> Deakin University

<sup>2</sup> Telethon Kids Institute

<sup>5</sup> The University of Sydney

<sup>3</sup> La Trobe University

<sup>6</sup> KU and UZ Leuven, Belgium



Australian Government

National Health and Medical Research Council

# Aims of AQUA

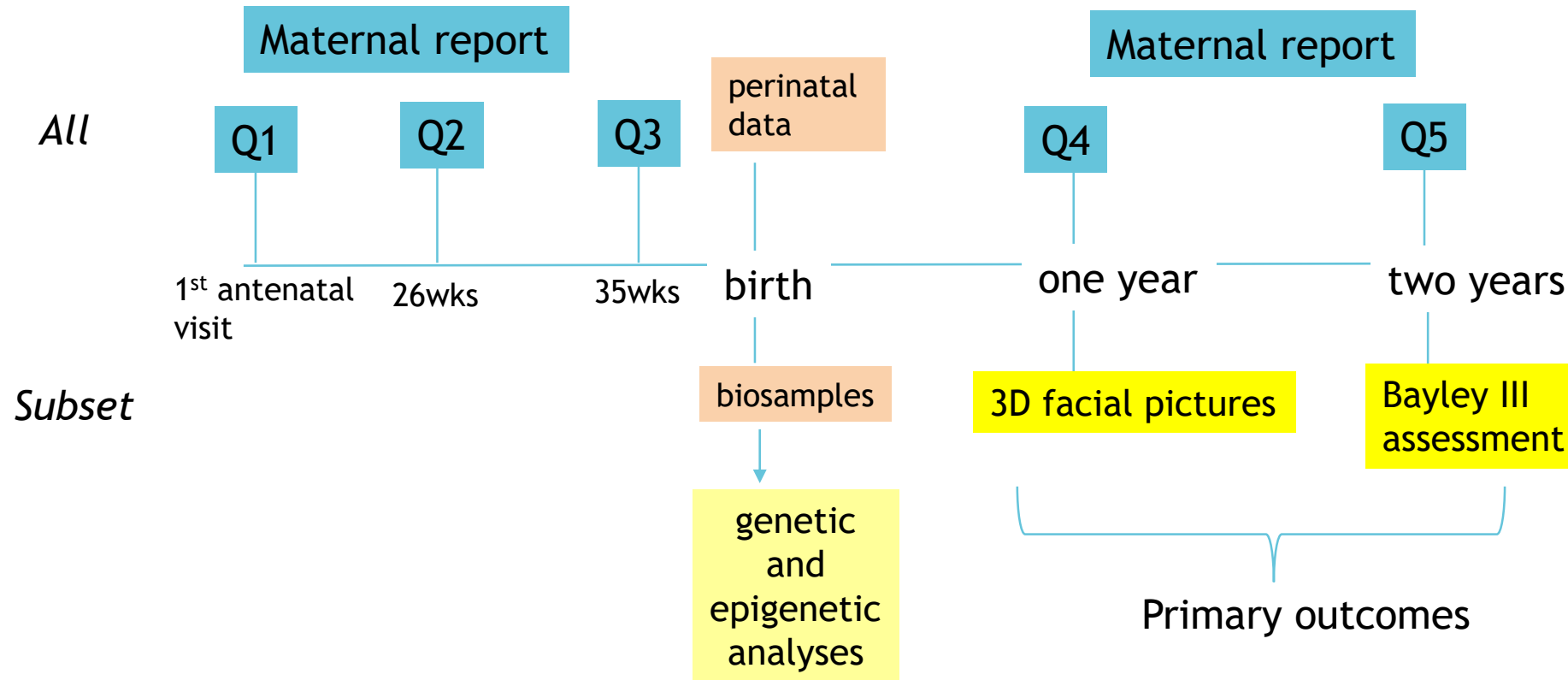
To collect detailed information about all levels of alcohol consumption throughout pregnancy, especially sporadic binge and low exposure,

as well as collecting other possible influences on the unborn child, e.g. socio-economic variation, diet, smoking,

in order to detect early/subtle signs of FASD:

- 1) facial dysmorphology at one year of age, using 3D photography
- 2) neurodevelopmental problems at two years of age using the Bayley III scales and maternally reported sensory/behavioural profiles.

