



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

17 March 2022 Dr Connie Chong Addiction Medicine Registrar Paediatrics & Adolescent Medicine Advanced Trainee



Key Ideas...

**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?



Day/Month/Year

Page 3

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



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)

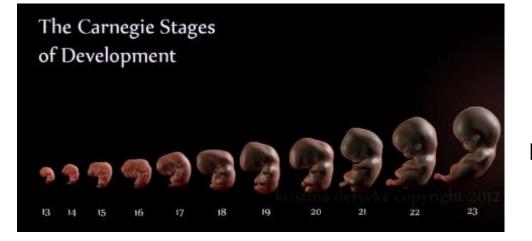


## I. Foetal Impact





## I. Foetal Impact



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

Day/Month/Year

Page 6

# Opioids (and metabolites) freely cross the placenta

Footnote to go here



## II. Neonatal Impact





## **II. Neonatal Impact**



#### Neonatal Abstinence Syndrome Central and autonomic nervous system & gastrointestinal system dysfunction

Day/Month/Year

Page 8

DATE:	SCORE	TIME
High pitched cry: inconsolable >15 sec.	2	
OR intermittently for <5 min.		
High pitched cry: inconsolable >15 sec.	3	
AND intermittently for ≥5 min.		
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	
s90% of birth weight	2	
Excessive irritability	1-3	
Total score		
Initials of scorer		

Foomore to go mere



"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

Day/Month/Year

Page 9



## III. Developmental Impact



Volume 139, Issue 2 February 2017

## III. Developmental Impact



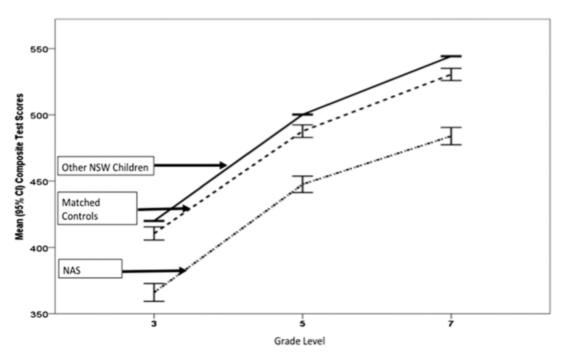
#### **Neonatal Abstinence Syndrome and High School Performance**

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.



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.







