

Diagnosi e terapia dell'insonnia in età pediatrica: Updates da European Consensus Conference

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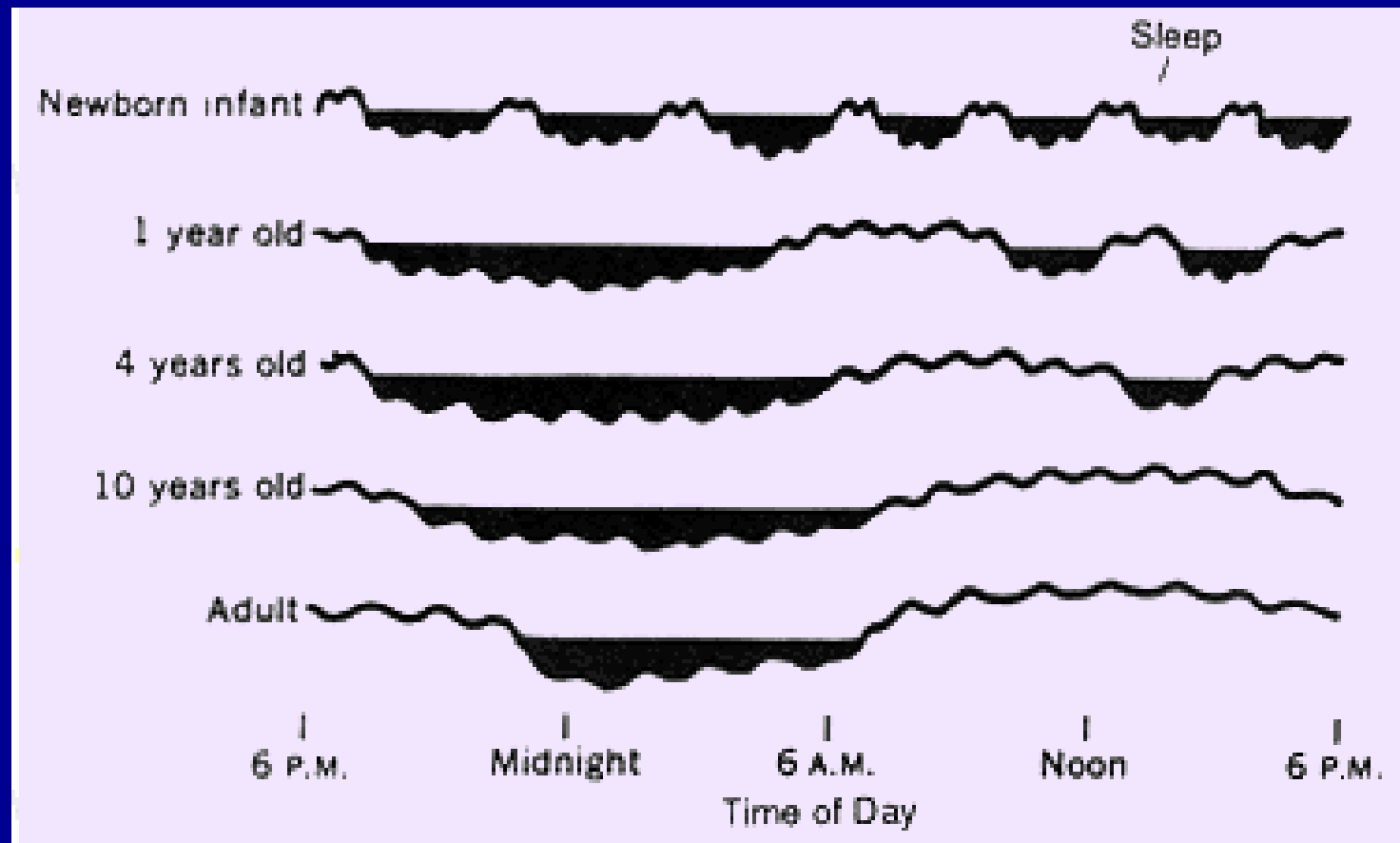
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Sleep in children

- Sleep cycles of children are briefer than in adults
- Neonatal sleep cycle (about 50 min):
 - REM sleep and NREM sleep
 - Equally distributed in the 24 hrs
- Infant sleep cycle (about 70 min)
 - Initial NREM sleep differentiation
 - Prevalent during night
- Children sleep cycle (about 90-120 min)
 - Complete NREM sleep differentiation
 - 4-5 cycles over the night-time

Sleep in children



Sleep and neurodevelopment

- The unique characteristics of neonatal sleep may promote learning
- REM sleep in infancy appears to set the stage for later learning
- Infants are likely to learn new information while asleep

Sleep and neuroplasticity

- Sleep promotes brain development and facilitates neural maturation
- REM and N-REM sleep influence experience-dependent neural plasticity mechanisms
- Sleep plays a role in memory consolidation through synaptic remodeling

Insomnia in children

Table 1

Diagnoses relevant to childhood insomnias

	Sleep Onset Association Disorder	Limit Setting Sleep Disorder	Adult Insomnia
Prevalence	25%–30%	25%–30%	4%–11%
Age group	6–36 months	>18 months	>18 years
Clinical features	• Delayed sleep onset and night time awakenings • Sleep onset becomes associated with exogenous cue(s) • Sleep onset at bedtime and/or the middle of the night will not occur without cue(s)	• Delayed bedtime • Parents reinforce undesirable behavior at bedtime • Inconsistent parental limit setting • Otherwise normal nocturnal sleep	• Difficulty with sleep initiation, maintenance, duration, consolidation or quality • Symptoms occur despite adequate time or opportunity to sleep • Symptoms are associated with decreased total sleep time, decreased sleep efficiency and daytime impairment (eg, sleepiness, inattention, fatigue, mood disturbance, loss of motivation, worry about sleep) • Symptom duration of >1 month

From American Academy of Sleep Medicine. The International Classification of Sleep disorders: Diagnostic and Coding Manual, ICSD-2. 2nd edition. Westchester, IL: American Academy of Sleep Medicine; 2005; with permission.

Insomnia in children

- Different subtypes, all characterized by difficulty initiating or maintaining sleep, or poor sleep quality and associated daytime impairment:
 - Psychophysiological Insomnia (PI) → conditioned sleep problems that may be associated with somatized tension or cognitive arousal at transitions from wake to sleep
 - Paradoxical Insomnia → perceived arousals or wakefulness during periods of objectively confirmed sleep
 - Idiopathic Insomnia → “lifelong history” of sleep problems, with an age of onset in infancy or childhood and no discernible cause

Insomnia in children

- There are no criteria or guidance for making a differential diagnosis among childhood insomnias, and there is no consensus among pediatric sleep specialists on the definition of insomnia in childhood
- Problems with sleep onset can begin at any age
- 15% to 22% of children have a persistent problem with sleep onset or maintenance
- In a sample of European adolescents the rate of insomnia was 5.8%

Insomnia in children

- For didactic purposes, the sleep-onset association and limit-setting subtypes of childhood insomnias are defined as separate entities. However, in reality, the two often coexist, and many children present with both bedtime delays and night wakings, which is the combined subtype
- Management begins with consistent implementation of good sleep hygiene and a consistent sleep-wake schedule, with night-time melatonin and/or morning bright light therapy as needed

Insomnia in children

- For didactic purposes, the sleep-onset association and limit-setting subtypes of BIC are defined as separate entities. However, in reality, the two often coexist, and many children present with both bedtime delays and night wakings, which is the combined subtype

Sleep disorders in childhood

- Huge amount of studies on children with neurodevelopmental disabilities (and/or autism, ADHD, etc.)
- Some studies on epilepsy, headache, pain
- Several data on neuroprotective properties (infants with HIE)
- Very few data on normal children (mainly school-age or adolescents) and for DSPS
- *No data on normal infants despite the fact that, at least in Italy, melatonin is the most commonly used drug by pediatricians for infants and toddlers with sleep problems*

Melatonin prescription by pediatricians?

The Sleep Knowledge of Pediatricians and Child Neuropsychiatrists

Oliviero Bruni, M.D., Cristiano Violani, Ph.D.*, Anna Luchetti, M.D.,
Silvia Miano, M.D., Elisabetta Verrillo, M.D., Carlo Di Brina,
Donatella Valente, Ph.D., P.T.

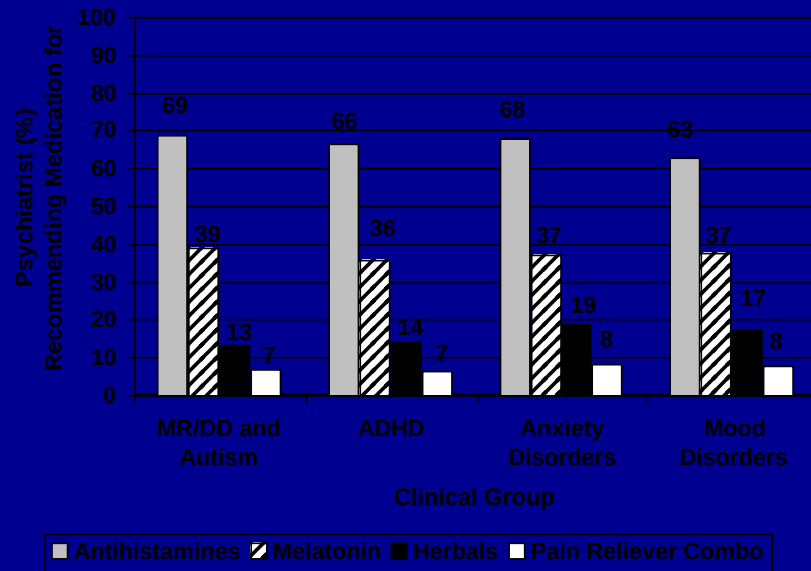
Sleep and Hypnosis, 6:3, 2004

	PED %	ChNP %	p
Antihistamines	52.03	43.97	NS
Benzodiazepines	4.55	22.41	<.0001
Imidazopyridines	3.58	6.03	NS
Neuroleptics	2.11	4.31	NS
Phytotherapy	19.84	18.10	NS
Herbal infuse	53.01	32.76	<.0005

Owens JA, Rosen CL, Mindell JA. Medication Use in the Treatment of Pediatric Insomnia: Results of a Survey of Community-Based Pediatricians. *Pediatrics* 2003;111:e628–e635

<u>Respondents, %</u>	0-2	3-5 y	6-12y	13y	Tot
Antihistamines	48.6	58.2	46.5	34.1	67.9
Combination	15.7	16.9	17.2	20.4	29.2
Melatonin	1.7	7.7	15.4	18.9	24.9
Herbal	13.5	12.7	13.3	15.6	22.2

*Owens et al. Use of Pharmacotherapy
for Insomnia in Child Psychiatry
Practice. Sleep Med, 2010*



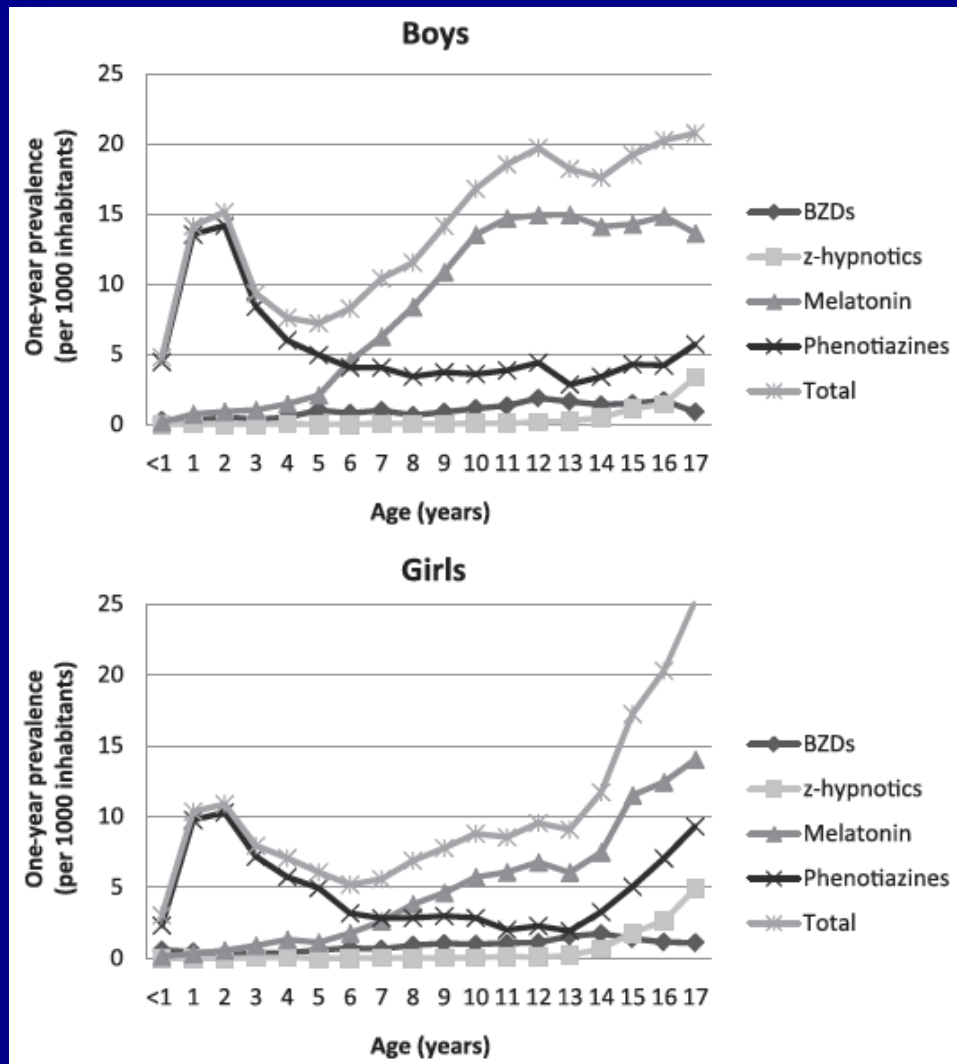
Most used:

- Antihistamines
- Melatonin
- Alpha agonists
- Trazodone
- Sedating antidepressants

Heussler H et al. Pharmacological and non-pharmacological management of sleep disturbance in children. Sleep Med. 2013

- 101/180 (56%) PEDS prescribed MLT for:
 - sleep onset insomnia (89.1%)
 - delayed sleep phase (66.3%)
 - nighttime wakings (30.7%)
- In:
 - children with autism (85.2%)
 - developmental delay (76.2%)
 - ADHD (54.5%)
 - behavioral disorders (42.6%)
 - visual impairment (40.6%),
 - anxiety disorders (25.7%)
 - **typically developing (54.5%)**

Hartz, I ; Furu, K ; Bratlid, T ; Handal, M ; Skurtveit, S. Hypnotic drug use among 0-17 year olds during 2004-2011: A nationwide prescription database study. Scand J Pub Health, 2012, 40(8):704-7



- Hypnotic drug use in 0–17 year olds increased during the period, from 8.9 to 12.3 per 1000, mainly owing to **doubling of melatonin use.**
- **Hypnotic drug use peaked at 15 per 1000 among those aged 1–2 years.**
- Melatonin use increased steadily from 6 to 12 years of age
- **Melatonin was dispensed in the highest annual amount of all hypnotic drugs**

DOSAGE

Table 2 Dose of melatonin prescribed

	Median	Range	25–75% interquartile
Starting dose (mg)	2.5	1.0–5.0	2.0–3.0
Lower maintenance dose (mg)	3	0.5–10.0	2.0–3.0
Higher maintenance dose (mg)	6	2.0–20.0	6.0–9.0
Maximum dose used (mg)	8	2.0–24.0	6.0–10.0
	0–2.0 mg	2.1–3.0 mg	>3.0 mg
Starting dose	63 (44%)	70 (49%)	9 (7%)
Lower maintenance dose	42 (30%)	69 (48%)	31 (22%)
	0–5 mg	6–9 mg	>9 mg
Higher maintenance dose	34 (24%)	82 (58%)	26 (18%)
	Immediate release	Slow release	Both
Formulation of melatonin	89 (68.5%)	3 (2.3%)	38 (29.2%)

Waldron DL, Bramble D, Gringras P. Melatonin: prescribing practices and adverse events. Arch Dis Child 2005;90:1206–7

Waldron DL, Bramble D, Gringras P. Melatonin: prescribing practices and adverse events. Arch Dis Child 2005;90:1206–7.