# Prospective cohort data collection



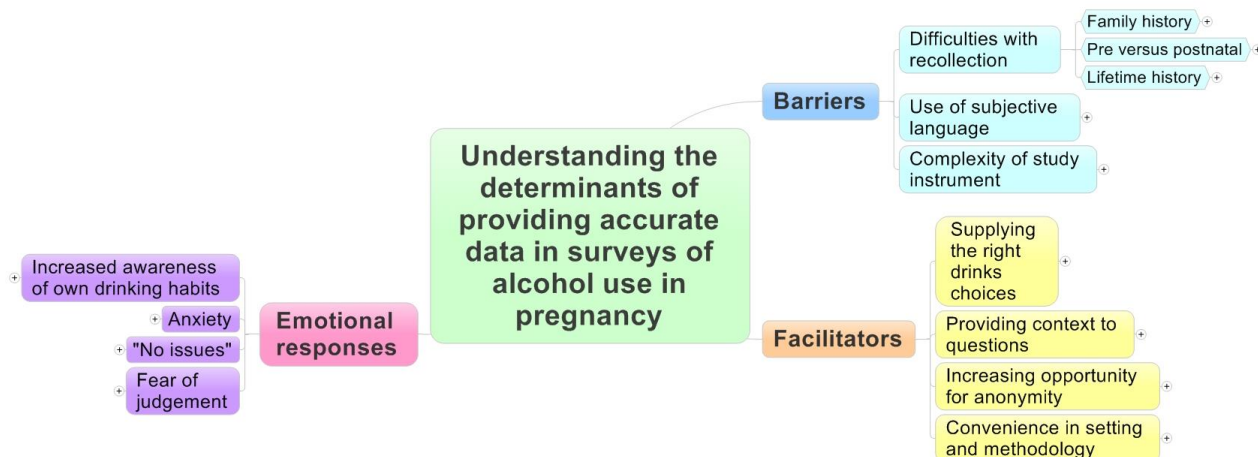
Evi Muggli, Colleen O’Leary, Della Forster, Peter Anderson, Sharon Lewis, Cate Nagle, Jeffrey Craig, Susan Donath, Elizabeth Elliott, Jane Halliday. *Asking QUestions about Alcohol in pregnancy (AQUA): a longitudinal cohort study of fetal effects of low to moderate alcohol exposure*. BMC Pregnancy and Childbirth, 14:302 (2014)

# Challenge: Accurate prenatal alcohol exposure measure

Sceptics ++

Low risk population with vested interest

Focus groups

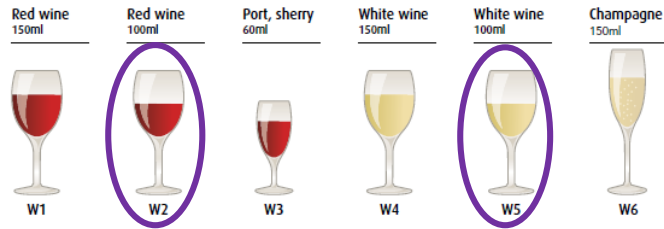


## Increasing accurate self-report in surveys of pregnancy alcohol use

Evelyn Muggli, MPH (Senior Research Officer)<sup>a,h\*</sup>, Brendan Cook, MPH (Research Assistant)<sup>a,c</sup>, Colleen O'Leary, PhD (Post Doctoral Research Fellow)<sup>d</sup>, Della Forster, PhD (Professor)<sup>e,f</sup>, Jane Halliday, PhD (Professor)<sup>a,b</sup>

Midwifery(2014), <http://dx.doi.org/10.1016/j.midw.2014.11.003>

Wine including fortified wines



Beer including cider



Spirits including mixed drinks



# Drinks choices: pregnancy alcohol exposure (PAE) assessment

10g of absolute alcohol (AA) = 1 standard drink

## Definition of exposure level:

- LOW:  $\leq 20\text{gAA}/\text{occasion}$ , and  $< 70\text{gAA}/\text{week}$ ;
- MODERATE:  $21\text{-}49\text{gAA}/\text{occasion}$ , and  $\leq 70\text{gAA}/\text{week}$ ;
- HIGH:  $> 70\text{gAA}/\text{week}$ ;
- BINGE:  $\geq 50\text{gAA}/\text{occasion}$

# Beer including cider



# Spirits including mixed drinks

Nip, shot  
30ml



S1

55. Using the code(s) provided in the Drinks Guide (on the inner back cover of this booklet), please complete the table below, including;
- what type of drink(s) you usually drank in this period,
  - how often you usually drank this type of alcohol (for each), and
  - how many of these would you usually drink on each occasion (for each type of drink).

	CODE FOR DRINK TYPE	FREQUENCY	NUMBER PER OCCASION
1.	B 2	less than once a month <input type="checkbox"/> 1 to 2 days per month <input type="checkbox"/> 1 to 2 days per week <input checked="" type="checkbox"/> 3 to 4 days per week <input type="checkbox"/> 5 or more days per week <input type="checkbox"/>	less than 1 drink <input type="checkbox"/> 1 to 2 drinks <input checked="" type="checkbox"/> 3 to 4 drinks <input type="checkbox"/> 5 to 6 drinks <input type="checkbox"/> 7 or more drinks <input type="checkbox"/>
2.	S 1	less than once a month <input type="checkbox"/> 1 to 2 days per month <input type="checkbox"/> 1 to 2 days per week <input type="checkbox"/> 3 to 4 days per week <input checked="" type="checkbox"/> 5 or more days per week <input type="checkbox"/>	less than 1 drink <input type="checkbox"/> 1 to 2 drinks <input checked="" type="checkbox"/> 3 to 4 drinks <input type="checkbox"/> 5 to 6 drinks <input type="checkbox"/> 7 or more drinks <input type="checkbox"/>
3.		less than once a month <input type="checkbox"/> 1 to 2 days per month <input type="checkbox"/> 1 to 2 days per week <input type="checkbox"/> 3 to 4 days per week <input type="checkbox"/> 5 or more days per week <input type="checkbox"/>	less than 1 drink <input type="checkbox"/> 1 to 2 drinks <input type="checkbox"/> 3 to 4 drinks <input type="checkbox"/> 5 to 6 drinks <input type="checkbox"/> 7 or more drinks <input type="checkbox"/>
4.		less than once a month <input type="checkbox"/> 1 to 2 days per month <input type="checkbox"/> 1 to 2 days per week <input type="checkbox"/> 3 to 4 days per week <input type="checkbox"/> 5 or more days per week <input type="checkbox"/>	less than 1 drink <input type="checkbox"/> 1 to 2 drinks <input type="checkbox"/> 3 to 4 drinks <input type="checkbox"/> 5 to 6 drinks <input type="checkbox"/> 7 or more drinks <input type="checkbox"/>

