Figures

Figure 1

Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

Figure 2 (Analysis 2.1)

Study or Subgroup	Melatonin Mean	Melatonin SD	Melatonin Total	Placebo Mean	Placebo SD	Placebo Total	Weight	Mean Difference IV, Random, 95% CI
Gringras 2017 (1)	51.16	10.46	52	18.73	10.82	48	38.0%	32.43 [28.25, 36.61]
Cotesi 2012b (2)	505.01	31.18	35	445.13	48.37	33	30.8%	59.88 [40.41, 79.35]
Cortesi 2012a (3)	481.1	33.15	34	416.23	43.6	32	31.2%	64.87 [46.10, 83.64]
Total (95% CI)			121			113	100.0%	50.99 [26.89, 75.10]

Heterogeneity: Tau² = 393.03; Chi² = 17.45, df = 2 (P = 0.0002); I² = 89%
Test for overall effect: Z = 4.15 (P < 0.0001)

Footnotes
(1) Sleep diary measured sleep times
(2) Actigraph measured sleep times
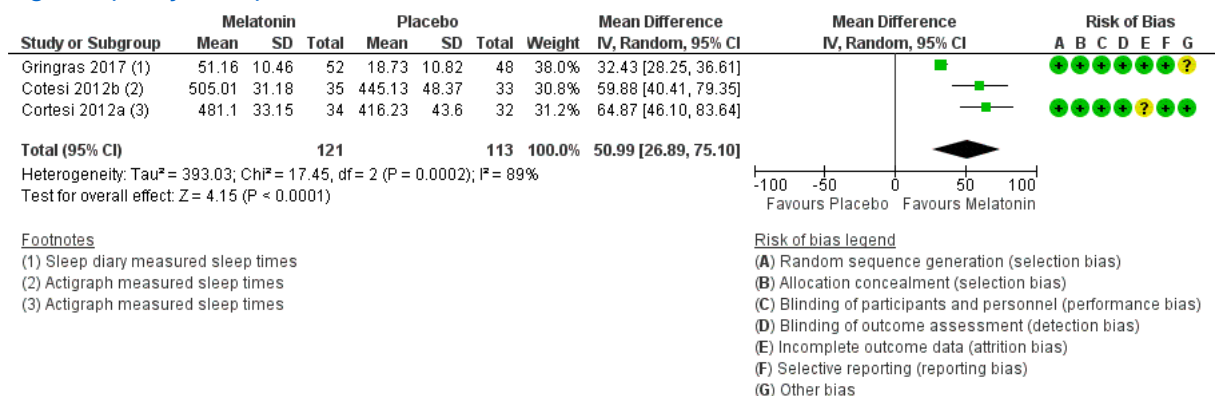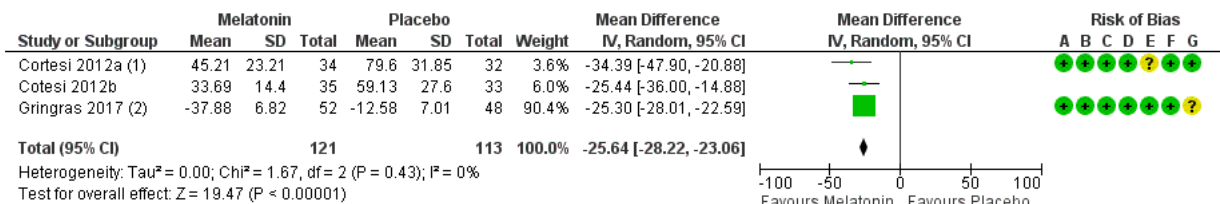(3) Actigraph measured sleep times

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Forest plot of comparison: 2 Mealtonin vs. placebo, outcome: 2.1 Total sovetid, min (total sleep time).

Figure 3 (Analysis 2.2)

Study or Subgroup	Melatonin Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Cortesi 2012a (1)	45.21	23.21	34	79.6	31.85	32	3.6%	-34.39 [-47.90, -20.88]
Cotesi 2012b	33.69	14.4	35	59.13	27.6	33	6.0%	-25.44 [-36.00, -14.88]
Gringras 2017 (2)	-37.88	6.82	52	-12.58	7.01	48	90.4%	-25.30 [-28.01, -22.59]
Total (95% CI)			**121**			**113**	**100.0%**	**-25.64 [-28.22, -23.06]**

Heterogeneity: Tau² = 0.00; Chi² = 1.67, df = 2 (P = 0.43); I² = 0%
Test for overall effect: Z = 19.47 (P < 0.00001)

Mean Difference IV, Random, 95% CI — Favours Melatonin / Favours Placebo (-100, -50, 0, 50, 100)

