

# Obstructive sleep apnoea in Down syndrome

## *Current knowledge and future directions*

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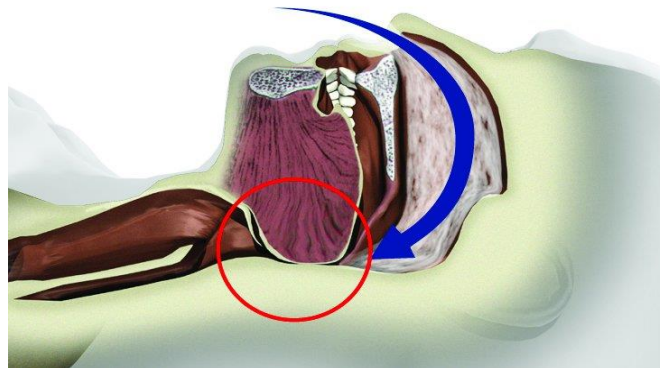
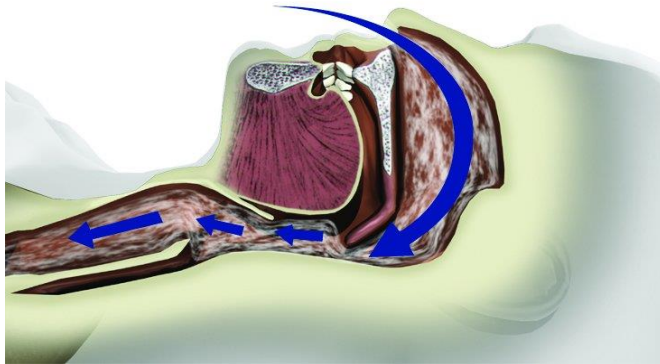


# OSA is a relatively new concept!

*The stupid-lazy child who frequently suffers from headaches at school, breaths through his mouth instead of his nose, snores and is restless at night, and wakes up with a dry mouth in the morning, is well worthy of the solicitous attention of the school medical officer. BMJ 1889*

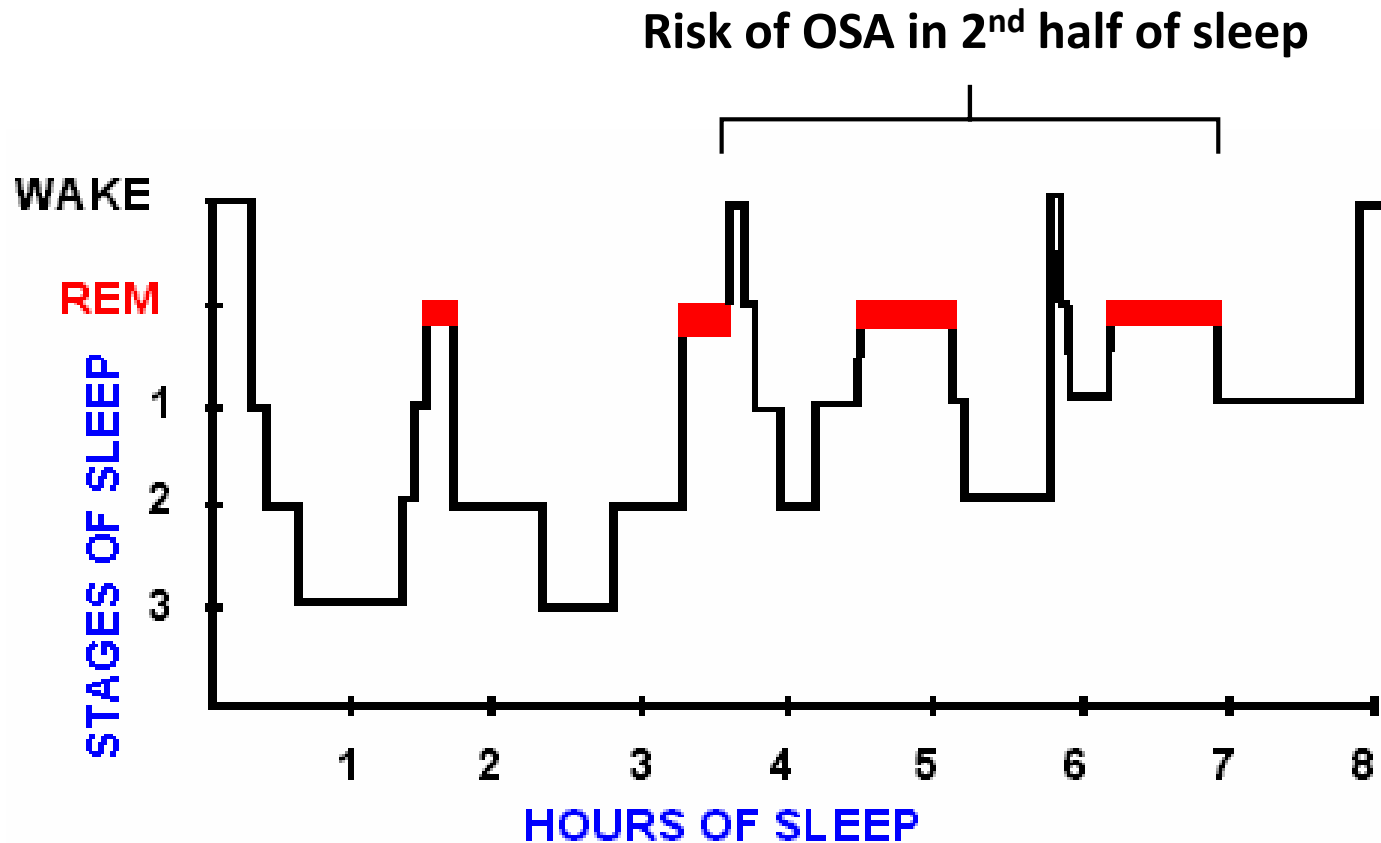
- 1962 first report of obstructive apnoeas in sleep in obese adults (called Pickwickian syndrome)
- 1976, first description of paediatric OSA was published describing 8 children '*with a sleep apnea syndrome similar to that seen in adults*'.