# Special occasion question

79. Did you ever drink more than you would normally have done (as you described above), for example on special occasions or during difficult times?

no  (please go to question 82)

yes

80. Approximately, how many times did this occur in the time since you became pregnant, but before you knew you were pregnant?  
(please provide number of occasions)

occasions

81. Using the code(s) provided in the Drinks Guide (on the inner back cover of this booklet), please complete the table below to show;

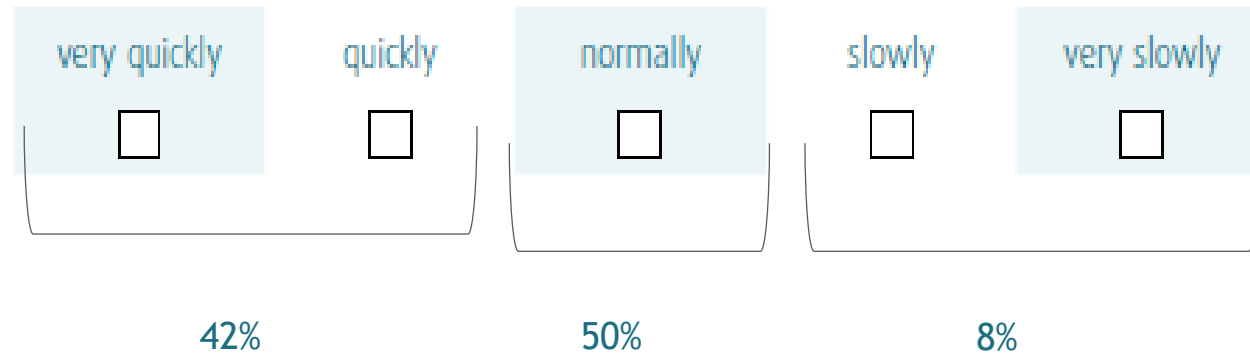
- what type of drink(s) you usually drank on these special occasions or during difficult times, and
- how many of these would you usually drink on each occasion (for each type of drink)

	CODE FOR DRINK TYPE	NUMBER PER OCCASION				
1.	<input type="text"/>	less than 1 drink <input type="checkbox"/>	1 to 2 drinks <input type="checkbox"/>	3 to 4 drinks <input type="checkbox"/>	5 to 6 drinks <input type="checkbox"/>	7 or more drinks <input type="checkbox"/>