- Autism (68%) and ADHD (44%) most frequent clinical diagnoses in the children prescribed melatonin.
- Over 95% of respondents found melatonin “usually” or “always” effective.
- Adverse events were reported by 18%: seizure (n=5), hyperactivity (n=5), agitation/behavioural changes (n=6), worsening sleep pattern (n=6), nightmares (n=2), and constipation (n=2).

When to administer?

Is DLMO evaluation useful?

- Administration of exogenous melatonin in children with insomnia shifts DLMO as well as sleep onset to an earlier time in the evening, ameliorating the insomnia problems (Smits et al. 2001, 2003; Van der Heijden et al. 2007)
- The largest phase-advancing therapeutic effects of melatonin can be expected when administration occurs approximately **5 to 6 h before the individual DLMO**
- **The earlier melatonin is administered the larger the phase advance of sleep onset is.** (Van der Heijden et al. 2005)

- Most studies apply a melatonin dosage of 5 mg, although melatonin plasma concentrations in children are generally higher than in adults due to the fixed size of the pineal gland in humans during development, while the body volume increases (Waldhauser et al. 1988; Schmidt et al. 1995; Griefahn et al. 2003).
- Children metabolize melatonin more quickly than adults (Cavallo and Dolan 1996; Cavallo and Ritschel 1996).
- Several small studies and case reports on the efficacy of melatonin for childhood insomnia have been published, with pharmacological doses of 2–12 mg showing that melatonin treatment is effective and safe in children with sleep onset disorders with or without comorbidity (Jan et al. 1994, 2000; McArthur and Budden 1998; Jan 2000; Smits et al. 2001, 2003; Coppola et al. 2004; Weiss et al. 2006; Van der Heijden et al. 2007; Wasdell et al. 2008).
- Recently, several reviews concluded that melatonin is effective and safe in children irrespective of the dosage (Pandi-Perumal et al. 2007; Owens and Moturi 2009; Bendz and Scates 2010).

Serotoninenrgic dysfunction

- Insomnia
- Parasomnias
- Headache/migraine
- Depression
- Mood disorders



No difficulties in falling asleep

Mid-night awakenings



L-5-HTP

MLT

Dopaminergic dysfunction

- Anemia
- RLS
- PLM
- Growing pains
- Breath-holding spells



Difficulty in falling asleep (kicking legs)

Noct. hyperactivity (a horse in the bed)

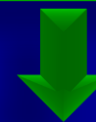


Iron

Gabapentin, DA, MLT

Histaminergic dysfunction

- Atopic dermatitis
- Milk intolerance
- Cow's milk allergy
- GER?



Difficulty in falling asleep

Several night awakenings (all night)



Antihistaminics

MLT

Appleton RE, Gringras P. Melatonin: helping to
MEND impaired sleep. Arch Dis Child
2013;98:216–217.

- **MLT is not a panacea for every child with a ‘sleep problem’**
- Melatonin is often prescribed as a short-term measure
- The MENDS (The use of MElatonin in children with Neurodevelopmental Disorders and impaired Sleep) study informed paediatricians when melatonin could be prescribed.
- Low doses (0.5 mg) can be effective for some children, and with diminishing benefit with doses exceeding 6 mg.
- No significant adverse side effects:
 - headaches, confusion, dizziness, cough and rashes
 - Previous reports of poor seizure control, poor asthma control and adverse endocrinological problems during puberty not confirmed
- *Our collective personal experience of over 18 years would suggest that many children continue to require melatonin indefinitely*

SOME QUESTIONS TO BE ANSWERED

- Dosage in infants, children and adolescents
- Timing of administration
- More rational and optimal administration by measuring salivary melatonin?
- Is DLMO useful and practical?
- Immediate release vs. controlled release?
- In which type of insomnia?
- For how long?
- Association with other drugs?
- Awareness campaign for pediatricians?

Melatonin

- Mechanism: mimics effects endogenous pineal hormone with both hypnotic and chronobiotic properties
- Pharmacokinetics: plasma levels peak 1 hr
- Effects sleep architecture: minimal
- Side effects (???): BP, bradycardia; decreases seizure threshold; potential suppression hypothalamic-gonadal axis (trigger precocious puberty)
- National Sleep Foundation has warned against using melatonin in patients with immune disorders, lymphoproliferative disorders, and in those taking corticosteroids or other immunosuppressants, given its ability to enhance immune function
- Dosing: 0.1-1 mg younger, 2.5-3mg older, 5 mg adol; up to 10 mg special needs reported; timing of dose dependent on DLMO (5-7 hrs prior)?

GRINGRAS P. WHEN TO USE DRUGS TO HELP SLEEP. ARCH DIS CHILD 2008;93:976-981

- © The reason why exogenous melatonin may work in paediatric sleep disorders remains unclear
 - a) melatonin acts to entrain a problematic circadian rhythm disorder
 - b) treats an endogenous melatonin deficiency state
 - c) acts as a soporific
 - d) increases the duration of particularly important sleep stages
- © Best efficacy on sleep onset latency
- © Fast release seems to be more effective in children

Melatonin:

1. Strong chronobiotic with hypnotic properties*

– Absorption is influenced by filler material of tablets / capsules**

– Usually long term treatment is necessary

- *Stopping melatonin treatment in children too early:*

*insomnia increases, but positive influence on parenting stress remains present***.*

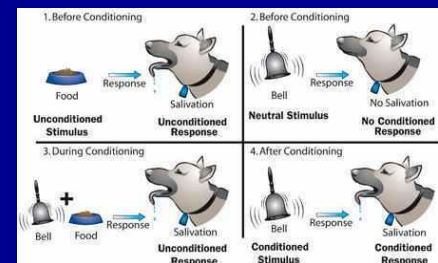
- *Classical conditioning is ineffective ****.*

*J.Sleep Res (1996) 137-141

**Int.J. Pharm (209) 9-16

***Sleep Medicine (2011, 875-879.

**** submitted



Melatonin

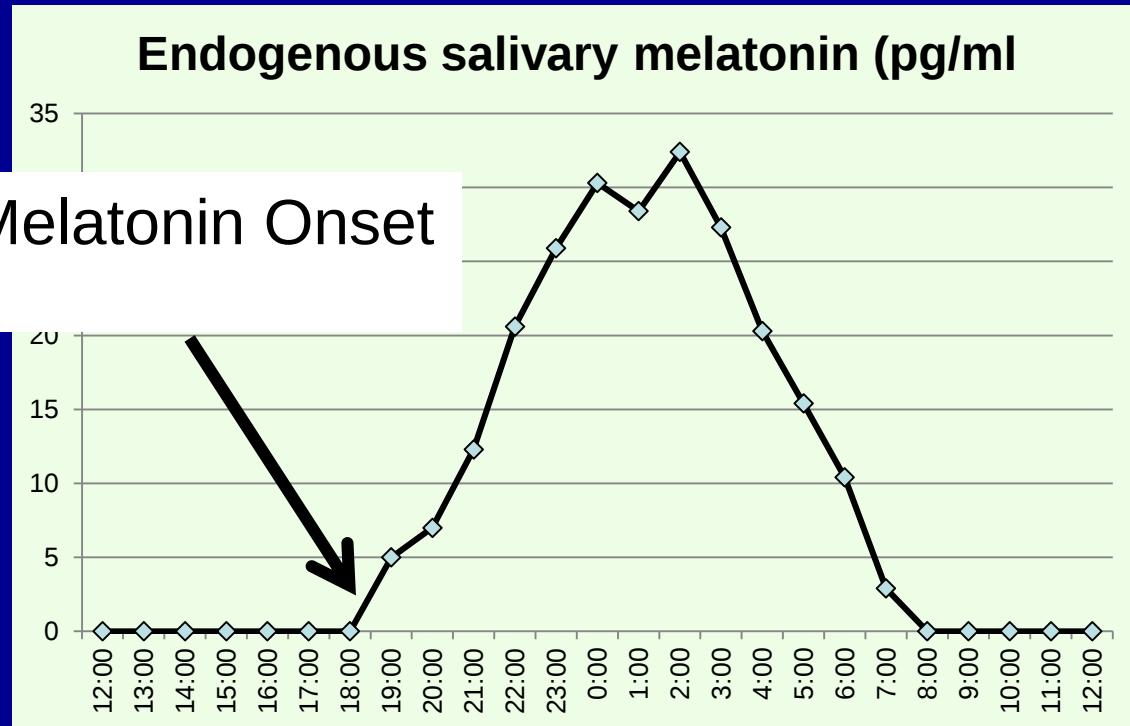
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2. Extraordinarily because of:

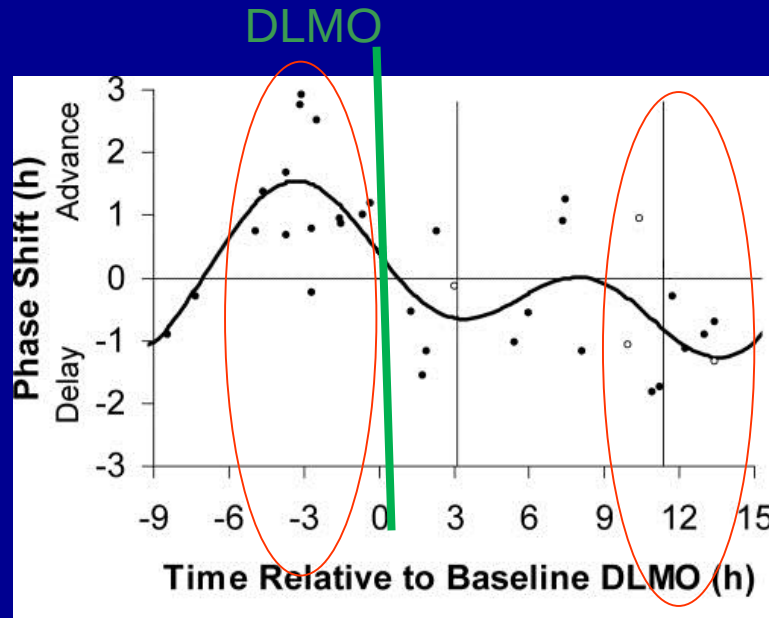
- Timing
 - When administered at the wrong time:
 - No effect
 - Opposite effect
- Dosing:
 - When the dose is too high
 - melatonin has no effect (See lecture of W. Braam)

For optimal timing DLMO should be known

Dim Light Melatonin Onset
(DLMO)



Timing of melatonin administration



To advance sleep wake rhythm

(advance sleep onset time and or advance wake-up time):

- Adults: 5 hours before Dim Light Melatonin Onset (**DLMO**)
- Children: 2-3 hours before **DLMO**

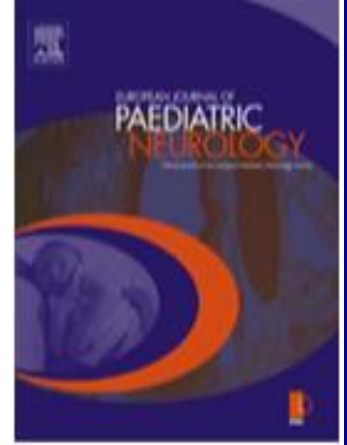
To delay sleep wake rhythm:

Adults and probably also children: 10 hours **after DLMO**

Current role of melatonin in pediatric neurology:

Clinical recommendations

Oliviero Bruni^a, Daniel Alonso-Alconada^{b,c}, Frank Besag^d,
Valerie Biran^{e,f}, Wiebe Braam^{g,h}, Samuele Cortese^{i,j,k},
Romina Moavero^{l,m}, Pasquale Parisiⁿ, Marcel Smits^{h,o},
Kristiaan Van der Heijden^p, Paolo Curatolo^{l,*}



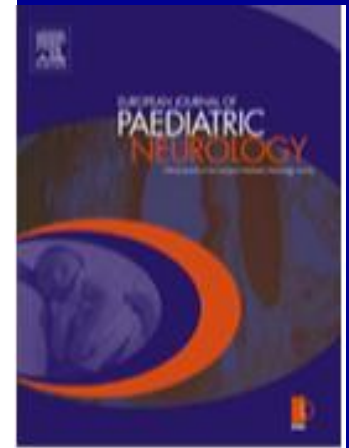
Pitfalls in melatonin treatment

1. Melatonin does not work although evidently disturbed circadian rhythm:
 - *Consider co-morbidity (severe ADHD, autism, depression, personality disorder)*
2. Efficacy melatonin treatment disappears:
 - *Dose was too high / slow melatonin metabolizer)*
 - *Melatonin intake time shifted to too late (e.g. because of strong hypnotic effect)*

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Pitfalls in melatonin treatment

- Sublingual melatonin tablets are not taken sublingually but are directly swallowed

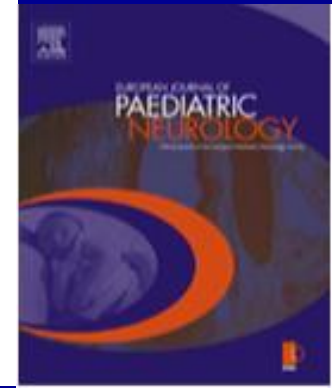
3. Sleep maintenance problems after start melatonin treatment:

- Melatonin dose is probably too high.

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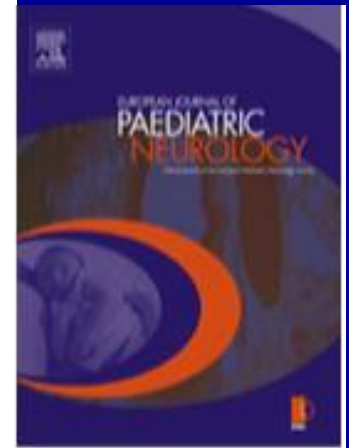
Recommendations for prescribing melatonin in children with sleep-wake rhythm disturbances

1. Measure DLMO
2. Time of administration: 2-3 hours before DLMO
3. Dosis: Start with 1 mg;
 - when after 1 week nothing happens: increase dose every week with 1 mg until effect appears.
 - Maximum dose:
 - < 40 mg: 3 mg.
 - > 40 kg: 5 mg
 - When 1 mg is effective: try to lower dose to 0.1 – 0.9 mg
 - Consider melatonin sublingually.

