



# Long-Term Outcomes of Prenatal Exposure to Methadone or Buprenorphine

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UNDER THE STEWARDSHIP OF MARY AIKENHEAD MINISTRIES

# Key Ideas...

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**The Big Idea...** opioid exposure during pregnancy has developmental consequences which is progressive over time.

**The Key Clinical Decision...** selecting a model of treatment that has the least evidence of harm.

**The Key Clinical Skills...** to learn how to talk to pregnant women about their substance use non-judgementally.

**The Main Scientific Mechanisms...** opioid receptors in foetal neurological structures.

**The Key Insight for Clinician as a Professional...** does my own bias interfere with identifying and treating pregnant women with opioid use disorder?

# Opioid Use Disorder and Pregnancy

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Prevalence in Australia is difficult to capture.

Amongst pregnant women, 2.4% reported using illicit substances before knowledge of pregnancy. National Drug Strategy

Household Survey (AIHW 2014)

## Neonatal Abstinence Syndrome (NAS)

- AUS: ~3 per 1000 live births
- USA: rapidly increasing, baby born every 25 minutes

# Opioid Use Disorder and Pregnancy

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## Maternal opioid use disorder > negative consequences

- maternal death (OR 4.6; 95%CI 1.8 to 12.1)
- intrauterine growth restriction (OR 2.7; 95%CI 2.4 to 2.9)
- preterm labour (OR 2.1; 95%CI 2.0 to 2.3)
- stillbirth (OR 1.5; 95%CI 1.3 to 1.8)

# I. Foetal Impact

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Opioid receptors are  
diffusely present in fetal  
neurologic structures from a  
very early gestational age

Opioids (and metabolites) freely  
cross the placenta

## II. Neonatal Impact

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### Neonatal Abstinence Syndrome

Central and autonomic nervous system &  
gastrointestinal system dysfunction





DATE:	SCORE	TIME
High pitched cry: inconsolable >15 sec. OR intermittently for <5 min.	2	
High pitched cry: inconsolable >15 sec. AND intermittently for ≥5 min.	3	
Sleeps <1 hour after feeding	3	
Sleeps <2 hours after feeding	2	
Sleeps <3 hours after feeding	1	
Hyperactive Moro	1	
Markedly hyperactive Moro	2	
Mild tremors: disturbed	1	
Moderate-severe tremors: disturbed	2	
Mild tremors: undisturbed	1	
Moderate-severe tremors: undisturbed	2	
Increased muscle tone	1-2	
Excoriation (indicate specific area): _____	1-2	
Generalized seizure	8	
Fever ≥37.2°C (99°F)	1	
Frequent yawning (≥4 in an interval)	1	
Sweating	1	
Nasal stuffiness	1	
Sneezing (≥4 in an interval)	1	
Tachypnea (rate >60/min.)	2	
Poor feeding	2	
Vomiting (or regurgitation)	2	
Loose stools	2	
≤90% of birth weight	2	
Excessive irritability	1-3	
Total score		
Initials of scorer		

*“That tremulous,  
unsettled,  
inconsolable baby  
with a high-pitched  
cry, red face, arching  
back, who is vomiting  
and feeding poorly”*

Oral morphine  
Phenobarbitol, Clonidine  
Average length of stay 17-23 days

## III. Developmental Impact


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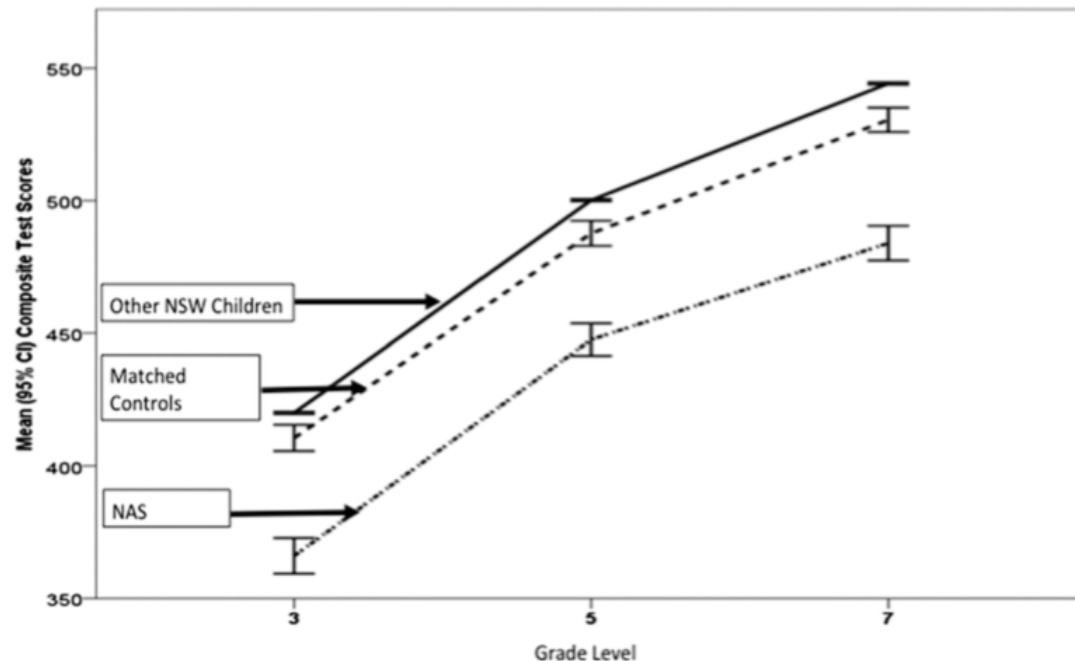