# Despite stabilization of the intrauterine environment through long-acting OMT







Day/Month/Year

Page 15

# Despite stabilization of the intrauterine environment through long-acting OMT

#### Majority of newborns show symptoms of NAS

&

#### Long-term neurodevelopmental data is lacking



Contents lists available at ScienceDirect

#### Early Human Development

journal homepage: www.elsevier.com/locate/earlhumdev

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

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

	No	n-user			OMT			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
1.1.1 Cognition									
Bauman 1986, 3-6 years	100.4	18.36	70	92.71	15.36	70	1.0%	0.45 [0.12, 0.79]	
Bernstein 1984, 4 months	115	14.7	23	109.9	12.8	17	0.8%	0.36 [-0.27, 0.99]	<u>+</u>
Chasnoff 1986, 12 months	105.8	8.1	27	99.6	10.6	20	0.8%	0.66 [0.07, 1.25]	
Chasnoff 1986, 24 months	96.2	15.9	14	98.7	16	16	0.7%	-0.15 [-0.87, 0.57]	
Chasnoff 1986, 3 months	99.2	9	34	104.2	11.1	36	0.9%	-0.49 [-0.96, -0.01]	
Chasnoff 1986, 6 months	111	12.3	29	103.6	13.5	26	0.9%	0.57 [0.03, 1.11]	
Davis 1988, 6-15 years	96.32	8.72	28	89.58	10.32	12	0.7%	0.72 [0.02, 1.41]	
Hans 2001, 12 months	109	13.7	45	107	14.3	33	0.9%	0.14 [-0.31, 0.59]	
Hans 2001, 18 months	103	13.1	45	95	16.3	33	0.9%	0.55 [0.09, 1.00]	
Hans 2001, 24 months	96	12.3	45	92	12.7	33	0.9%	0.32 [-0.13, 0.77]	<b>—</b>
Hans 2001, 4 months	114	15.1	45	111	12.3	33	0.9%	0.21 [-0.24, 0.66]	<del></del>
Hans 2001, 8 months	120	20.2	45	116	19.5	33	0.9%	0.20 [-0.25, 0.65]	
Hunt 2008, 18 months	105.02	23	61	88.2	16.4	79	1.0%	0.86 [0.51, 1.21]	
Hunt 2008, 3 years	107.5	13.4	44	99.9	15.1	67	1.0%	0.52 [0.14, 0.91]	
Kaltenbach 1979, 12 months	109.4	9.35	27	103.4	9.26	26	0.9%	0.64 [0.08, 1.19]	
Kaltenbach 1979, 24 months	94.62	11.93	24	90.88	8.26	17	0.8%	0.35 [-0.28, 0.97]	
Kaltenbach 1987, 6 months	104.4	12	63	103.5	12	105	1.0%	0.07 [-0.24, 0.39]	<u> </u>
Kaltenbach 1989, 12 months	106.5	6.41	17	102.5	11.38	17	0.8%	0.42 [-0.26, 1.10]	
Kaltenbach 1989, 24 months	103.9	11.49	17	100.9	18.04	27	0.8%	0.19 [-0.42, 0.79]	
Kaltenbach 1989, 4 years	106.1	13.1	17	106.5	12.96	27	0.8%	-0.03 [-0.64, 0.58]	
Kaltenbach 1989, 6 months	105.6	7.31	17	107.9	12.23	27	0.8%	-0.21 [-0.82, 0.40]	
Konijnenberg 2015a, 4 years	0.43	0.46	31	0.38	0.58	35	0.9%	0.09 [-0.39, 0.58]	
Lifschitz 1985, 3-5 years	89.4	10.8	41	90.4	13	26	0.9%	-0.08 [-0.58, 0.41]	
Rosen 1985, 12 months	107	2.8	22	98.4	2.7	41	0.7%	3.11 [2.34, 3.87]	
Rosen 1985, 18 months	106.4	3.6	23	96	2.3	38	0.7%	3.60 [2.76, 4.44]	
Rosen 1985, 24 months	96.9	3.1	22	90.4	2.6	34	0.8%	2.28 [1.59, 2.98]	
Rosen 1985, 3 years	46.3	2.3	22	44.6	2.0	39	0.8%	0.77 [0.22, 1.32]	
Rosen 1985, 6 months	100.7	4.2	23	44.0	2.5	41	0.8%		
Rosen 1985, 6 years	88.9	3.2	10	89.22	3.4	18	0.8%	1.76 [1.16, 2.35] -0.09 [-0.87, 0.68]	
			13						
Salo 2009, 3 years	10.54	1.26		8.91	0.73	21	0.7%	1.65 [0.84, 2.46]	
Salo 2010, 7 months	105.11	7.61	57	92.33	10.73	15 25	0.8%	1.52 [0.89, 2.14]	
Strauss 1976, 12 months	114.8	11.3	26	113.4	10.2		0.9%	0.13 [-0.42, 0.68]	-
Strauss 1976, 3 months	115.3	13.5	26	112.5	11.5	25	0.9%	0.22 [-0.33, 0.77]	
Strauss 1976, 6 months	114.3	20.9	26	115.7	16.8	25	0.9%	-0.07 [-0.62, 0.48]	
Strauss 1979, 5 years	86.2	16.2	30	86.8	13.3	33	0.9%	-0.04 [-0.53, 0.45]	1
van Baar 1990, 12 months	114	17	34	108	12	26	0.9%	0.39 [-0.12, 0.91]	
van Baar 1990, 18 months	99	19	34	92	14	22	0.9%	0.40 [-0.14, 0.94]	
van Baar 1990, 24 months	98	16	34	86	15	26	0.9%	0.76 [0.23, 1.29]	
van Baar 1990, 30 months	101	20	34	87	18	25	0.9%	0.72 [0.19, 1.25]	
van Baar 1990, 6 months	107	13	37	106	13	27	0.9%	0.08 [-0.42, 0.57]	
van Baar 1994, 3 1/2 years	109	11	32	99	9	23	0.8%	0.96 [0.40, 1.53]	
van Baar 1994, 4 1/2 years	103	15	31	85	11	23	0.8%	1.32 [0.72, 1.92]	
van Baar 1994, 5 1/2 years	102	17	30	90	12	22	0.8%	0.78 [0.21, 1.35]	
Wilson 1981, 9 months	105.5	15.6	55	99.3	15.5	35	0.9%	0.40 [-0.03, 0.82]	
Wilson 1989, 18 months	97.4	14.4	42	92	14.5	29	0.9%	0.37 [-0.11, 0.85]	
Wilson 1989, 24 months	90.2	14.6	48	88.8	15.5	32	0.9%	0.09 [-0.35, 0.54]	
Subtotal (95% CI)			1519			1460	39.1%	0.56 [0.38, 0.74]	●