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Kristiaan Van der Heijden ^p, Paolo Curatolo ^{l,*}



Recommendations

(continued)

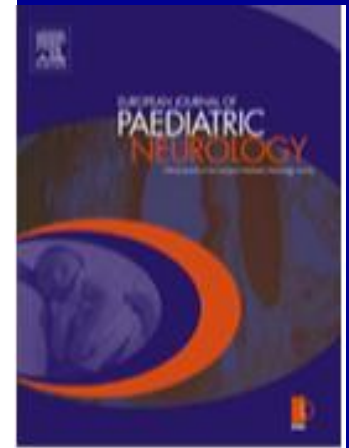
4. Treatment duration:

- try to stop every summer holidays
- Usually children can stop:
 - either just before puberty (age around 12 yrs)
 - or shortly after puberty (age between 18 and 24 yrs).

Current role of melatonin in pediatric neurology:

Clinical recommendations

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Recommendations

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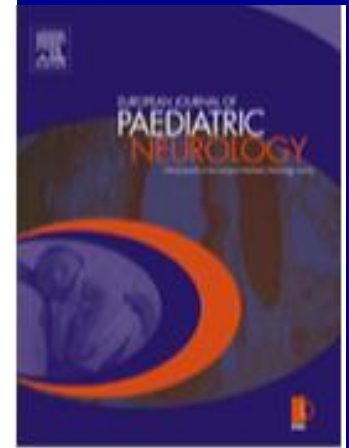
5. When melatonin treatment is not effective (anymore):

- check timing (children might take melatonin later because hypnotic effect starts too early)
- Reconsider diagnosis (wrong DLMO because melatonin treatment was stopped too short before DLMO measurement)
- Look for (hidden) comorbidity (e.g. ADD, Personality disorder / autism, child depression) and treat that together with the insomnia.
- Sublingual melatonin does not work because children did swallow the tablets
- When very severe delayed sleep wake rhythm: consider chronotherapy

Current role of melatonin in pediatric neurology:

Clinical recommendations

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What to do when DLMO cannot be measured?

- Start 1 mg melatonin at 7 or 8 p.m. and increase dose weekly until effect is seen (max. 3-5 mg)
- When melatonin does not work within 6 weeks:
 - Stop treatment
 - Reconsider diagnosis

Delayed Sleep Phase Disorder (DSPD)

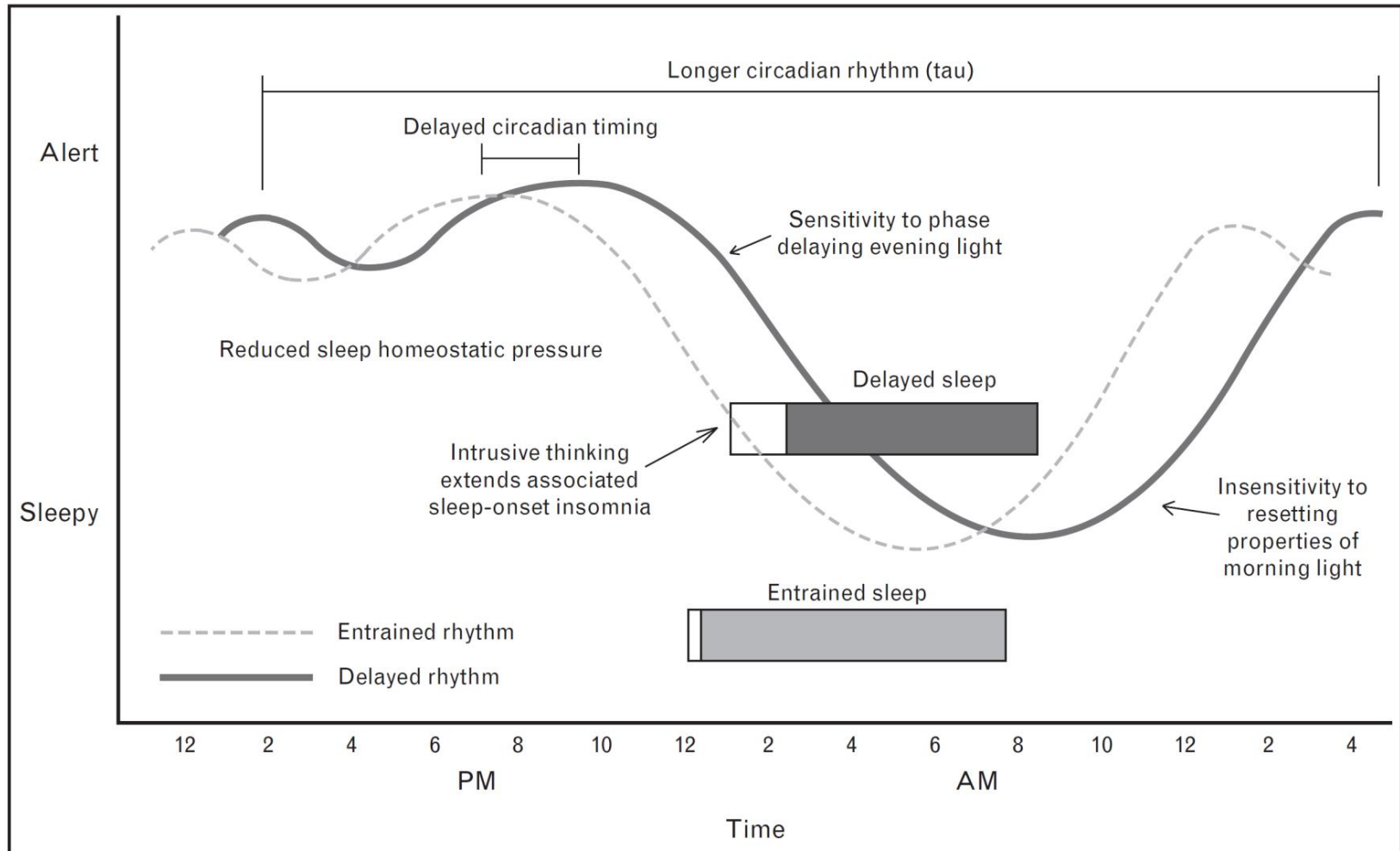


FIGURE 1. Contributing factors to delayed sleep phase disorder.

Melatonin and DSPD

	Age	Dose	Timing	Effect				Adverse events
				Sleep phase	Sleep length	Sleepiness	Health/behavior/Cognition	
Smits et al 2001	6-12	5	6 pm	+	+		0	Mild (MT)
Smits et al 2003	6-12	5	7 pm	+	0		+	Mild (MT/PL)
Van Geijlswijk et al 2010	6-12	0.05-0.15 mg/kg bw	5:30-7:30 pm	+				Mild (MT/PL)
Eckerberg et al 2012	14-19	1	4:30-6:00 pm	+	+	+		Mild (MT)
Wilhelmsen-Langeland et al 2013	16-25	3	> 8 pm			0	0	
Saxvig et al 2014	16-25	3	> 8 pm	0	0			

Melatonin and DSPD

Melatonin for primary DSPD in children:

- Advances sleep-wake rhythm (level 1b)
- Advances DLMO (level 1b)
- Possibly lengthens sleep moderately (level 1b)
- Safe on short term (and long term: Van Geijlswijk ea, 2011; Hoebert ea, 2009)

More studies needed:

- Adolescents
- Daytime sleepiness
- Health/behavior/cognition

Classification schemes

Category of evidence:

Ia—evidence for meta-analysis of randomised controlled trials

Ib—evidence from at least one randomised controlled trial

IIa—evidence from at least one controlled study without randomisation

IIb—evidence from at least one other type of quasi-experimental study

III—evidence from non-experimental descriptive studies, such as comparative studies, correlation studies, and case-control studies

IV—evidence from expert committee reports or opinions or clinical experience of respected authorities, or both

BMJ VOLUME 318 27 FEBRUARY 1999

Melatonin for perinatal hypoxia-ischemia

- Melatonin is safe even at high intravenous doses
- Melatonin's metabolites amplify neuroprotection
- Relatively easy to administer even during transfer
- Melatonin augmented hypothermic neuroprotection after HI
- More work needed
 - Therapeutic window
 - Lowest effective dose with and without cooling

Brain damages neonates

Term

HIE

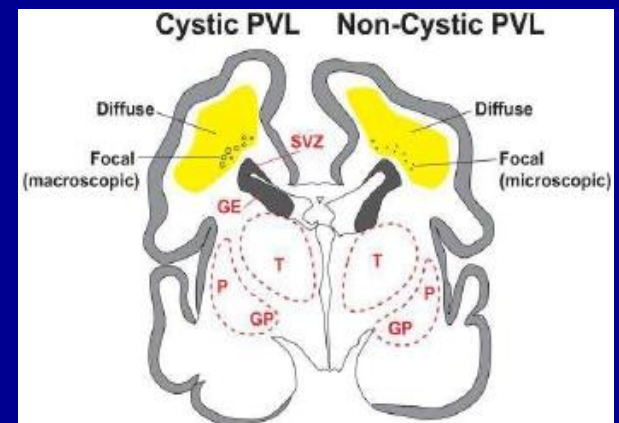
Stroke

Preterm

Intraventricular/parenchymal haemorrhage ↓

Cystic white matter damage ↓

Diffuse white matter damage ↑



Volpe, 2001, 2009

Neuroprotection and melatonin

Neurodevelopmental disabilities (cognitive deficiencies) from preterm birth

Neuroprotective effect of melatonin in various independant experimental models

Neuroprotective effect of melatonin in preterm infants?

PREMELIP trial

MINT trial

Many new promising strategies to protect the developing brain:

Melatonin +

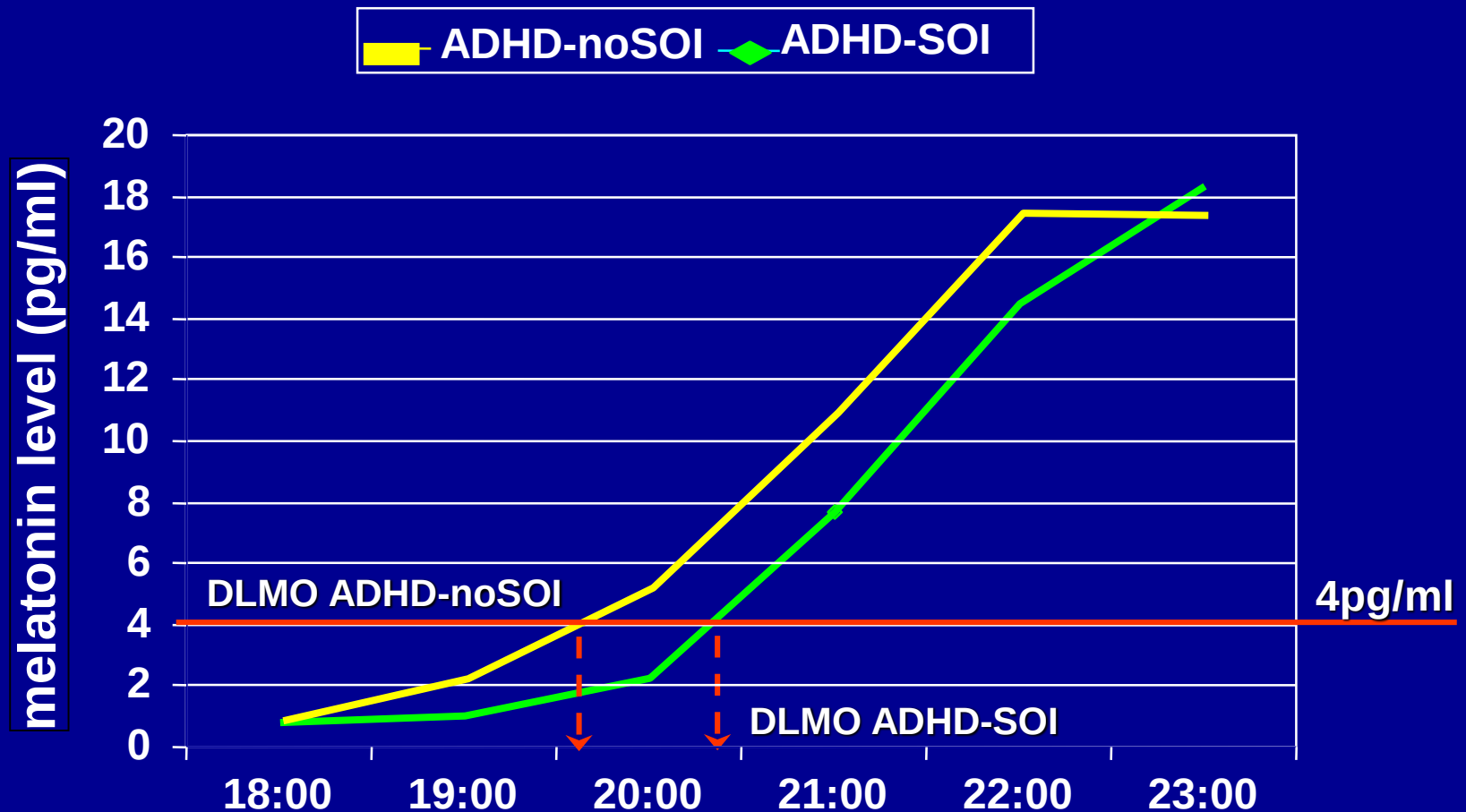
NO

Steroid

Magnesium Sulfate ...