Risk of Bias: A B C D E F G

Footnotes
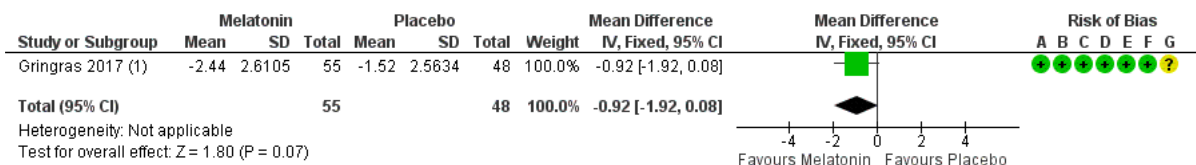(1) Actigraph measured sleep times
(2) Sleep diary measured sleep times

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Forest plot of comparison: 2 Mealtonin vs. placebo, outcome: 2.2 Indsovningstid, min (sleep onset latency).

Figure 5 (Analysis 2.4)

Study or Subgroup	Melatonin Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Gringras 2017 (1)	-2.44	2.6105	55	-1.52	2.5634	48	100.0%	-0.92 [-1.92, 0.08]
Total (95% CI)			**55**			**48**	**100.0%**	**-0.92 [-1.92, 0.08]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.80 (P = 0.07)

Mean Difference IV, Fixed, 95% CI — Favours Melatonin / Favours Placebo (-4, -2, 0, 2, 4)
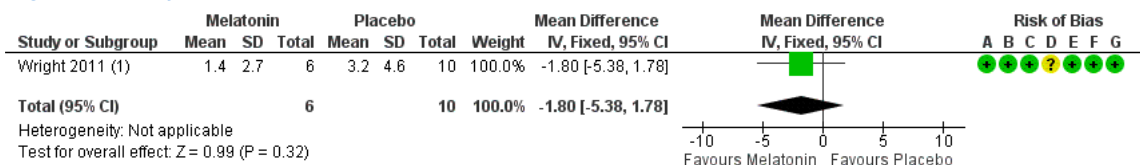
Risk of Bias: A B C D E F G

Footnotes
(1) CSDI, total score

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Forest plot of comparison: 2 Mealtonin vs. placebo, outcome: 2.4 Søvnkvalitet generelt (sleep quality).

Figure 6 (Analysis 2.5)

Study or Subgroup	Melatonin Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Wright 2011 (1)	1.4	2.7	6	3.2	4.6	10	100.0%	-1.80 [-5.38, 1.78]
Total (95% CI)			**6**			**10**	**100.0%**	**-1.80 [-5.38, 1.78]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.99 (P = 0.32)

Mean Difference IV, Fixed, 95% CI — Favours Melatonin / Favours Placebo (-10, -5, 0, 5, 10)
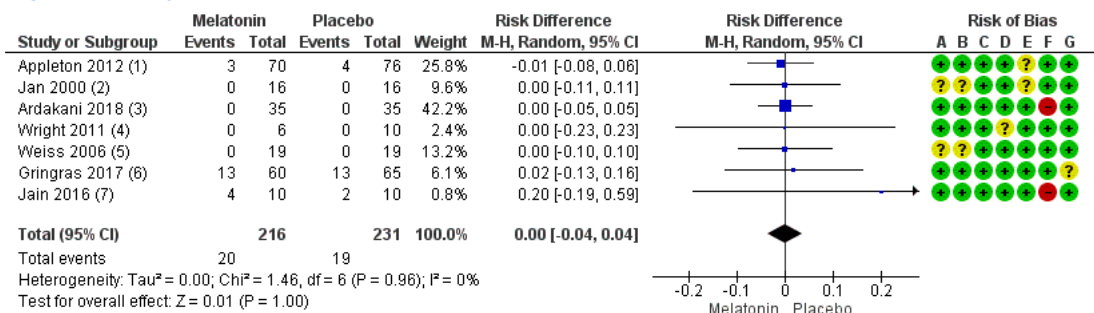
Risk of Bias: A B C D E F G

Footnotes
(1) GHQ

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Forest plot of comparison: 2 Mealtonin vs. placebo, outcome: 2.5 Forældretrivsel (caregivers wellbeing).