Heterogeneity: Tau<sup>2</sup> = 0.31; Chi<sup>2</sup> = 246.74, df = 45 (P < 0.00001); l<sup>2</sup> = 82% Test for overall effect: Z = 6.08 (P < 0.00001)

**Favours OMT** 

Favours non-exposed Day/Month/Year

٠

Α

Footnote to go here

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

	No	n-user			OMT		:	Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
1.1.1 Cognition									
Bauman 1986, 3-6 years	100.4	18.36	70	92.71	15.36	70	1.0%	0.45 [0.12, 0.79]	
Bernstein 1984, 4 months	115	14.7	23	109.9	12.8	17	0.8%	0.36 [-0.27, 0.99]	
Chasnoff 1986, 12 months	105.8	8.1	27	99.6	10.6	20	0.8%	0.66 [0.07, 1.25]	
Chasnoff 1986, 24 months	96.2	15.9	14	98.7	16	16	0.7%	-0.15 [-0.87, 0.57]	
Chasnoff 1986, 3 months	99.2	9	34	104.2	11.1	36	0.9%	-0.49 [-0.96, -0.01]	
Chasnoff 1986, 6 months	111	12.3	29	103.6	13.5	26	0.9%	0.57 [0.03, 1.11]	
Davis 1988, 6-15 years	96.32	8.72	28	89.58	10.32	12	0.7%	0.72 [0.02, 1.41]	
Hans 2001, 12 months	109	13.7	45	107	14.3	33	0.9%	0.14 [-0.31, 0.59]	
Hans 2001, 18 months	103	13.1	45	95	16.3	33	0.9%	0.55 [0.09, 1.00]	
Hans 2001, 24 months	96	12.3	45	92	12.7	33	0.9%	0.32 [-0.13, 0.77]	
Hans 2001, 4 months	114	15.1	45	111	12.3	33	0.9%	0.21 [-0.24, 0.66]	+
Hans 2001, 8 months	120	20.2	45	116	19.5	33	0.9%	0.20 [-0.25, 0.65]	
Hunt 2008, 18 months	105.02	23	61	88.2	16.4	79	1.0%	0.86 [0.51, 1.21]	
Hunt 2008, 3 years	107.5	13.4	44	99.9	15.1	67	1.0%	0.52 [0.14, 0.91]	
Kaltenbach 1979, 12 months	109.4	9.35	27	103.4	9.26	26	0.9%	0.64 [0.08, 1.19]	
Kaltenbach 1979, 24 months	94.62	11.93	24	90.88	8.26	17	0.8%	0.35 [-0.28, 0.97]	
Kaltenbach 1987, 6 months	104.4	12	63	103.5	12	105	1.0%	0.07 [-0.24, 0.39]	<u> </u>
Kaltenbach 1989, 12 months	106.5	6.41	17	102.5	11.38	17	0.8%	0.42 [-0.26, 1.10]	
Kaltenbach 1989, 24 months	103.9	11,49	17	100.9	18.04	27	0.8%	0.19 [-0.42, 0.79]	
Kaltenbach 1989, 4 years	106.1	13.1	17	106.5	12.96	27	0.8%	-0.03 [-0.64, 0.58]	
Kaltenbach 1989, 6 months	105.6	7.31	17	107.9	12.23	27	0.8%	-0.21 [-0.82, 0.40]	
Konijnenberg 2015a, 4 years	0.43	0.46	31	0.38	0.58	35	0.9%	0.09 [-0.39, 0.58]	