Delayed dim light melatonin onset in ADHD



*Courtesy by Kristiaan van der Heijden et al., AACAP meeting 2005;
Chrono Biol Int, 2005*

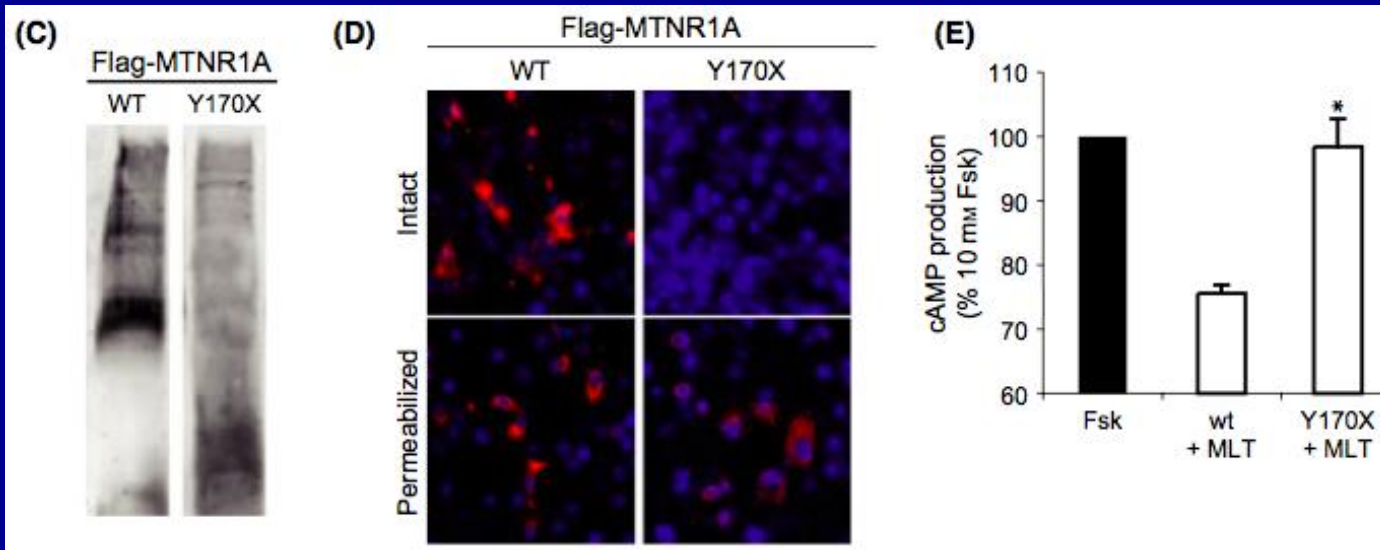
Genetics

J. Pineal Res. 2011; 51:394–399

Doi:10.1111/j.1600-079X.2011.00902.x

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Journal of Pineal Research

Genetic variations of the melatonin pathway in patients with attention-deficit and hyperactivity disorders



ASDs and sleep disorders

- Reduced total sleep and longer sleep latency as well as nocturnal and early morning awakenings are often reported in children with ASD
- Nocturnal secretion of melatonin is often low in ASD
- Melatonin has shown promise in reducing sleep latency and can be effective in treating children with ASD

Genetic Variation in Melatonin Pathway Enzymes in Children with Autism Spectrum Disorder and Comorbid Sleep Onset Delay

**Olivia J. Veatch • Julie S. Pendergast • Melissa J. Allen • Roberta M. Leu •
Carl Hirschie Johnson • Sarah H. Elsea • Beth A. Malow**

- Patients with disappearing effect of melatonin CYP1A2 poor metabolizer (Braam 2010)
- Disappearing efficacy of exogenous melatonin might be caused by slow melatonin metabolism because of a SNP in the CYP1A2 gene (Braam 2013)
- Sleep onset delay in children with ASD relates to melatonin pathway genes (Veatch 2014)

Melatonin in ASDs

- The majority of ASD children respond to 1-3 mg dose given 30 minutes before bedtime with improvement in sleep latency
- Melatonin is well tolerated with minimal adverse effects
- The mechanisms of action whereby supplemental melatonin affect sleep in children with ASD require further studies

Melatonin and seizures

- There is great interest in knowing whether melatonin is likely to precipitate seizures in those who do not already have epilepsy or to exacerbate seizures in those who already have epilepsy
- Case studies and small case series have yielded conflicting results with regard to the effect of melatonin on seizures; most reports targeted sleep, not epilepsy

Melatonin and seizures

- The data are insufficient to allow any definitive conclusions to be drawn
- However, there is a suggestion that melatonin might improve seizure control from human data and there is extensive animal work that would support this
- In contrast, there appears to be no unequivocal data to prove that melatonin exacerbate seizures

Melatonin and Headache

- An alteration of neurotransmitter pathway (serotonergic and dopaminergic) could predispose, at different age (earlier for sleep disorders and later for headache), to both these disorders, as consequence of a supposed neurotransmitter imbalance
- The connection between headache disorders and circadian biology and melatonin is fascinating, but it is only in its first step toward a more definitive understanding
- Available data are discordant and we do not have a definitive consensus about therapeutic use of melatonin for headache in children

Melatonin in Intellectual Disability

Melatonin is widely used in children with an intellectual disability.

There are no guidelines on how to prescribe melatonin.

It is considered to be safe without serious side effects.

Loss of response to melatonin

Melatonin levels 12:00 and 16:00: >50pg/ml

Hypothesis: CYP1A2 poor metaboliser

Braam W et al. Loss of response to melatonin treatment is associated with slow melatonin metabolism. J Intellect Disabil Res. 2010 Jun;54(6):547-55.

Loss of response to melatonin

In 40 / 76 non-melatonin users at first visit (52,8%) we found loss of effect and high day time melatonin levels after 4 – 12 weeks of melatonin treatment

Melatonin in Intellectual Disability

Start with a low dose of 0.2–0.5 mg fast release melatonin one hour before bedtime; increase by 0.2 - 0.5 mg every 2 weeks as needed (maximum 3 mg) until effect

Melatonin in Intellectual Disability

Slow-release melatonin may only be useful for children with sleep maintenance difficulties if there are sleep onset problems as well.

Melatonin in Intellectual Disability

Reduce dose if possible to the lowest dose that is effective

Wean slowly 12 weeks after a normal sleep cycle is established

Melatonin in Intellectual Disability

Be aware that loss of efficacy of melatonin treatment most likely is caused by slow melatonin metabolism.

Therefore dose reduction is strongly advised (one week wash out) instead of dose escalation.

Melatonin in Intellectual Disability

Be aware of interactions of melatonin with other medication:

Metabolism slower: oral contraceptives, cimetidine, fluvoxamine

Metabolism faster: carbamazepine, esomeprazole, omeprazole,

Melatonin in Intellectual Disability

Sleep problems are much more frequent in children with neurodevelopmental problems (such as ASD, ADHD, ID) than in the general population

A meta-analysis of randomized double-blind placebo-controlled crossover studies showed significant improvements with large effect size in sleep duration and sleep onset latency, but not in night-time awakenings in individuals with ASD who took melatonin

The majority of children with ASD responded to a dose of 1-3 mg given 30 min before bedtime, with improvement in sleep latency and total sleep duration The overall improvement rate with melatonin was 80%. Melatonin was well tolerated with minimal adverse effects

Currently, there is no established consensus on how to treat sleep disorders in ADHD and the grade of available empirical evidence is generally low. Melatonin may be an option, at least when sleep onset insomnia is related to a delayed sleep phase disorder

Melatonin given in doses ranging from 3 to 6 mg/night significantly reduced sleep onset delay and increased total sleep duration, but did not impact on daytime ADHD core symptoms as might have been expected, considering that better sleep

Current role of melatonin in pediatric neurology:

Bruni et al, EJPN 2015

Clinical recommendations

Oliviero Bruni ^a, Daniel Alonso-Alconada ^{b,c}, Frank Besag ^d,
Valerie Biran ^{e,f}, Wiebe Braam ^{g,h}, Samuele Cortese ^{i,j,k},
Romina Moavero ^{l,m}, Pasquale Parisi ⁿ, Marcel Smits ^{h,o},
Kristiaan Van der Heijden ^p, Paolo Curatolo ^{l,*}



- Sleep problems are much more frequent in children with neurodevelopmental problems (such as ASD, ADHD, ID) than in the general population
- A meta-analysis of randomized double-blind placebo-controlled crossover studies showed significant improvements with large effect size in sleep duration and sleep onset latency, but not in night-time awakenings in individuals with ASD who took melatonin
- The majority of children with ASD responded to a dose of 1-3 mg given 30 min before bedtime, with improvement in sleep latency and total sleep duration The overall improvement rate with melatonin was 80%. Melatonin was well tolerated with minimal adverse effects
- Currently, there is no established consensus on how to treat sleep disorders in ADHD and the grade of available empirical evidence is generally low. Melatonin may be an option, at least when sleep onset insomnia is related to a delayed sleep phase disorder
- Melatonin given in doses ranging from 3 to 6 mg/night significantly reduced sleep onset delay and increased total sleep duration, but did not impact on daytime ADHD core symptoms as might have been expected, considering that better sleep quantity/quality has been related to improvement in cognitive and behavioral functioning
- In ID melatonin decreased sleep latency and increased total sleep time, less significantly decreasing the number of awakenings per night



X CONGRESSO NAZIONALE FIMP 2016

1000 Giorni 

fimp Federazione Italiana Medici Pediatri

 AIM GROUP ASSOCIAZIONE ITALIANA MEDICI

Progetto BUONANOTTE

Mattia Doria

pediatra di famiglia

Coordinatore FIMP del Progetto



fimp Federazione Italiana Medici Pediatri



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razionale

- La **carenza di sonno** in età pediatrica è all'origine di molti **disturbi** dell'infanzia e della preadolescenza, sia di natura psicologica sia fisica.
- Numerose evidenze segnalano l'importanza dell'**igiene del sonno** per crescere un bambino in **buona salute**.
- **Deprivazione e disturbi del sonno:**
 - Disturbi di **attenzione**, di **iperattività** e di controllo degli **impulsi**
 - Scarso **rendimento scolastico**
 - Deficit nel **decision making**
 - Maggiore rischio di **addiction** per videogiochi, tablet, smartphone
 - Maggior rischio di **abuso di sostanze** (alcol, sigarette, marijuana)

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obiettivi

- Obiettivo primario:
indagare le **abitudini relative al sonno** nei bambini della fascia di età **12 mesi – 5 anni**, mettendole a confronto con le linee guida della National Sleep Foundation (2015), procedendo a una **descrizione e valutazione epidemiologica** dei disturbi del sonno nei bambini italiani.
- Obiettivo secondario
correlare le **abitudini relative al sonno** dei bambini studiati con **parametri comportamentali** quali l'utilizzo di nuove tecnologie e dispositivi informatici (smartphone, tablet, internet, tv digitale), per l'identificazione precoce di comportamenti che possano essere predittivi di un disturbo di controllo e disturbo ipercinetico degli impulsi in età adolescenziale



Progetto BUONANOTTE popolazione

- **Da 1 anno** (12 mesi e 0 giorni) **a 5 anni** (5 anni, 11 mesi, 22 giorni)
- **Accesso allo studio del pediatra di famiglia**
per motivi diversi da malattia acuta
- **Autocompilazione da parte del genitore**

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Codice Identificativo: _____ ☐ Maschio ☐ Femmina Data di nascita _____

Gravidanza pretermine: _____ ☐ No ☐ Sì Settimane alla nascita _____

È stato allattato al seno: ☐ No ☐ Sì Se Sì, fino a che mese _____

Ordine di nascita: (primogenito, secondogenito...) _____

Numero di fratelli o sorelle più grandi _____ Numero di fratelli o sorelle più piccoli _____

Ruolo dell'intervistato: ☐ Mamma ☐ Papà altro (specificare) _____

Mamma (dati obbligatori): Età _____ Titolo di studio _____

Papà (dati obbligatori): Età _____ Titolo di studio _____

Professione _____ Cittadinanza _____

Durante la settimana il bambino frequenta: ☐ Asilo nido ☐ Scuola materna ☐ Altro (es. ludoteca) _____

Quante ore la settimana? _____

Durante la settimana il bambino sta con: ☐ Baby sitter ☐ Nonni

Quante ore la settimana? _____

Quante ore la settimana? _____

Si prega di dare una sola risposta ad ogni domanda. Grazie per l'aiuto.

1. Generalmente in quanto tempo si addormenta il bambino dopo essere andato a letto
☐ Un quarto d'ora ☐ Mezz'ora ☐ 45 min. ☐ 1 ora ☐ Più di un'ora
2. Di solito la sera a che ora va a letto il vostro bambino
☐ 19.30 ☐ 20.00 ☐ 20.30 ☐ 21.00 ☐ 21.30 ☐ 22.00 ☐ 22.30 ☐ 23.00 ☐ Oltre le 23
3. Di solito quanto dura il riposo diurno (se riposa più volte sommare i tempi)
☐ Non dorme ☐ Mezz'ora ☐ Circa 1 ora ☐ Circa 2 ore ☐ più di 2 ore
4. Di solito al mattino a che ora si sveglia il vostro bambino (fascia oraria)
☐ 6.00 ☐ 6.30 ☐ 7.00 ☐ 7.30 ☐ 8.00 ☐ 8.30 ☐ 9.00 ☐ 9.30 ☐ Oltre le 10
5. Il vostro bambino porta il pannolino?
☐ di giorno e di notte ☐ solo di notte ☐ non lo porta Tolto a mesi _____
6. Come si addormenta il vostro bambino? (è possibile indicare anche più di una risposta)
☐ bevendo latte o altro liquido ☐ leggendo un libro/racconto una favola
☐ guardando tv o cartoni animati in streaming ☐ vicino a un genitore ☐ Altro (specificare) _____
7. Di solito dove dorme il vostro bambino per la maggior parte delle ore notturne
☐ Nel suo letto/lettino da solo ☐ Nel suo lettino in camera con fratelli o sorelle
☐ Nel suo lettino in camera dei genitori ☐ Nel lettone con i genitori ☐ Altro (specificare) _____

Si prega di dare una sola risposta ad ogni domanda. Grazie per l'aiuto.

	4 - sempre (ogni giorno)	3 - spesso (3 o 5 volte a settimana)	2 - qualche volta (1 o 2 a settimana)	1 - occasionalmente (1 o 2 volte al mese o meno)	0 - mai
8. Il vostro bambino fa i capricci per andare a letto?	0	1	2	3	4
9. Il vostro bambino si sveglia più di due volte per notte e vi costringe ad alzarvi e rimanere a lungo (almeno 30 minuti) con lui per farlo riaddormentare?	0	1	2	3	4
10. Il vostro bambino se si sveglia di notte vuole che voi gli diate un qualche oggetto (sacchetti, pupazzo...) che lo rassicuri?	0	1	2	3	4
11. Il vostro bambino si sveglia con difficoltà al mattino ed è stanco?	0	1	2	3	4
12. Il vostro bambino fa la pipì a letto? (non rispondere se il bambino porta il pannolino)	0	1	2	3	4
13. Il vostro bambino soffre di incubi?	0	1	2	3	4
14. Il vostro bambino fa i capricci per mangiare?	0	1	2	3	4
15. Il vostro bambino gioca con bambole, peluche, pupazzi, macchinine...?	0	1	2	3	4
16. Il vostro bambino gioca con le costruzioni (lego, pile...)?	0	1	2	3	4
17. Il vostro bambino legge libri?	0	1	2	3	4
18. Il vostro bambino gioca con colori, tempere, album colorati, disegna?	0	1	2	3	4
19. Il vostro bambino gioca con tablet e/o smartphone?	0	1	2	3	4
In quale momento della giornata gioca? ☐ mattina ☐ pomeriggio ☐ sera, prima di cena ☐ sera, prima di addormentarsi					
Per quanto tempo gioca nell'arco di tutta la giornata? ☐ 15 min ☐ 30-45 min ☐ 1 ora ☐ più di 1 ora					
20. Il vostro bambino gioca con videogiochi?	0	1	2	3	4
In quale momento della giornata gioca? ☐ mattina ☐ pomeriggio ☐ sera, prima di cena ☐ sera, prima di addormentarsi					
Per quanto tempo gioca nell'arco di tutta la giornata? ☐ 15 min ☐ 30-45 min ☐ 1 ora ☐ più di 1 ora					
21. Il vostro bambino gioca all'aperto?	0	1	2	3	4
☐ In qualunque stagione, purché il tempo sia bello ☐ Solo durante la bella stagione					
Quando gioca per quanto tempo? ☐ meno di 1 ora ☐ circa 2 ore ☐ più di 2 ore					
22. Il vostro bambino guarda la TV (anche in streaming su tablet, telefoni e Dvd)?	0	1	2	3	4
In quale momento della giornata gioca? ☐ mattina ☐ pomeriggio ☐ sera, prima di cena ☐ sera, prima di addormentarsi					
Per quanto tempo guarda la TV nell'arco di tutta la giornata? ☐ 30 min ☐ 1 ora ☐ 2 ore ☐ più di 2 ore					



Si prega di dare una sola risposta ad ogni domanda. Grazie per l'aiuto.