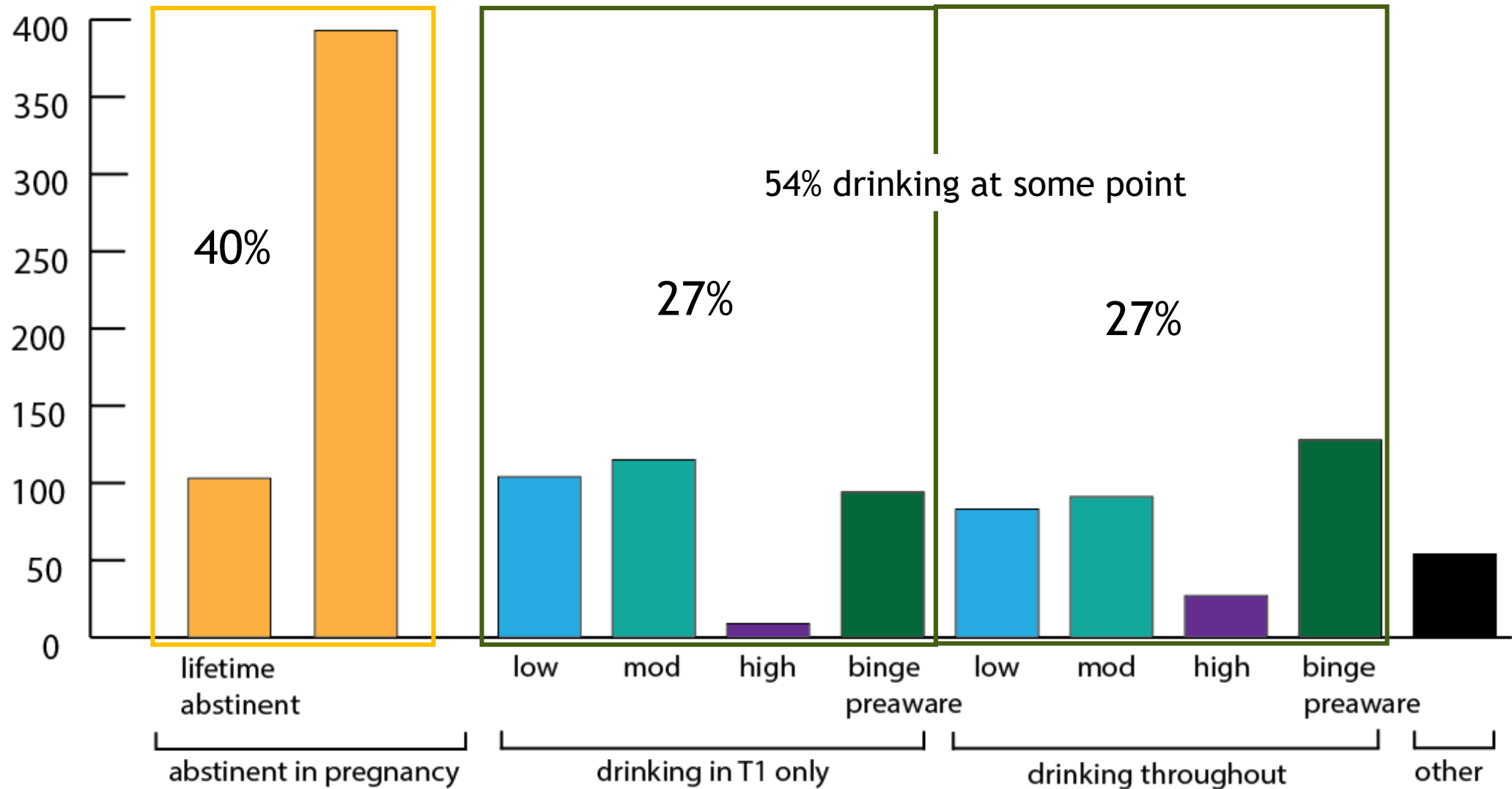


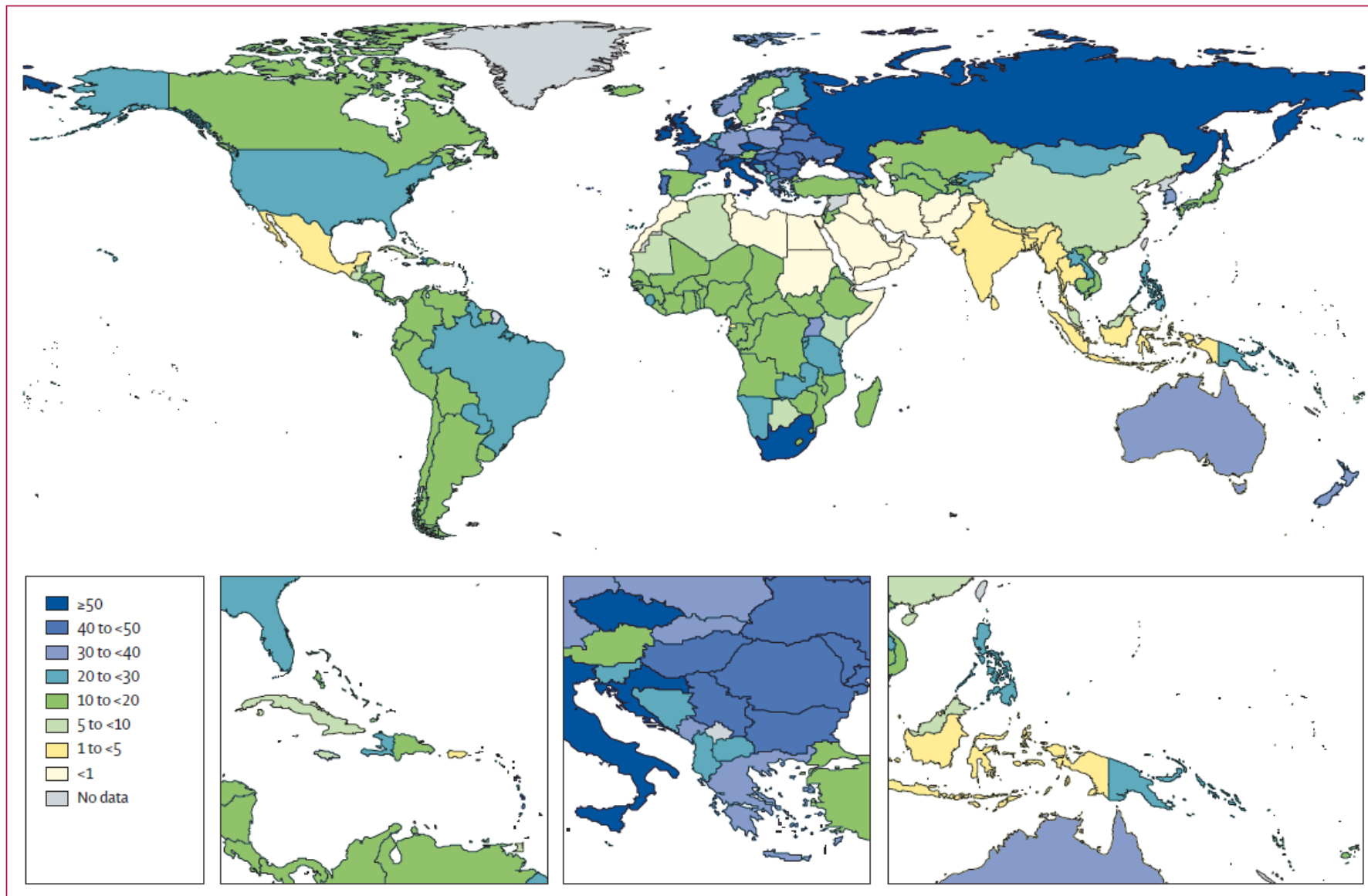
# “Feeling the effect of alcohol”