Lifschitz 1985, 3-5 years	89.4	10.8	41	90.4	13	26	0.9%	-0.08 [-0.58, 0.41]	
Rosen 1985, 12 months	107	2.8	22	98.4	2.7	41	0.7%	3.11 [2.34, 3.87]	
Rosen 1985, 18 months	106.4	3.6	23	96	2.3	38	0.7%	3.60 [2.76, 4.44]	
Rosen 1985, 24 months	96.9	3.1	22	90.4	2.6	34	0.8%	2.28 [1.59, 2.98]	-
Rosen 1985, 3 years	46.3	2.3	21	44.6	2.1	39	0.9%	0.77 [0.22, 1.32]	
Rosen 1985, 6 months	100.7	4.2	23	95	2.5	41	0.8%	1.76 [1.16, 2.35]	
Rosen 1985, 6 years	88.9	3.2	10	89.22	3.4	18	0.7%	-0.09 [-0.87, 0.68]	
Salo 2009, 3 years	10.54	1.26	13	8.91	0.73	21	0.7%	1.65 [0.84, 2.46]	
Salo 2010, 7 months	105.11	7.61	57	92.33	10.73	15	0.8%	1.52 [0.89, 2.14]	
Strauss 1976, 12 months	114.8	11.3	26	113.4	10.2	25	0.9%	0.13 [-0.42, 0.68]	
Strauss 1976, 3 months	115.3	13.5	26	112.5	11.5	25	0.9%	0.22 [-0.33, 0.77]	
Strauss 1976, 6 months	114.3	20.9	26	115.7	16.8	25	0.9%	-0.07 [-0.62, 0.48]	
Strauss 1979, 5 years	86.2	16.2	30	86.8	13.3	33	0.9%	-0.04 [-0.53, 0.45]	
van Baar 1990, 12 months	114	17	34	108	12	26	0.9%	0.39 [-0.12, 0.91]	
van Baar 1990, 18 months	99	19	34	92	14	22	0.9%	0.40 [-0.14, 0.94]	
van Baar 1990, 24 months	98	16	34	86	15	26	0.9%	0.76 [0.23, 1.29]	
van Baar 1990, 30 months	101	20	34	87	18	25	0.9%	0.72 [0.19, 1.25]	
van Baar 1990, 6 months	107	13	37	106	13	27	0.9%	0.08 [-0.42, 0.57]	
van Baar 1994, 3 1/2 years	109	11	32	99	9	23	0.8%	0.96 [0.40, 1.53]	
van Baar 1994, 4 1/2 years	103	15	31	85	11	23	0.8%	1.32 [0.72, 1.92]	
van Baar 1994, 4 1/2 years van Baar 1994, 5 1/2 years	103	17	30	90	12	23	0.8%	0.78 [0.21, 1.35]	
Wilson 1981, 9 months	102	15.6	55	90.3	12	35	0.8%	0.40 [-0.03, 0.82]	
Wilson 1989, 18 months	97.4	14.4	42	99.3	14.5	29	0.9%		
Wilson 1989, 18 months Wilson 1989, 24 months	97.4	14.4	42	92 88.8	14.5	32	0.9%	0.37 [-0.11, 0.85]	
Subtotal (95% CI)	90.2	14.6	48 1519	6.60	10.5	32 1460	0.9%	0.09 [-0.35, 0.54] 0.56 [0.38, 0.74]	Ĩ <b>▲</b>
Heterogeneity: Tau <sup>2</sup> = 0.31; Chi <sup>2</sup> = 2	246 74 df - 4	15 /D / /		12 - 82	96	.400	00.170	2100 [0100] 0114]	•
			1.00001	1. 17 = 82					

#### **OMT vs Non-exposed**

Ά

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 7point IQ difference.