Le seguenti affermazioni rappresentano alcuni stili comportamentali rispetto ai quali vi chiediamo di esprimere il vostro parere valutando gli stili di comportamento del vostro bambino.

Il vostro bambino...

	2 - Sì (molto vero o spesso vero)		
	1 - In parte vero o qualche volta vero		
	0 - No (non vero)		
23. ...è socievole	0	1	2
24. ...tende ad arrabbiarsi facilmente	0	1	2
25. ...è dispettoso o litiga spesso	0	1	2
26. ...è disobbediente	0	1	2
27. ...tende ad avere atteggiamenti di sfida nei confronti dell'autorità (genitori, nonni, maestri...)	0	1	2
28. ...non sopporta di aspettare, vuole tutto subito	0	1	2
29. ...distrugge le cose	0	1	2
30. ...non sembra sentirsi in colpa dopo essersi comportato male	0	1	2
31. ...non riesce a stare fermo/seduto dimostrando irrequietezza/iperattività	0	1	2
32. ...le punizioni non cambiano il suo comportamento	0	1	2
33. ...condivide facilmente i suoi giochi	0	1	2
34. ...picchia gli altri	0	1	2



Progetto BUONANOTTE

11 regioni

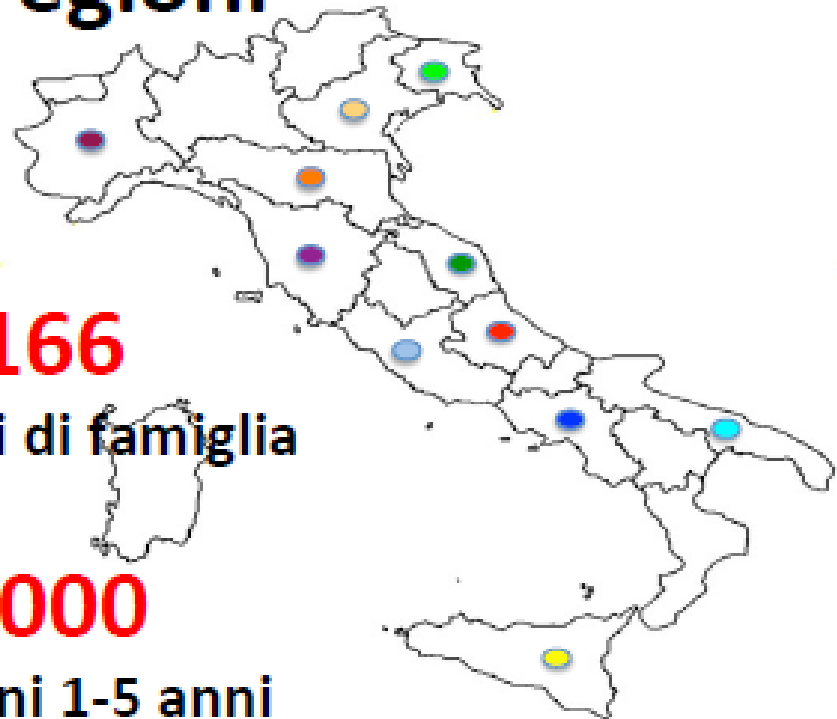
- **Abruzzo** (A. Lamborghini)
- **Campania** (M. Sticco)
- **Friuli Venezia Giulia** (F. Ceschin)
- **Emilia Romagna** (A. Antonelli)
- **Lazio** (G. Cerimoniale)
- **Marche** (A. Bottiglieri)
- **Piemonte** (E. Bruno)
- **Puglia** (T. Cazzato)
- **Sicilia** (G. Bottaro)
- **Toscana** (M.M. Mariani)
- **Veneto** (A. Pasinato e M. Tommasi)

166

pediatri di famiglia

4000

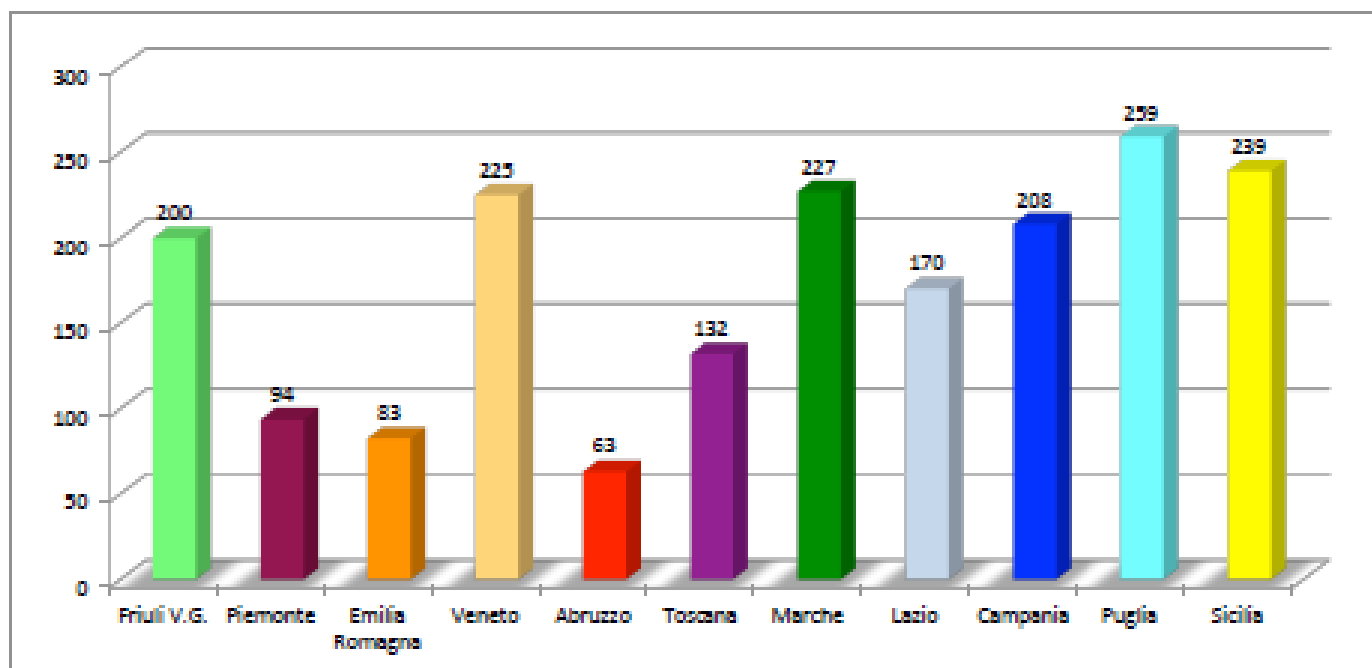
bambini 1-5 anni

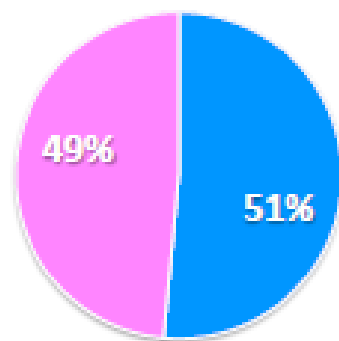


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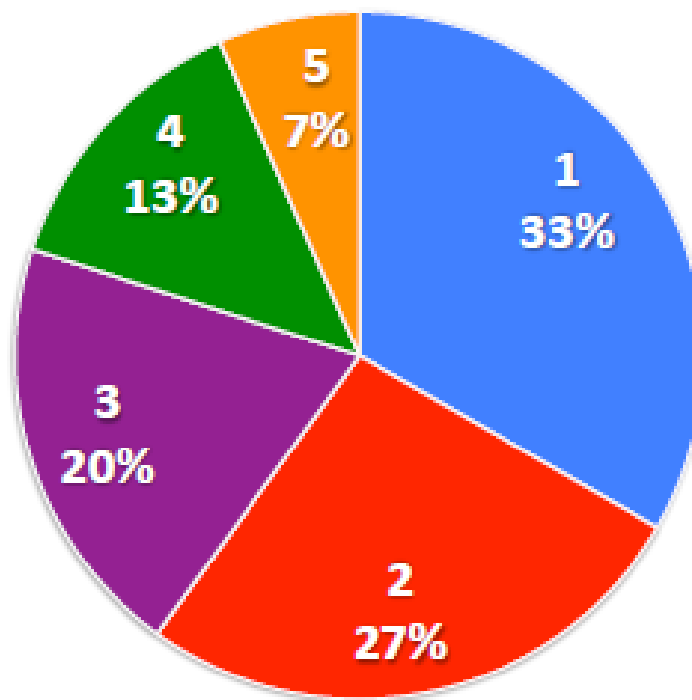
Progetto BUONANOTTE

numero di schede per regione
(tot. 1900 schede)

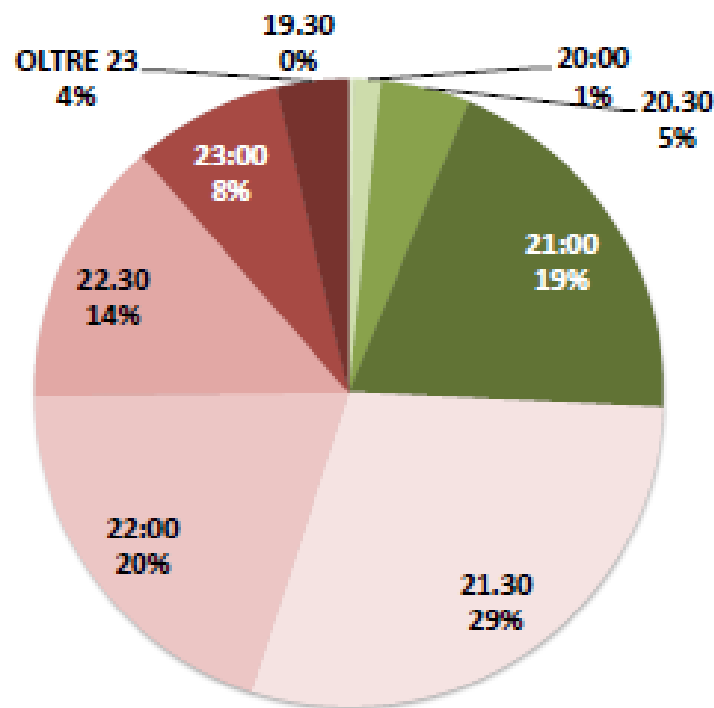




Progetto BUONANOTTE distribuzione per età



Progetto BUONANOTTE a che ora va a letto?