Figure 7 (Analysis 2.6)

Study or Subgroup	Melatonin Events	Total	Placebo Events	Total	Weight	Risk Difference M-H, Random, 95% CI
Appleton 2012 (1)	3	70	4	76	25.8%	-0.01 [-0.08, 0.06]
Jan 2000 (2)	0	16	0	16	9.6%	0.00 [-0.11, 0.11]
Ardakani 2018 (3)	0	35	0	35	42.2%	0.00 [-0.05, 0.05]
Wright 2011 (4)	0	6	0	10	2.4%	0.00 [-0.23, 0.23]
Weiss 2006 (5)	0	19	0	19	13.2%	0.00 [-0.10, 0.10]
Gringras 2017 (6)	13	60	13	65	6.1%	0.02 [-0.13, 0.16]
Jain 2016 (7)	4	10	2	10	0.8%	0.20 [-0.19, 0.59]
Total (95% CI)		**216**		**231**	**100.0%**	**0.00 [-0.04, 0.04]**
Total events	20		19			

Heterogeneity: Tau² = 0.00; Chi² = 1.46, df = 6 (P = 0.96); I² = 0%
Test for overall effect: Z = 0.01 (P = 1.00)

Risk Difference M-H, Random, 95% CI — Melatonin / Placebo (-0.2, -0.1, 0, 0.1, 0.2)

Risk of Bias: A B C D E F G

Footnotes
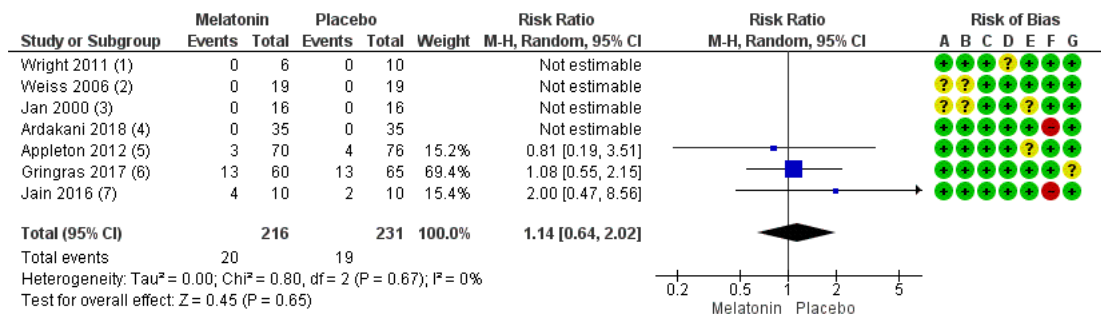(1) Mixed neurodevelopmental delays (41 % with ASD+developmental disorder)
(2) Mixed (10% out of 42 have ASD)
(3) atopic dermatitis
(4) Autism spectrum disorder
(5) ADHD
(6) Autism spectrum disorder
(7) epilepsy

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance...
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Forest plot of comparison: 2 Mealtonin vs. placebo, outcome: 2.6 Alvorlige bivirkninger, antal personer (serious adverse events), EoT -risk difference.

Figure 8 (Analysis 2.7)

Study or Subgroup	Melatonin Events	Melatonin Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Wright 2011 (1)	0	6	0	10		Not estimable
Weiss 2006 (2)	0	19	0	19		Not estimable
Jan 2000 (3)	0	16	0	16		Not estimable
Ardakani 2018 (4)	0	35	0	35		Not estimable
Appleton 2012 (5)	3	70	4	76	15.2%	0.81 [0.19, 3.51]
Gringras 2017 (6)	13	60	13	65	69.4%	1.08 [0.55, 2.15]
Jain 2016 (7)	4	10	2	10	15.4%	2.00 [0.47, 8.56]
Total (95% CI)		**216**		**231**	**100.0%**	**1.14 [0.64, 2.02]**
Total events	20		19			

Heterogeneity: Tau² = 0.00; Chi² = 0.80, df = 2 (P = 0.67); I² = 0%
Test for overall effect: Z = 0.45 (P = 0.65)

Footnotes
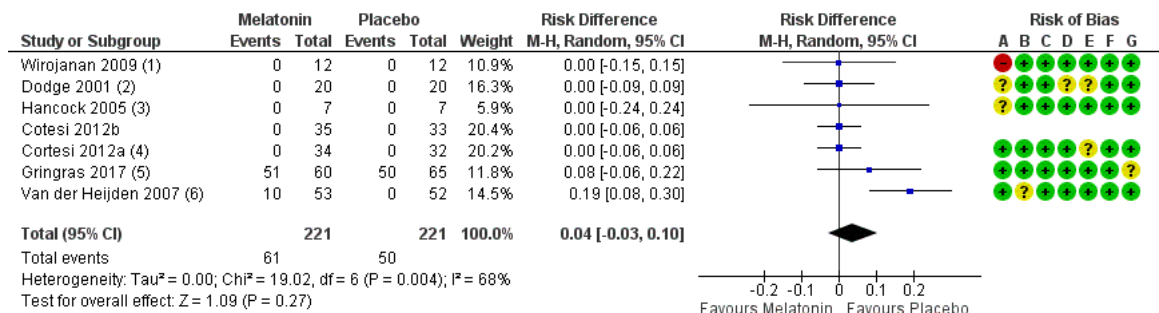(1) Autism spectrum disorder
(2) ADHD
(3) Mixed (10% out of 42 have ASD)
(4) atopic dermatitis
(5) Mixed neurodevelopmental delays (41 % with ASD+developmental disorder)
(6) Autism spectrum disorder
(7) epilepsy

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance...
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Forest plot of comparison: 2 Mealtonin vs. placebo, outcome: 2.7 Alvorlige bivirkninger, antal personer (serious adverse events), EoT.