Prior to this pregnancy, would you have described yourself as someone who felt the effects of alcohol: *(please tick ONE only)*

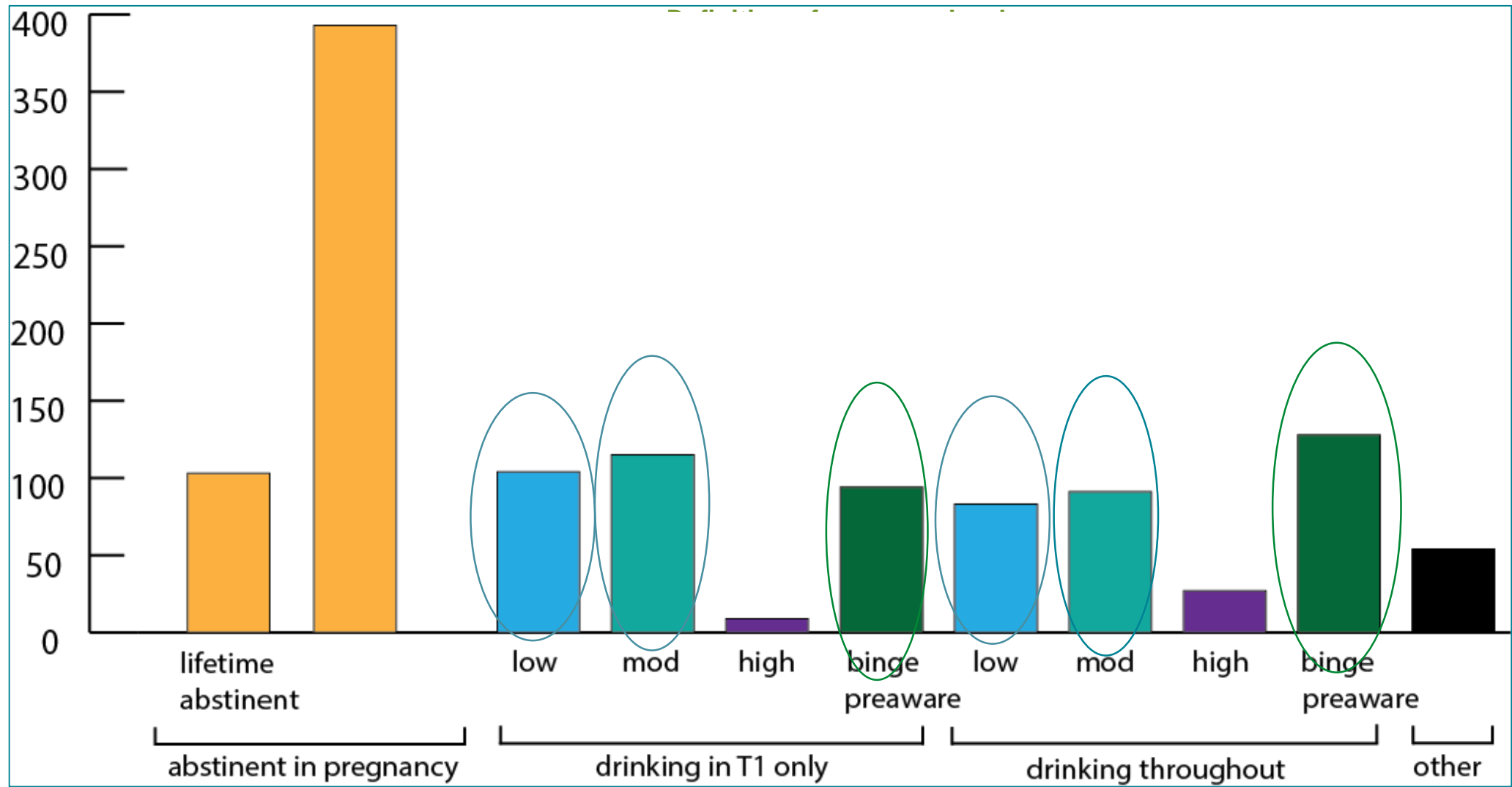


# Prenatal alcohol exposure (n=1200)





Global prevalence (%) of **alcohol use (any amount) in pregnancy** among the general antenatal population in 2012