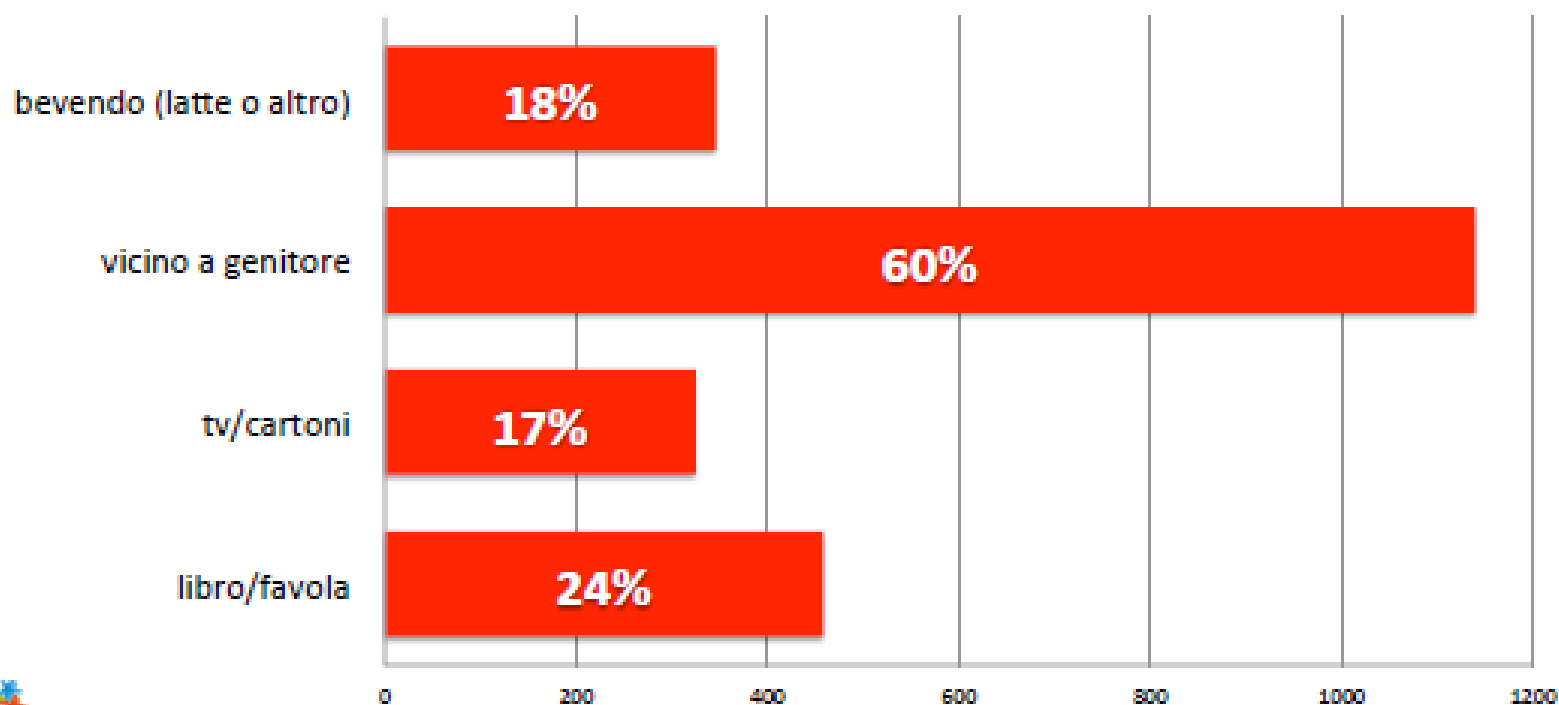
25% prima delle 21.00

63% 21.00-23.00

12% dopo le 23.00

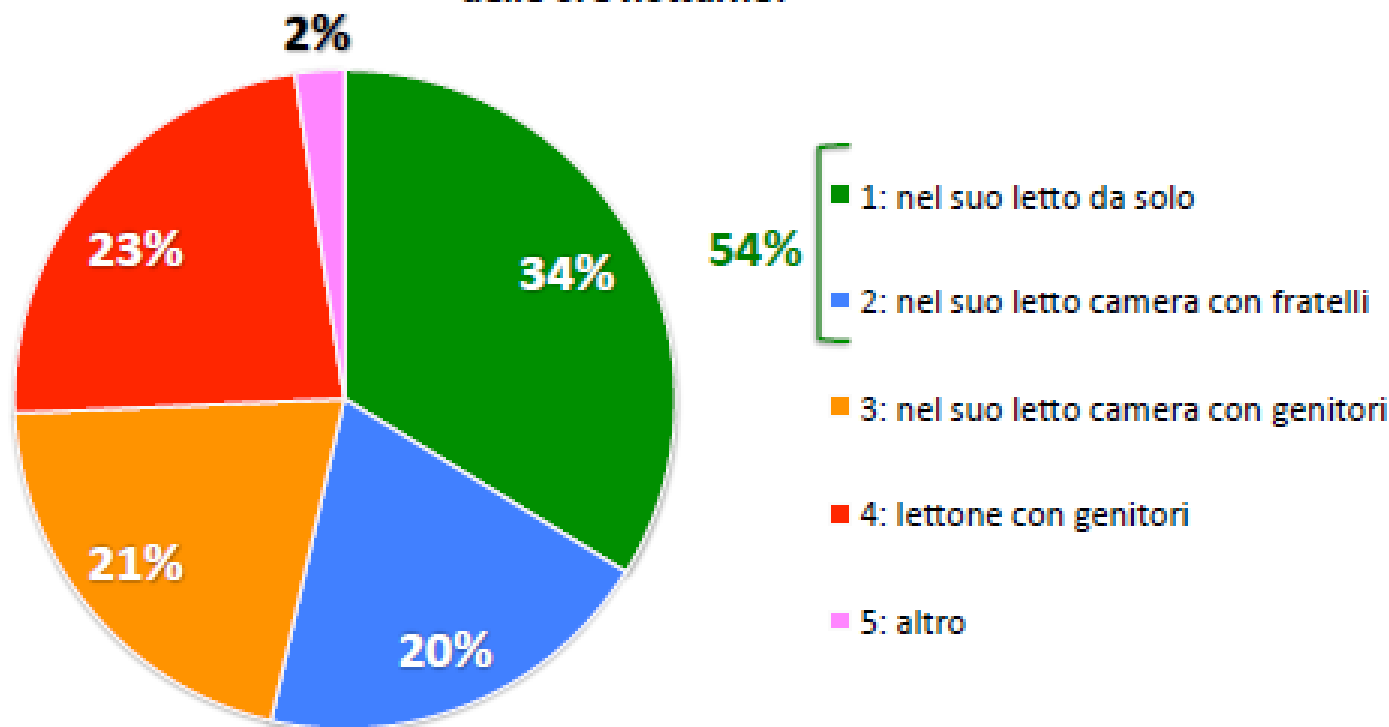
Progetto BUONANOTTE

Come si addormenta il vostro bambino?



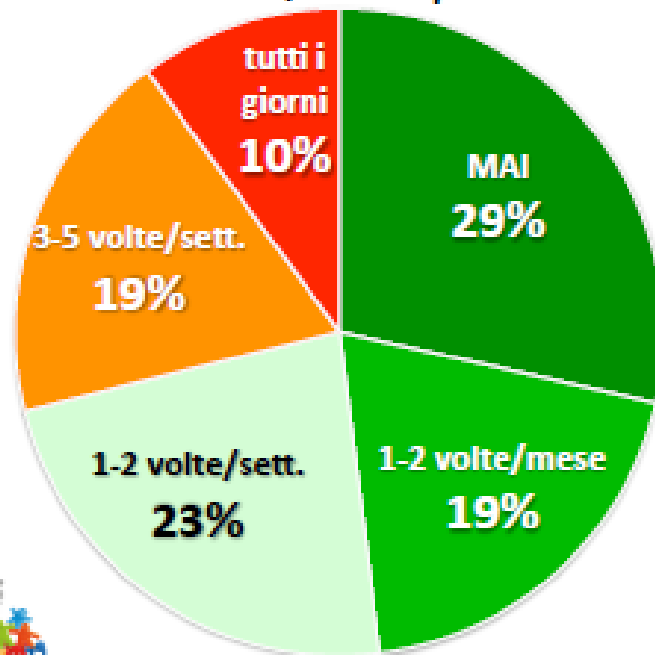
Progetto BUONANOTTE

Di solito dove dorme il vostro bambino per la maggior parte delle ore notturne?

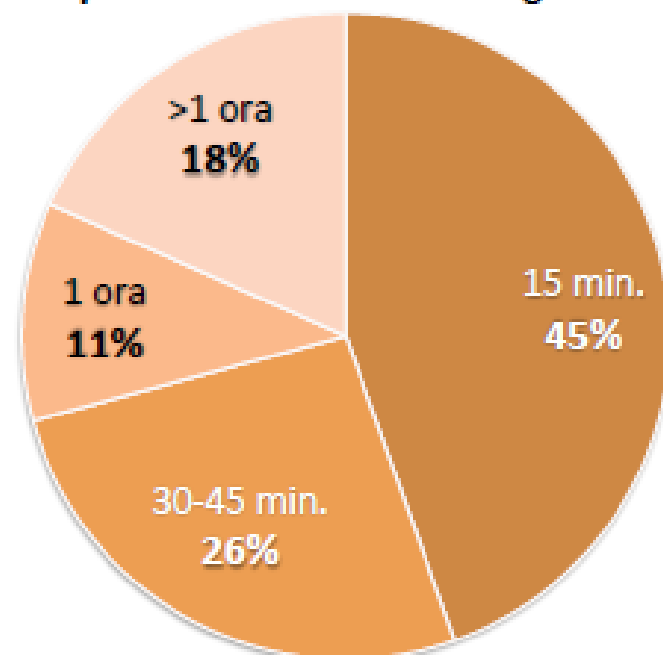


Progetto BUONANOTTE

Il vostro bambino gioca
con tablet e/o smartphone?

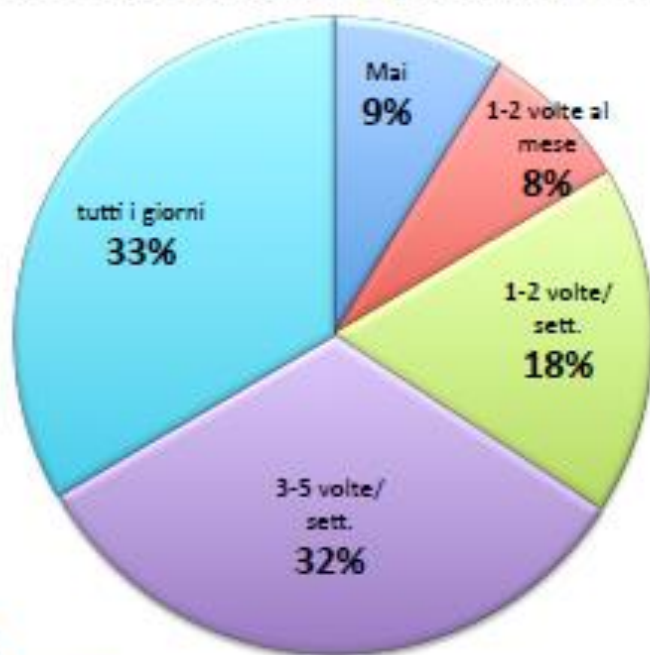


Per quanto tempo gioca con tablet e/o
smartphone nell'arco di tutta la giornata?

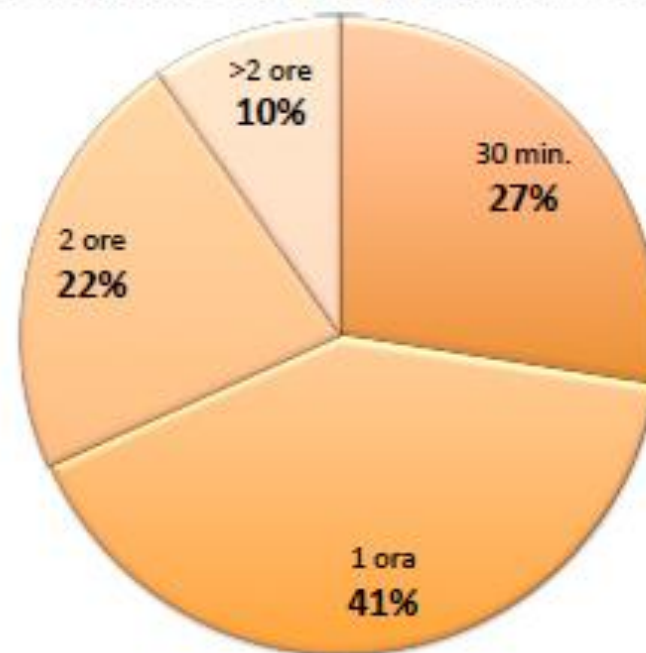


Progetto BUONANOTTE

il vostro bambino guarda la TV?



Per quanto tempo guarda la TV?



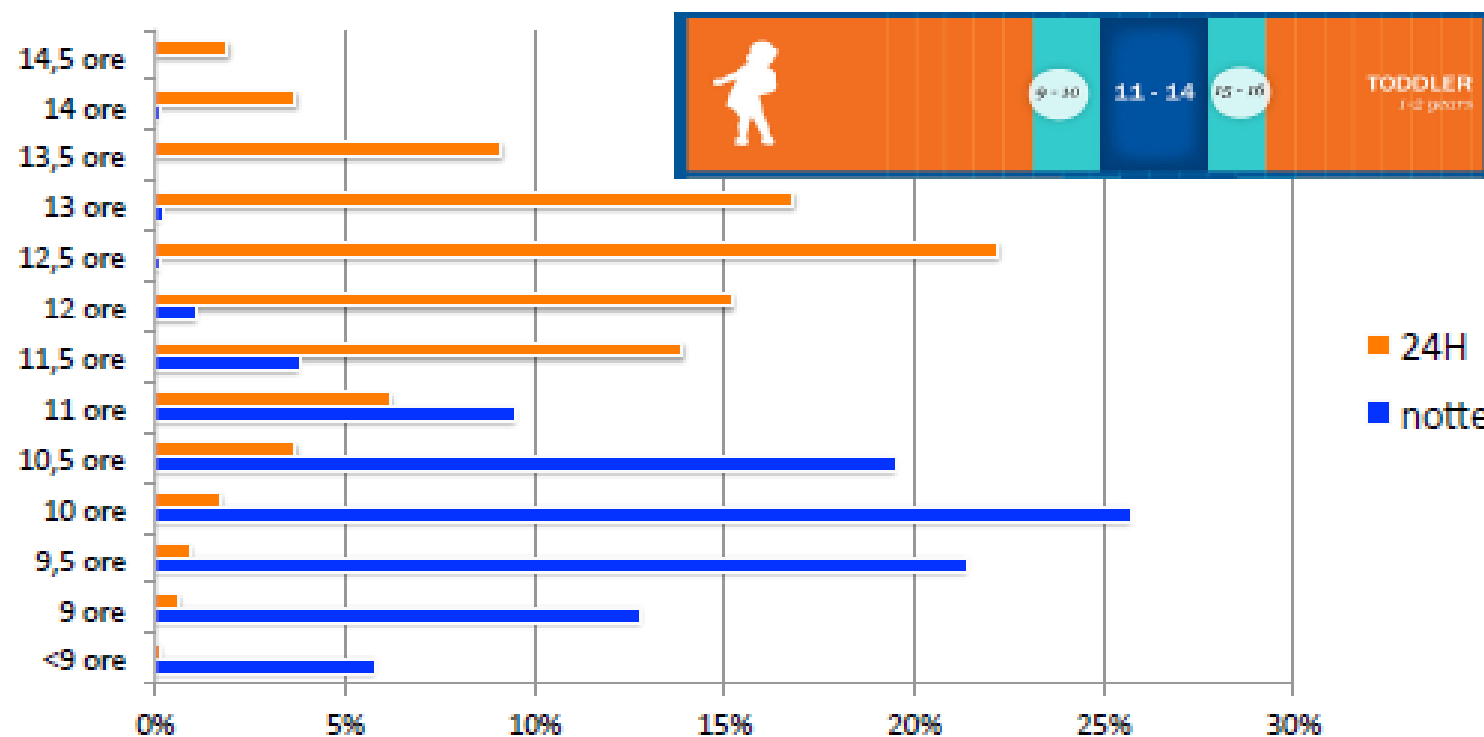
Progetto BUONANOTTE



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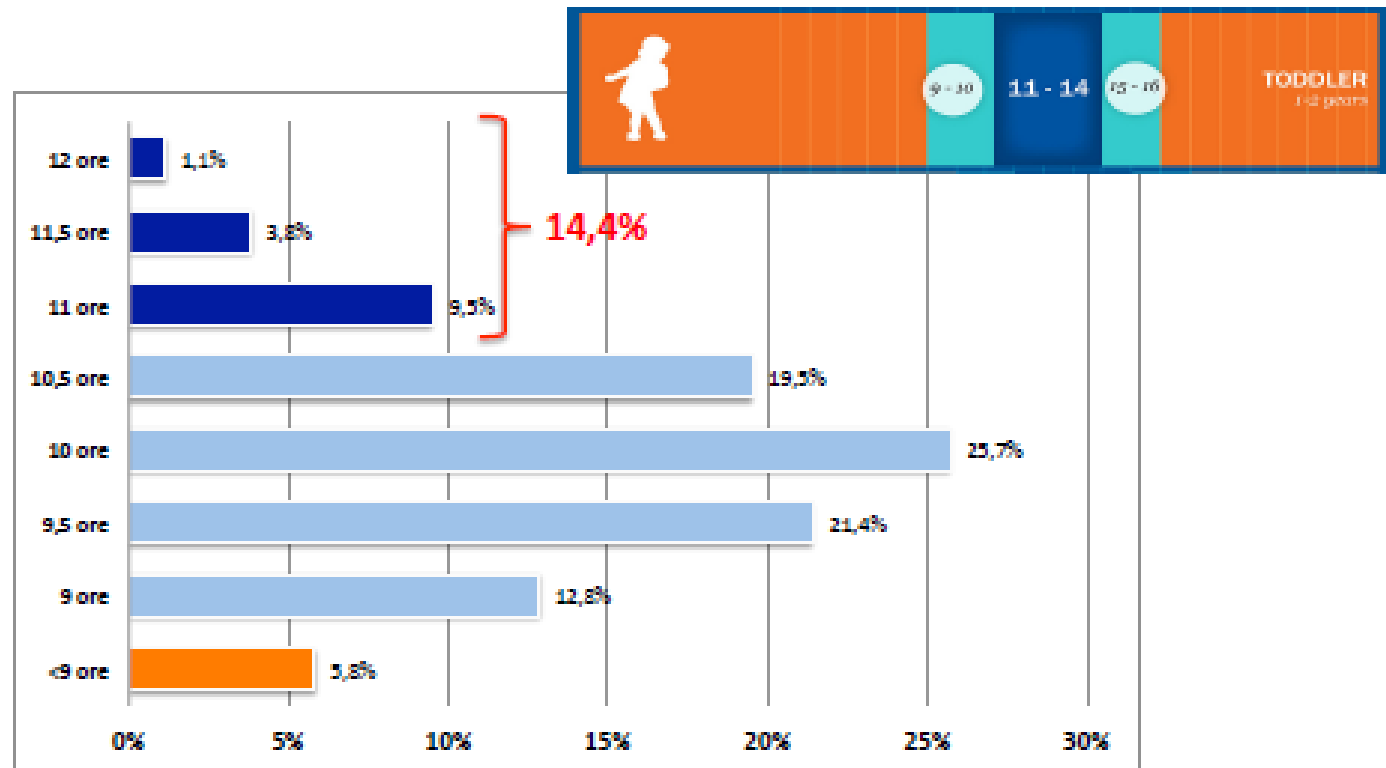
Progetto BUONANOTTE