## Neonatal Abstinence Syndrome and High School Performance

Ju Lee Oei, MD ; Edward Melhuish, PhD; Hannah Uebel; Nadin Azzam; Courtney Breen, PhD; Lucinda Burns, PhD; Lisa Hilder, MBBS; Barbara Bajuk, MPH; Mohamed E. Abdel-Latif, MD; Meredith Ward, FRACP; John M. Feller, FRACP; Janet Falconer, CNC; Sara Clews, CNC; John Eastwood, FRACP; Annie Li; Ian M. Wright, FRACP

- Data Linkage Study (2000-2006)
  - Perinatal Data Collection
  - Admitted Patient Data
  - NAPLAN database
- 468, 239 children
- Follow-up until Year 7

# Neonatal Abstinence Syndrome and High School Performance



NAS is associated with poorer academic performance at every grade and every domain of testing.

**Difference was progressive.**

Poor school performance increases the risk of myriad of poor adult outcomes.

# Treatment of Opioid Use Disorder in Pregnancy

Opioid Maintenance Therapy (OMT) has been the gold standard pharmacological treatment for opioid-dependent pregnant women. >5 decades of experience and substantial literature base supports its benefit.

# However...

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Despite stabilization of the intrauterine environment through  
long-acting OMT

# However...

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Despite stabilization of the intrauterine environment through  
long-acting OMT

Majority of newborns show symptoms of NAS

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Long-term neurodevelopmental data is lacking



ELSEVIER

## Prenatal exposure to methadone or buprenorphine and long-term outcomes: A meta-analysis

Jannike Mørch Andersen<sup>a,\*</sup>, Gudrun Høiseth<sup>a,b</sup>, Egil Nygaard<sup>c</sup>

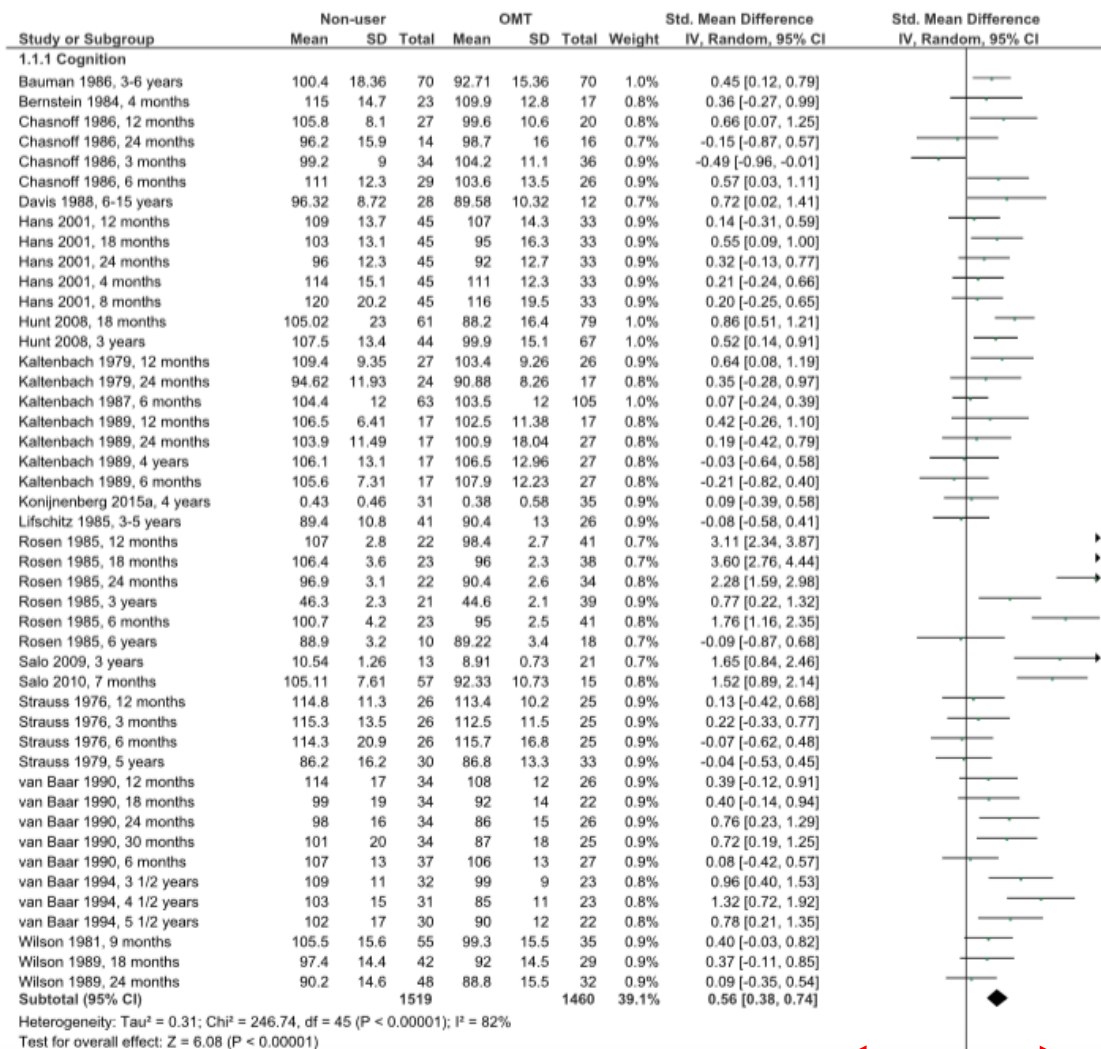
- Systemic literature search (1946 to 2018)
- 29 studies including 8,097 children
- Mean follow up 3.1 years (range 3 months-11 years)
- Measured cognition, motor function, attention, executive function, behaviour and vision