The survey by Murdoch Childrens Research Institute found 41 per cent did not drink during pregnancy. Picture: Supplied



AND 100% OF PREGNANT LOOKING MEN DRINK

### Lack of concern over drinking while pregnant

MORE than one third of pregnant women drink despite most knowing the harmful effects alcohol can have on unborn children, a study has found. A paper, to be presented at the Royal

# Aussie women 'just don't get it' on drinking while pregnant

## Don't risk your bub with booze



Lucie van den Berg and Courtney Crane

AUSSIE women have been criticised as incredibly ignorant about the danger of drinking alcohol during pregnancy. Liberal MP for Murray Sharnan Stone said yesterday it was a tragedy many women were still not fully aware of the dangers of fetal alcohol spectrum disorder, even though women now drank as "hard and long as the boys". "Every survey conducted in Australia of women's knowledge about alcohol consumption during pregnancy shows a shocking majority have not been informed," Dr Stone said. The National Health and Medical Research Council said there was no safe level of drinking during pregnancy or breastfeeding. But a cone of silence had long paralysed Australia's recognition and response to the dangers. "In the past 40 years, Australian women and men have stopped

VIC News

## Educated women more likely to continue drinking alcohol throughout pregnancy, study finds

"Did you ever drink more?" A detailed description of pregnant women's drinking patterns



Evelyne Muggli<sup>1,2\*</sup>, Colleen O'Leary<sup>3</sup>, Susan Donath<sup>1,2</sup>, Francesca Orsini<sup>1</sup>, Della Forster<sup>4,5</sup>, Peter J. Anderson<sup>1,2</sup>, Sharon Lewis<sup>1,2</sup>, Catherine Nagle<sup>6,7</sup>, Jeffrey M. Craig<sup>1,2</sup>, Elizabeth Elliott<sup>8</sup> and Jane Halliday<sup>1,2</sup>

BMC Public Health. 2016;16:683.

# Aim 1) facial dysmorphology at one year of age, using 3D photography

Is there an effect on facial shape of 12 month old children exposed to 'common' patterns of alcohol use in pregnancy?



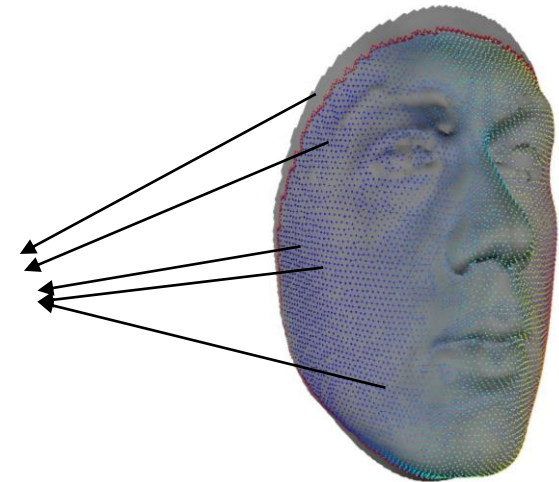
## Three sentinel facial features in FASD

- Short palpebral fissure
- Long, flat philtrum with loss of the central groove
- Thin upper vermillion, decreased lip volume

## Others

- Short, upturned nose; microcephaly; mid-face hypoplasia (inc malar flattening/micro/retrognathia); flat, low nasal bridge; inner canthal folds

YES - see Harry Matthew's talk later today



# 3D facial photography at one year of age

- Full range of alcohol exposure patterns
- Caucasian parents
- Image taken within 2 weeks of first birthday