ore di sonno a 1-2 anni



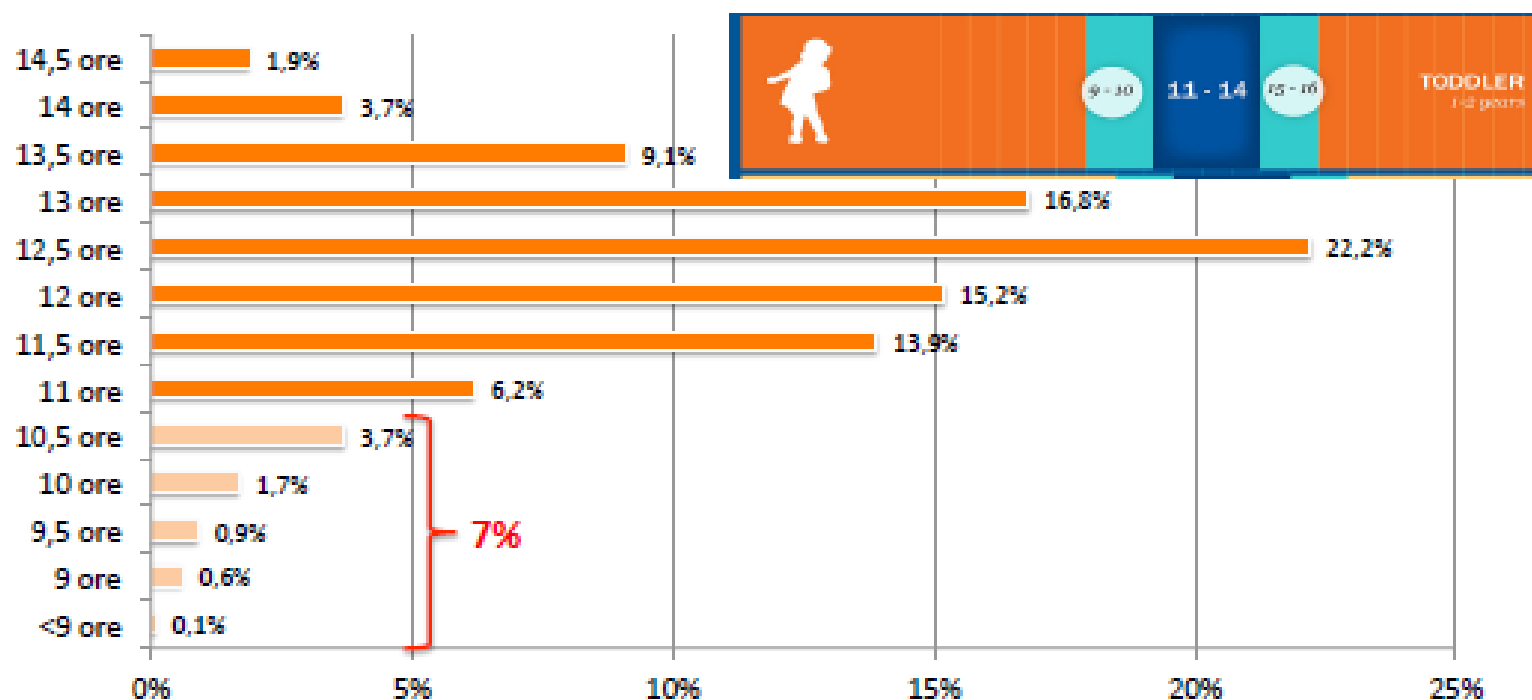
Progetto BUONANOTTE

ore di sonno notturno a 1-2 anni



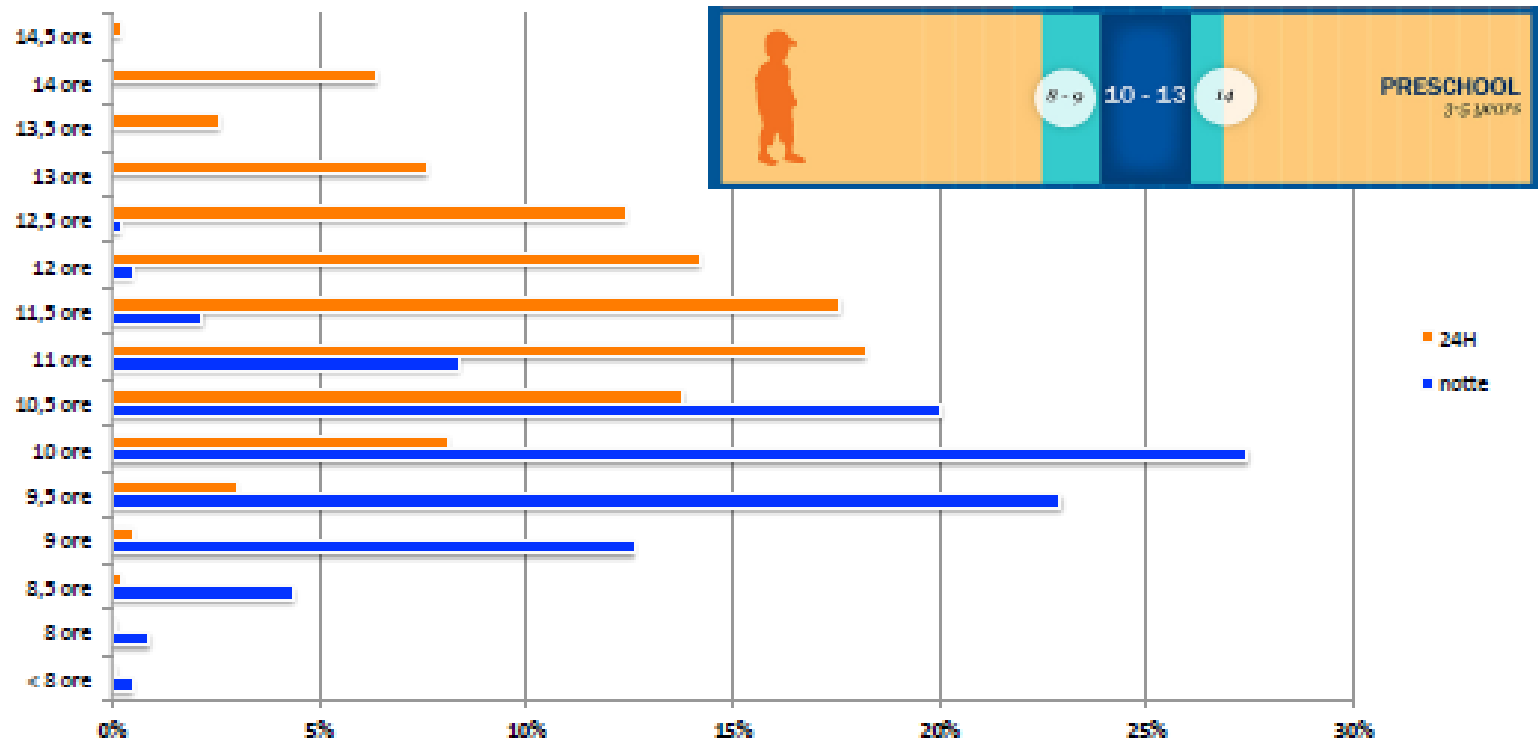
Progetto BUONANOTTE

ore di sonno 24H a 1-2 anni

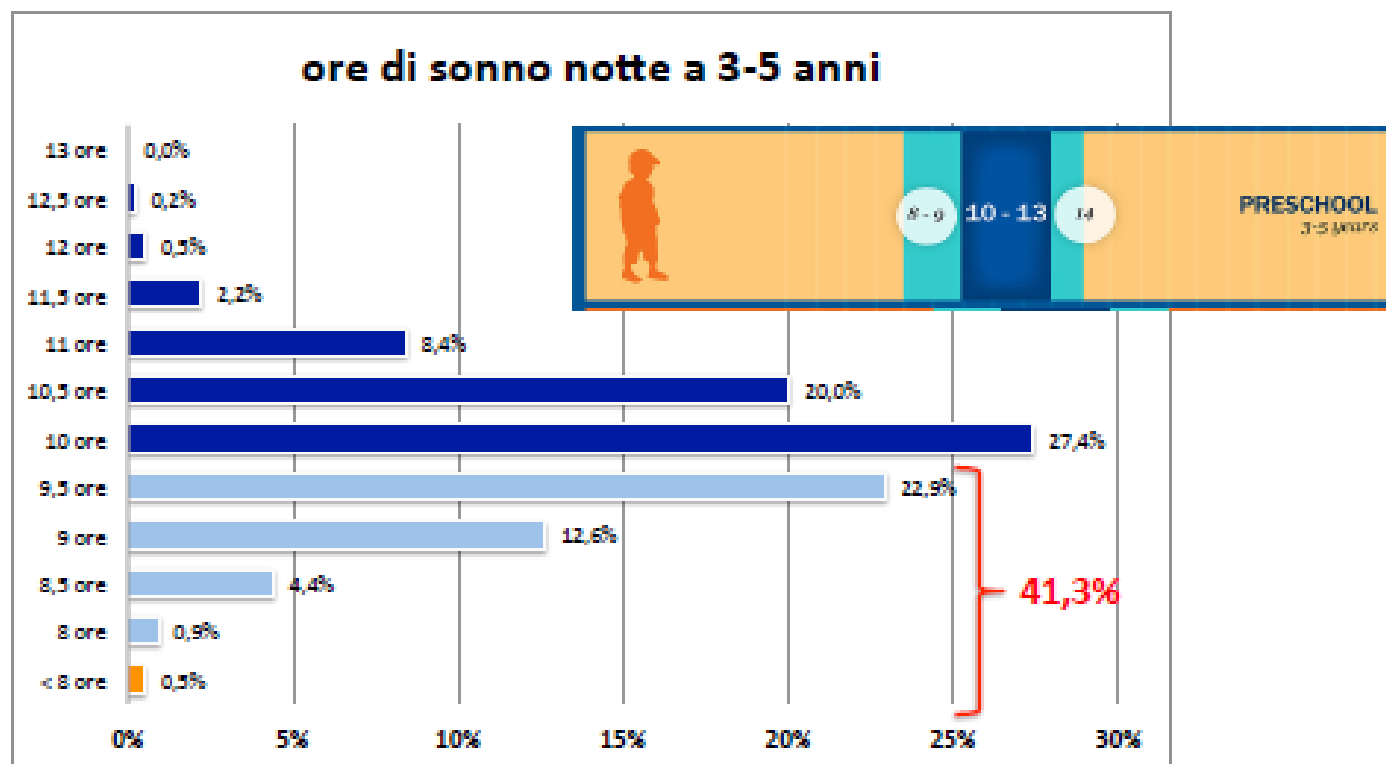


Progetto BUONANOTTE

ore di sonno: 3-5 anni

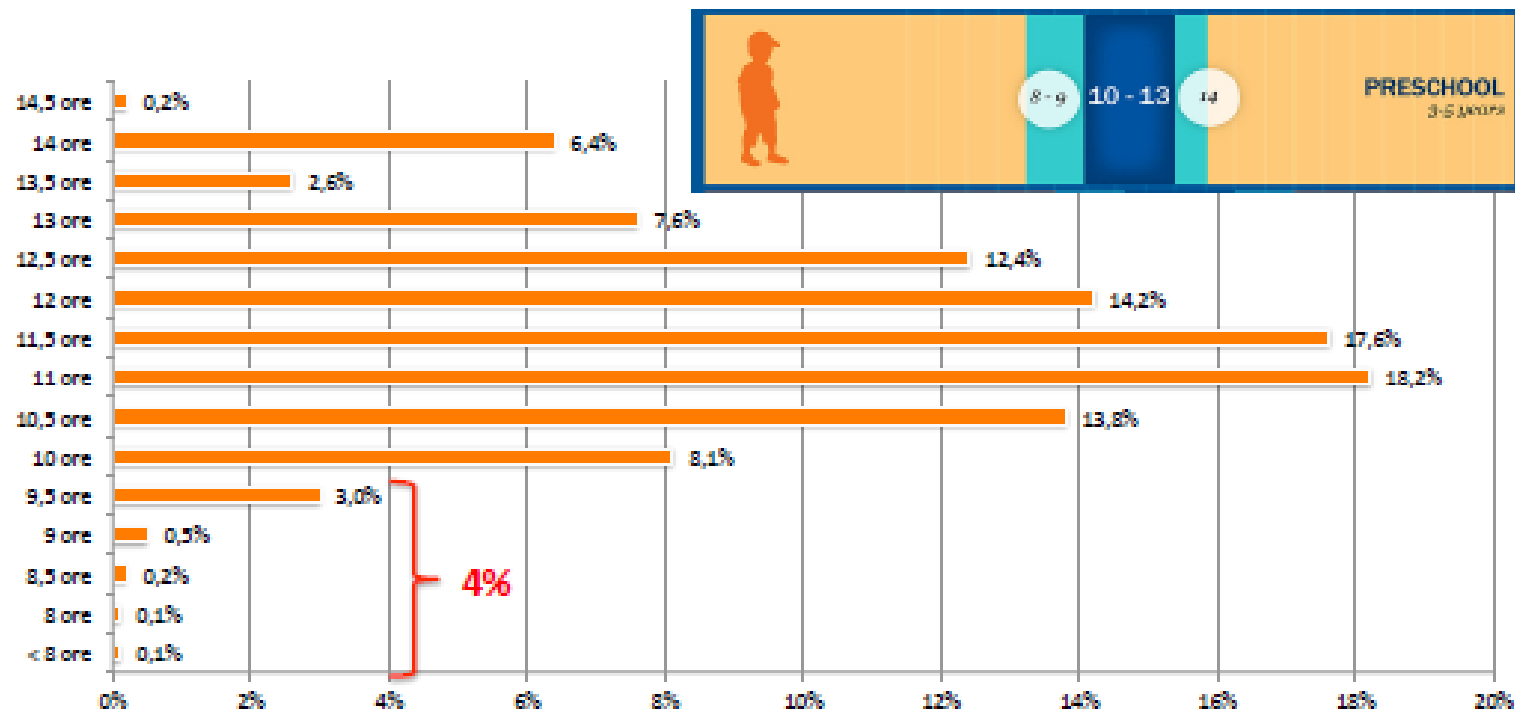


Progetto BUONANOTTE



Progetto BUONANOTTE

ore di sonno 24H 3-5 anni



Progetto BUONANOTTE

significatività dei dati

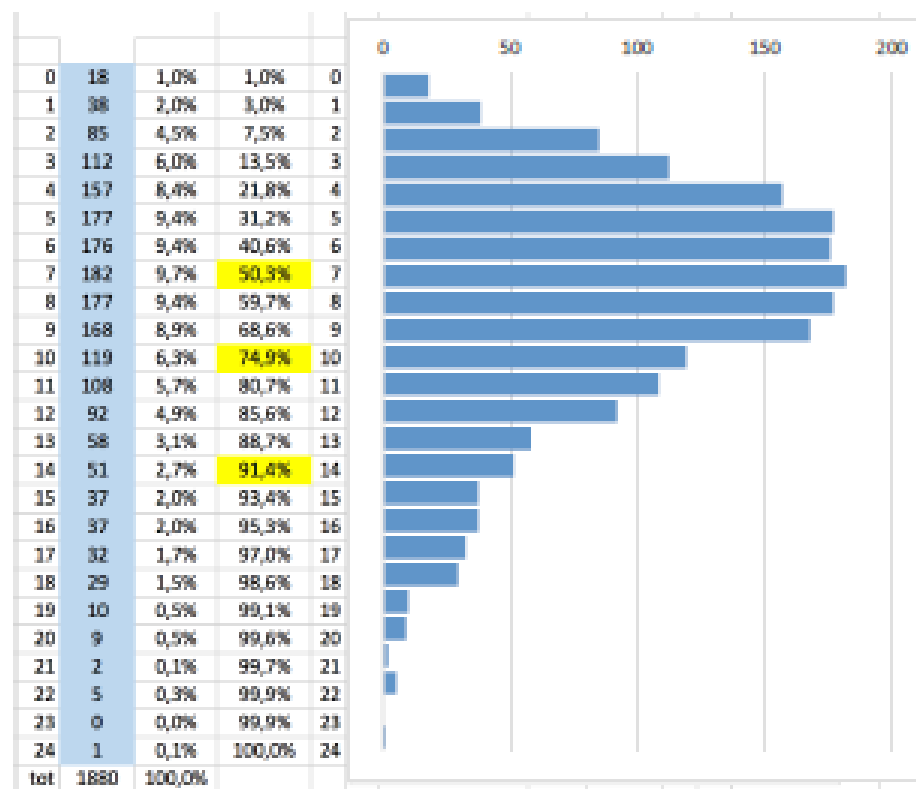
ODDS RATIO

misura dell'associazione tra due fattori

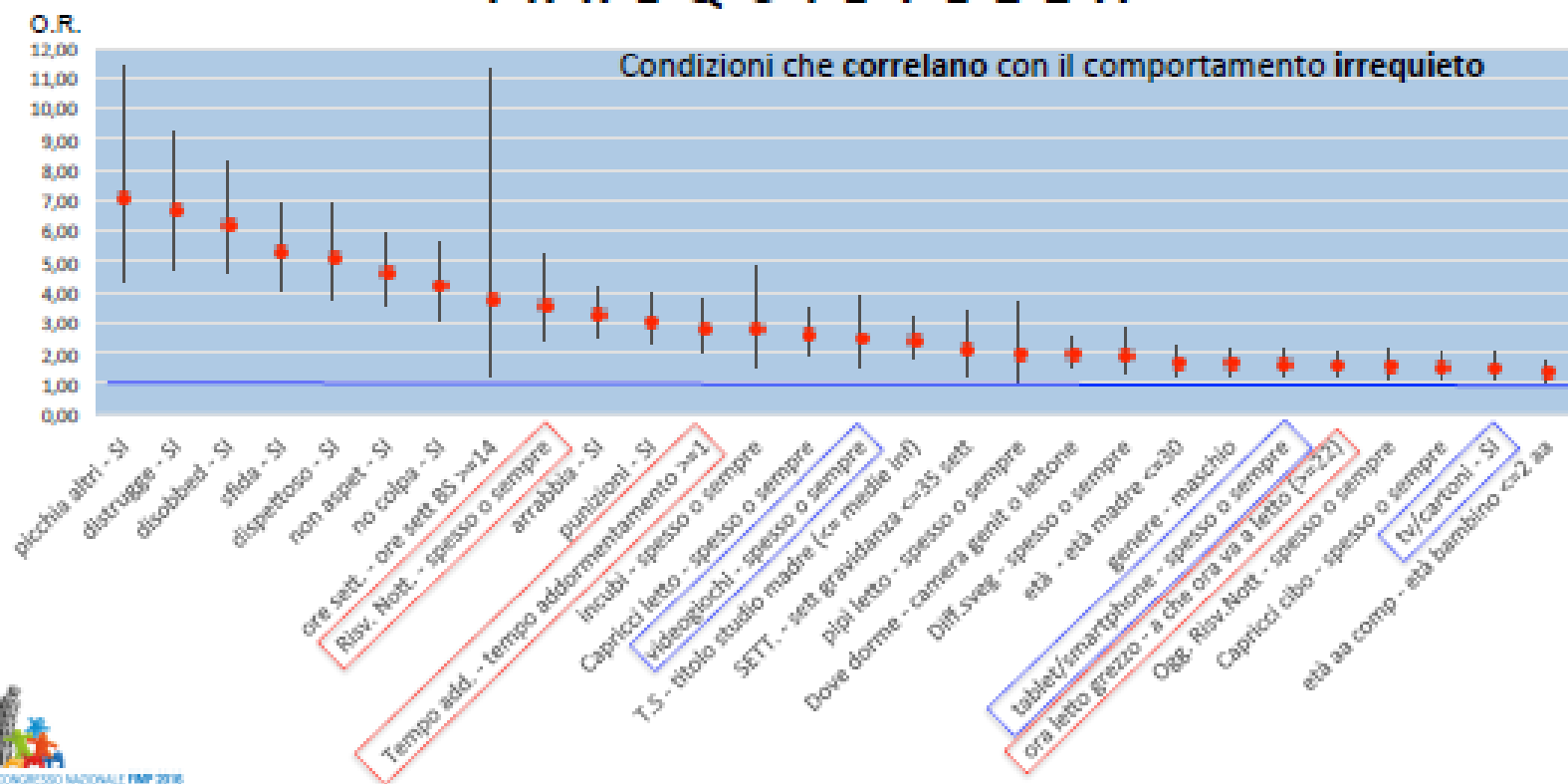