# Prenatal exposure to methadone or buprenorphine and long-term outcomes: A meta-analysis

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Jannike Mørch Andersen<sup>a,\*</sup>, Gudrun Høiseth<sup>a,b</sup>, Egil Nygaard<sup>c</sup>



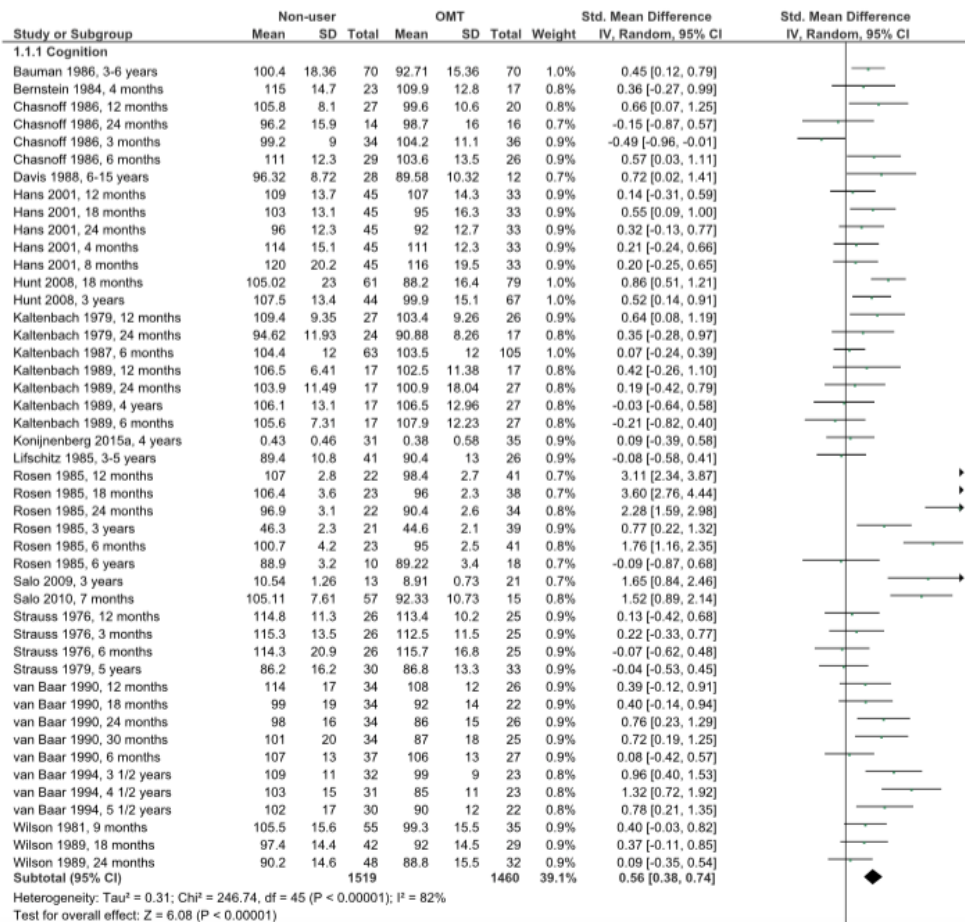
Favours OMT

Favours non-exposed

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## OMT vs Non-exposed

OMT group had worse developmental outcomes than non-exposed group.