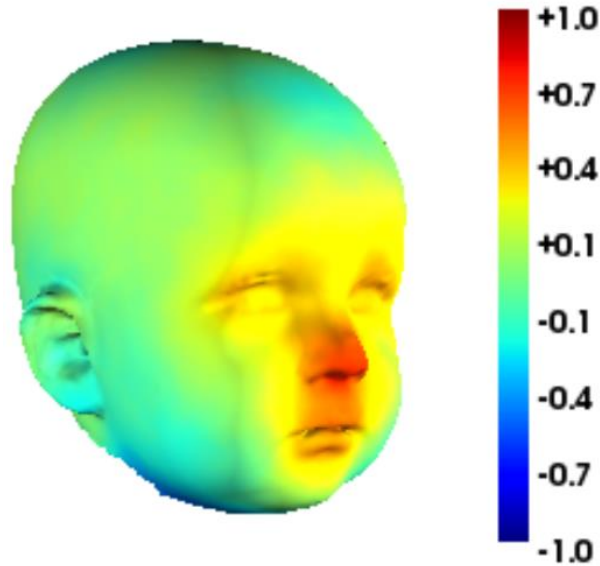


415 AQUA children had their 3D photo included in his analysis



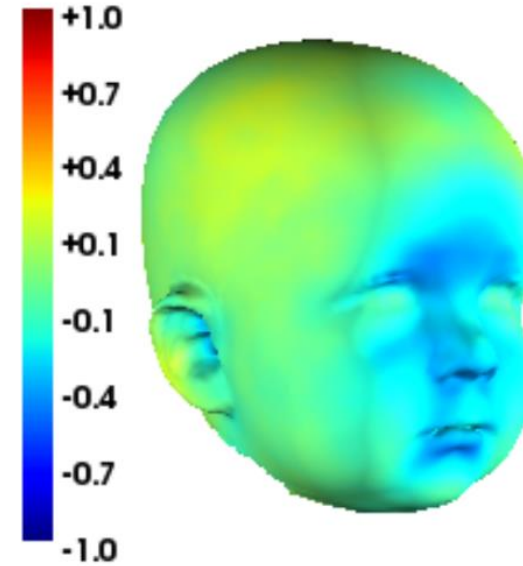
# Any alcohol exposure

Superior/inferior displacement (mm)



Mouth, upper-lip and  
base of nose

Anterior/posterior displacement (mm)



Midface

Change in facial pattern consistent with FASD

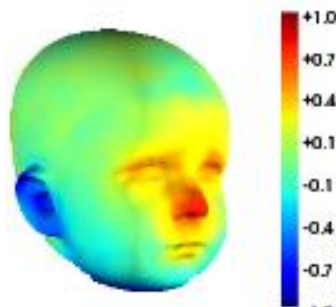


# Results- by exposure group, trimester 1 only

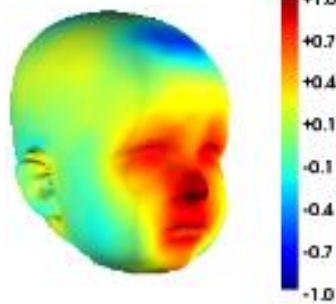
Superior/inferior displacement (mm)

Anterior/posterior displacement (mm)

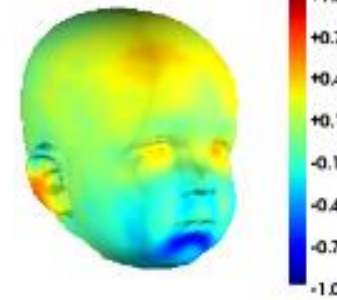
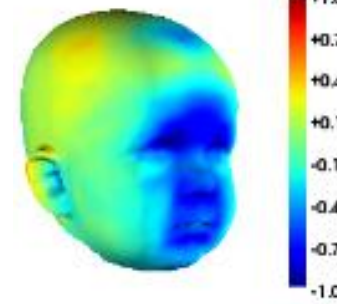
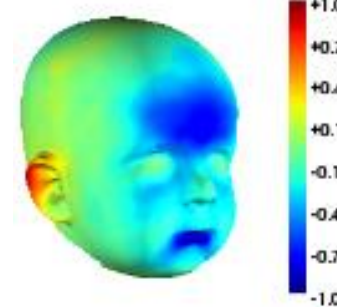
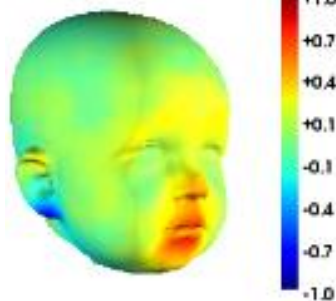
Low



Moderate



Binge pre-aware

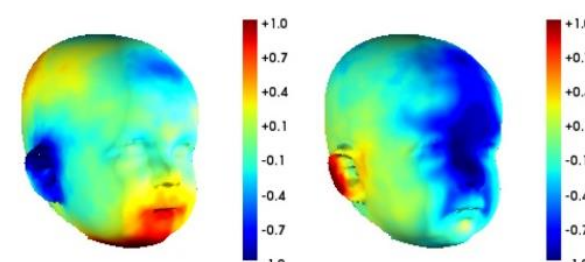
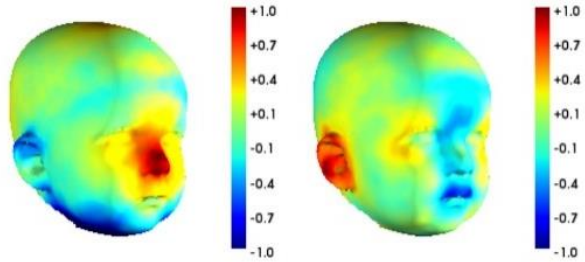


# Results- by alcohol sensitivity, exposure all pregnancy

Feel effect of alcohol 'normally'

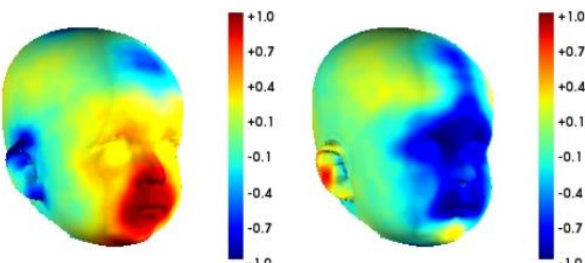
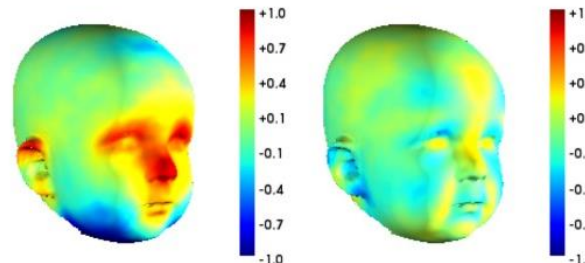
Feel effect of alcohol 'very/quickly'