esposizione/outcome

O.R. >1 l'outcome è più frequente nei soggetti esposti
O.R. <1 l'outcome è meno frequente nei soggetti esposti

Progetto BUONANOTTE

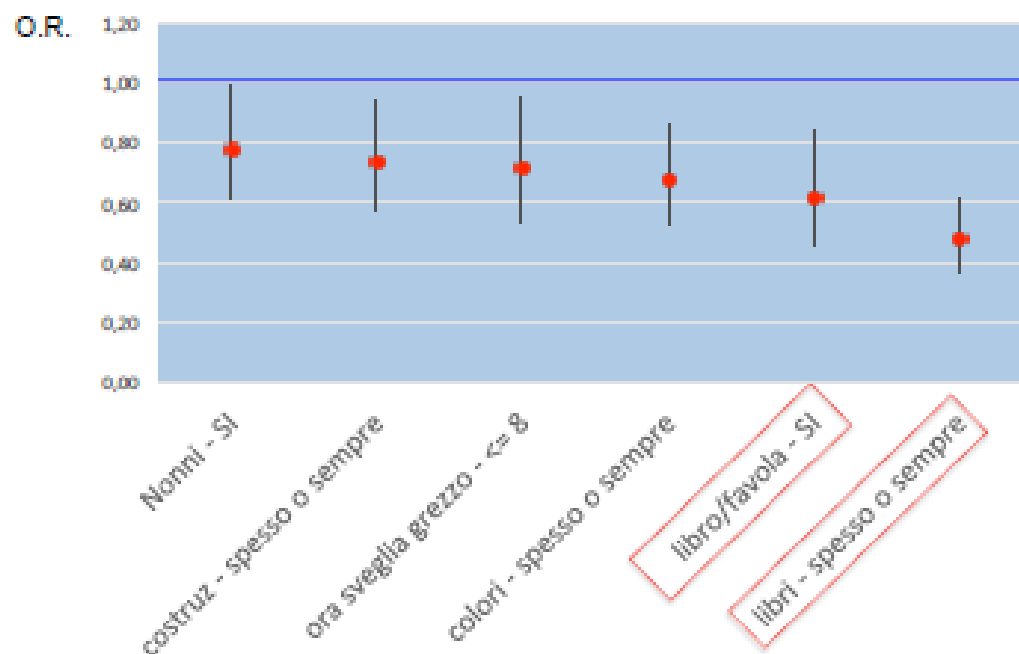


Progetto BUONANOTTE I R R E Q U I E T E Z Z A

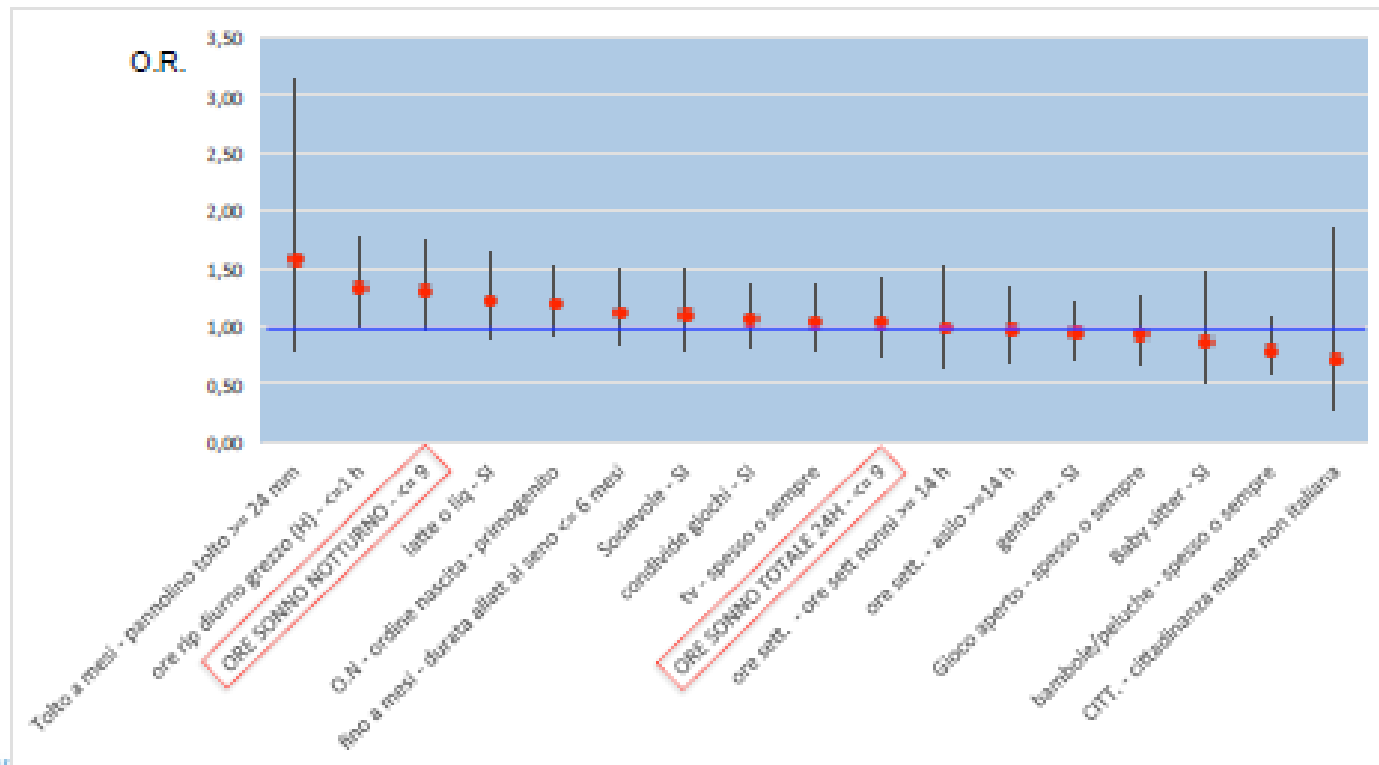


Progetto BUONANOTTE I R R E Q U I E T E Z Z A

Condizioni che non correlano con il comportamento irrequieto

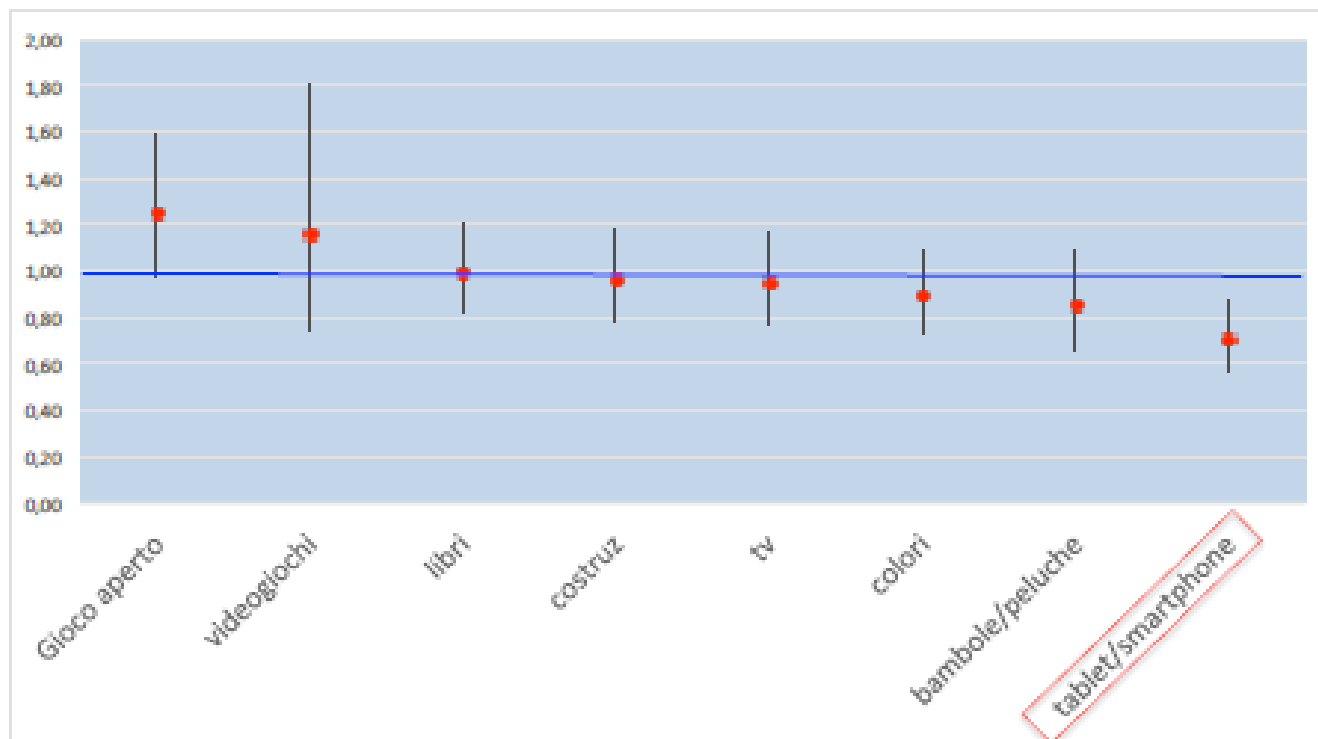


Progetto BUONANOTTE I R R E Q U I E T E Z Z A



Progetto BUONANOTTE

SONNO NOTTURNO ≥ 10 ore



Progetto BUONANOTTE

SONNO 24 ORE