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

	Un	treate	d		OMT			Std. Mean Difference	Std. Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	
2.1.1 Cognition										
Chasnoff 1986, 12 months	103.5	8.1	12	99.6	10.6	20	5.2%	0.39 [-0.33, 1.11]		
Chasnoff 1986, 24 months	104.8	15.1	9	98.7	16	16	4.1%	0.38 [-0.45, 1.20]		
Chasnoff 1986, 3 months	99	13.6	22	104.2	11.1	36	8.3%	-0.42 [-0.96, 0.11]		
Chasnoff 1986, 6 months	99.9	12.7	17	103.6	13.5	26	6.8%	-0.28 [-0.89, 0.34]		_
Davis 1988, 6-15 years	95.11	12.8	9	89.58	10.32	12	3.7%	0.46 [-0.41, 1.34]		OMT gro
Lifschitz 1985, 3-5 years	85.3	15.7	25	90.4	13	26	7.9%	-0.35 [-0.90, 0.20]		
Wilson 1981, 9 months	97.2	17.6	29	99.3	15.5	35	9.4%	-0.13 [-0.62, 0.37]		the untre
Wilson 1989, 18 months	86.5	10.7	27	92	14.5	29	8.5%	-0.42 [-0.95, 0.11]		
Wilson 1989, 24 months	84.4	16.4	27	88.8	15.5	32	8.8%	-0.27 [-0.79, 0.24]		heroin or
Subtotal (95% CI)			177			232	62.7%	-0.17 [-0.38, 0.03]	-	
Heterogeneity: Tau <sup>2</sup> = 0.00;	Chi <sup>2</sup> = 8	.42, df	= 8 (P	= 0.39)	;   <sup>2</sup> = 5%	b				
Test for overall effect: Z = 1	.66 (P =	0.10)								
2.1.2 Psychomotor tests										Difference
Chasnoff 1986, 12 months	98.1	12.3	12	104.4	11.9	20	5.1%	-0.51 [-1.24, 0.22]		
Chasnoff 1986, 24 months	97.9	10.1	9	100.3	14.2	16	4.2%	-0.18 [-1.00, 0.64]		was on t
Chasnoff 1986, 3 months	97.6	9.8	22	104.3	11.8	36	8.2%	-0.60 [-1.14, -0.05]		
Chasnoff 1986, 6 months	103.2	8.8	17	102.2	11.9	26	6.8%	0.09 [-0.52, 0.70]		significar
Davis 1988, 6-15 years	14.17	5.44	12	10.19	4.96	9	3.5%	0.73 [-0.17, 1.63]		5
Wilson 1981, 9 months	92.2	19.2		89.9	12.6	35	9.4%	0.14 [-0.35, 0.64]		
Subtotal (95% CI)			101			142	37.3%	-0.09 [-0.45, 0.27]	-	
Heterogeneity: Tau <sup>2</sup> = 0.09;	Chi <sup>2</sup> = 9	.04, df	= 5 (P	= 0.11)	<sup>2</sup> = 45	%				
Test for overall effect: Z = 0	.49 (P =	0.62)								
Total (95% CI)			278			374	100.0%	-0.14 [-0.32, 0.04]	•	
Heterogeneity: Tau <sup>2</sup> = 0.03;	Chi <sup>2</sup> = 1	7.66, 0	df = 14	(P = 0.2)	2);  2 =	21%				
Test for overall effect: Z = 1									-1 -0.5 0 0.5 1 Favours OMT Favours non-treated	
Test for subgroup difference	es: Chi <sup>2</sup> =	0.15,	df = 1	(P = 0.7	0), l <sup>2</sup> =	0%			Favours Own Favours non-realed	
				••• 00050				_		
								Favours	SOMT Favours	untreated

#### **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).

Page 19

Ά

Ά

Day/Month/Year

Page 20

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

#### 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

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

# **Authors' Conclusion**

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

6

Ά

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

# **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'

Ά



Key Ideas...

**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 substance use disorder?