Low (n= 18)



Low (n=20)

Moderate (n=58)



Moderate (n=20)

Research

JAMA Pediatrics | Original Investigation

## Association Between Prenatal Alcohol Exposure and Craniofacial Shape of Children at 12 Months of Age

Evelyne Muggli, MPH; Harold Matthews, BPsych(Hons); Anthony Penington, MDBS; Peter Claes, PhD; Colleen O'Leary, PhD; Della Forster, PhD; Susan Donath, MA; Peter J. Anderson, PhD; Sharon Lewis, PhD; Cate Nagle, PhD; Jeffrey M. Craig, PhD; Susan M. White, MBBS; Elizabeth J. Elliott, MD; Jane Halliday, PhD

← Editorial

← JAMA Pediatrics Patient Page

+ Supplemental content

## Aim 2) neurodevelopmental problems at two years of age

Is there an effect on neurodevelopment in two year old children exposed to 'common' patterns of alcohol use in pregnancy?

a) Clinical review by psychologists (n=565):  
Bayley-III Scales of Infant and Toddler Development



Cognition



Language



Motor

NO - but may be too early to detect subtle changes

## Aim 2) neurodevelopmental problems at two years of age - continued

b) Maternal report - completed by mother in the questionnaire (n~920)

Infant Toddler Sensory Profile - 4 quadrants,



Low registration



Sensory sensitivity



Sensation seeking



Sensation avoiding

NO - for low exposure, but YES for binge early and continued

### Healthy child development

Alcohol consumption in a general antenatal population and child neurodevelopment at 2 years

Jane L Halliday,<sup>1,2</sup> Evelyne Muggli,<sup>1,2</sup> Sharon Lewis,<sup>1,2</sup> Elizabeth J Elliott,<sup>1,3</sup> David J Amor,<sup>1,2</sup> Colleen O'Leary,<sup>4</sup> Susan Donath,<sup>1,2</sup> Della Forster,<sup>5,6</sup> Cate Nagle,<sup>7,8</sup> Jeffrey M Craig,<sup>1,2</sup> Peter J Anderson<sup>1</sup>

# Summary - outcomes if exposed to low levels of alcohol

- 3D photography suggests that any alcohol changes the face (seen at one year)
  - The clinical significance of these findings is yet to be determined
- Neurodevelopment at two years is not seriously affected, but may be too early to detect subtle changes.
- Early warning of sensory processing problems with binge PAE and continued drinking?

# Coming up

Genetic analysis - interaction between PAE and maternal or fetal genotype



Genome-wide epigenetic analysis of buccals

AQUA@6 NHMRC grant 2018-2021

Started already - recruiting 6-7 year olds for in-depth assessments:



- Neurodevelopment



- 3D imaging



- MRI - brain structure and function



# Acknowledgements

## Chief Investigators

Prof Jane Halliday  
Dr Colleen O'Leary  
Prof Della Forster  
A/Prof Susan Donath  
Prof Peter Anderson  
Dr Sharon Lewis  
Prof Elizabeth Elliott  
A/Prof Cate Nagle  
A/Prof Jeff Craig  
Evi Muggli

## Associate Investigators

Dr Sue White  
Prof Tony Pennington  
Dr Justine Ellis  
Dr Richard Saffery  
Joyce Cleary

## Project team

Evi Muggli  
Anne Glynn  
Turi Berg  
Helen Curd  
Anne Glynn  
Jo Kennedy  
Amanda Springer  
Dr Jane Loke  
(epigenetics)

## Facial analysis

Dr Peter Claes  
Harry Matthews

## 3D imaging

Robert Reitmaier  
Bert Di Paolo  
Alvin Aquino  
Lloyd Ellis

## Developmental assessments

Claire Corbett  
Michelle Livock  
Siobhan James

## Students

Michelle Livock (PhD)  
Wendy Pameh (MPH)  
Stephanie Badman (MGC)  
Mah Linh Ngyuen (Hon)  
Tara Sudarmana (SS)  
Hong Wu (SS)  
Lauren Rimmer (SS)  
Leah Marino (HIM, 2013)  
Taotao Zhu (HIM, 2012)  
Julie Price (HIM, 2011)  
Emily Lange (HIM, 2014)  
Whitney Blake (HIM, 2014)  
Megan McDonald (HIM, 2015)

## Recruitment staff

Simone Hamilton  
Jenny Saal  
Dianna Maxwell  
Clare Morrison  
Veronica Abruzzo  
Tina Viano  
Jenni Vaughan  
Janelle Blythe  
Turi Berg  
Michelle Burnett  
Kylie Black  
June Williams  
Bec Heylen

## Administrative support

RCH volunteers

## Statistical support

Francesca Orsini

## Database support

Luke Stevens