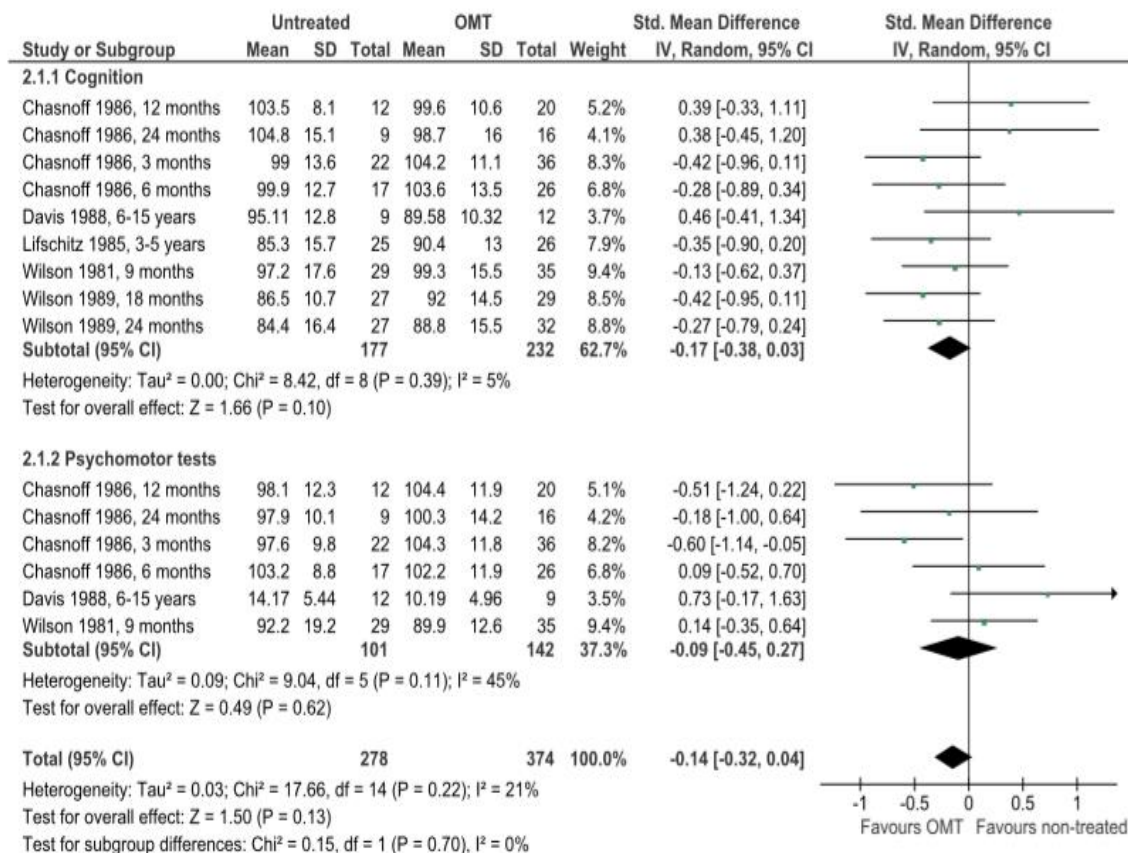
Effect size was small (0.49) but statistically significant ( $p < 0.00001$ ).

Practically translates into a 7-point IQ difference.

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## OMT vs Untreated

OMT group fared better than the untreated group (untreated heroin or polysubstance use).

Difference in cognitive abilities was on the border of statistical significance ( $p = 0.10$ ).

Favours OMT Favours untreated

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## Limitations

OMT and non-exposed groups were poorly matched  
> overestimation of difference

High risk of bias in most studies  
> researchers not blinded  
> attrition bias

Heterogeneity

Lack of studies of older children  
> underestimation of long-term difference

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## Authors' Conclusion

Mother in OMT is better for the child than a mother with untreated opioid addiction.

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## Authors' Conclusion

Mother in OMT is better for the child than a mother with untreated opioid addiction.

*‘However, potential worse outcomes in the OMT children compared to the non-exposed children emphasize the need to discuss whether OMT should continue to be the only preferred treatment during pregnancy or whether controlled tapering combined with psychosocial treatment should be recommended as an alternative, at least for motivated patients’*



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