Figure 9 (Analysis 2.8)

Study or Subgroup	Melatonin Events	Melatonin Total	Placebo Events	Placebo Total	Weight	Risk Difference M-H, Random, 95% CI
Wirojanan 2009 (1)	0	12	0	12	10.9%	0.00 [-0.15, 0.15]
Dodge 2001 (2)	0	20	0	20	16.3%	0.00 [-0.09, 0.09]
Hancock 2005 (3)	0	7	0	7	5.9%	0.00 [-0.24, 0.24]
Cotesi 2012b	0	35	0	33	20.4%	0.00 [-0.06, 0.06]
Cortesi 2012a (4)	0	34	0	32	20.2%	0.00 [-0.06, 0.06]
Gringras 2017 (5)	51	60	50	65	11.8%	0.08 [-0.06, 0.22]
Van der Heijden 2007 (6)	10	53	0	52	14.5%	0.19 [0.08, 0.30]
Total (95% CI)		**221**		**221**	**100.0%**	**0.04 [-0.03, 0.10]**
Total events	61		50			

Heterogeneity: Tau² = 0.00; Chi² = 19.02, df = 6 (P = 0.004); I² = 68%
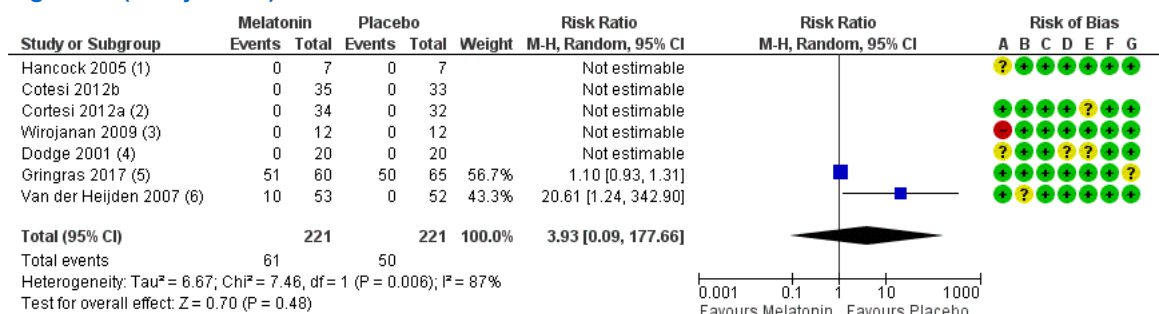Test for overall effect: Z = 1.09 (P = 0.27)

Footnotes
(1) ASD, fragile X syndrome or ASD+ Fragile x syndrome
(2) Developmental disability (including autism, genetic syndrome, Cerebral palsy, mental...
(3) Tuberous Sclerosis
(4) Autistic spectrum disorder
(5) Autistic spectrum disorder, with or without ADHD, Neurogenetic disorders
(6) ADHD

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Forest plot of comparison: 2 Mealtonin vs. placebo, outcome: 2.8 Bivirkninger, antal personer (adverse events) -risk difference.

Figure 10 (Analysis 2.9)

Study or Subgroup	Melatonin Events	Melatonin Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Hancock 2005 (1)	0	7	0	7		Not estimable
Cotesi 2012b	0	35	0	33		Not estimable
Cortesi 2012a (2)	0	34	0	32		Not estimable
Wirojanan 2009 (3)	0	12	0	12		Not estimable
Dodge 2001 (4)	0	20	0	20		Not estimable
Gringras 2017 (5)	51	60	50	65	56.7%	1.10 [0.93, 1.31]
Van der Heijden 2007 (6)	10	53	0	52	43.3%	20.61 [1.24, 342.90]
Total (95% CI)		**221**		**221**	**100.0%**	**3.93 [0.09, 177.66]**
Total events	61		50			

Heterogeneity: Tau² = 6.67; Chi² = 7.46, df = 1 (P = 0.006); I² = 87%
Test for overall effect: Z = 0.70 (P = 0.48)

Footnotes
(1) Tuberous Sclerosis
(2) Autistic spectrum disorder
(3) ASD, fragile X syndrome or ASD+ Fragile x syndrome
(4) Developmental disability (including autism, genetic syndrome, Cerebral palsy, mental...
(5) Autistic spectrum disorder, with or without ADHD, Neurogenetic disorders
(6) ADHD

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Forest plot of comparison: 2 Mealtonin vs. placebo, outcome: 2.9 Bivirkninger, antal personer (adverse events).