# Obstructive sleep apnoea (OSA)



- Negative intraluminal pressure in pharynx with inspiration NOT counterbalanced by dilator muscles
- Continued respiratory effort against a blocked upper airway in sleep
- Characterised by both complete (apnoea) or partial (hypopnoea) obstruction of the upper airway
- Causes combination of intermittent hypoxia, hypercapnia and brief arousals from sleep that restore airway patency, but fragment sleep.

# The landscape of sleep



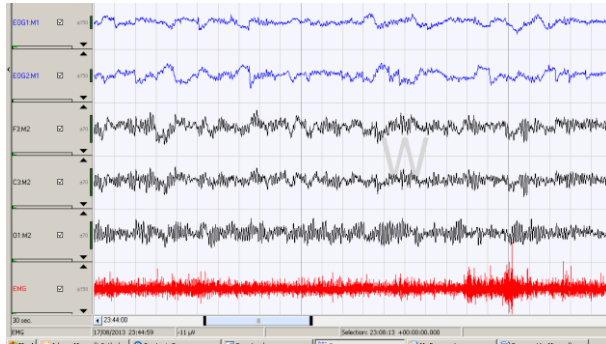
# Sleep and the upper airway

EOG →

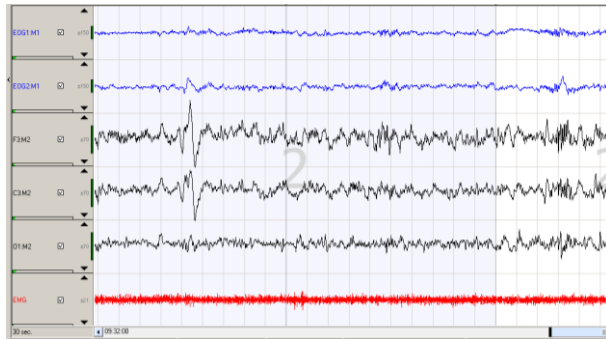
EEG →

CHIN →

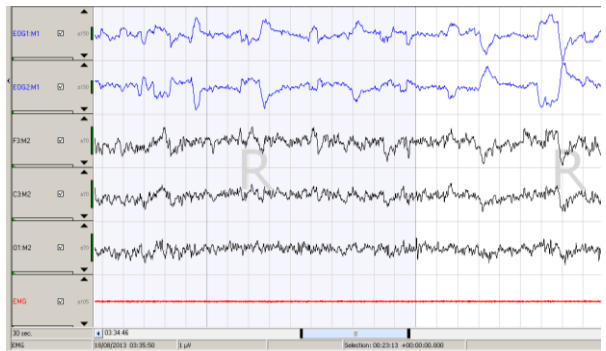
EMG



**Drowsy but awake**



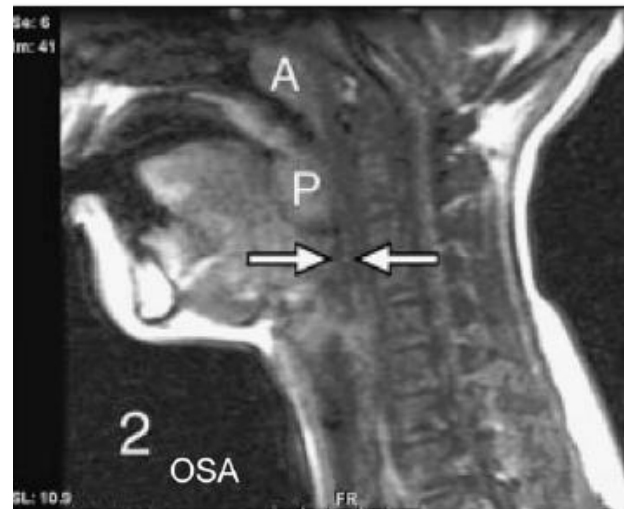
**N2: Muscle tone drops**



**REM: skeletal muscle atonia**

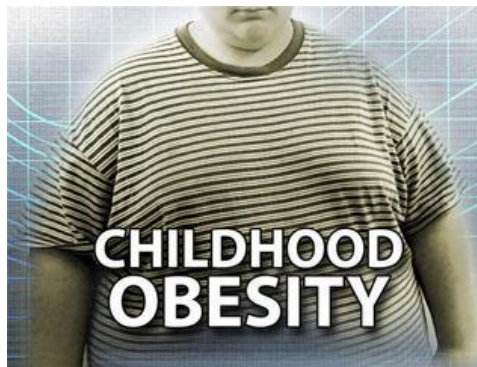
# Causes in children

- Adeno-tonsillar hypertrophy in pre-school years

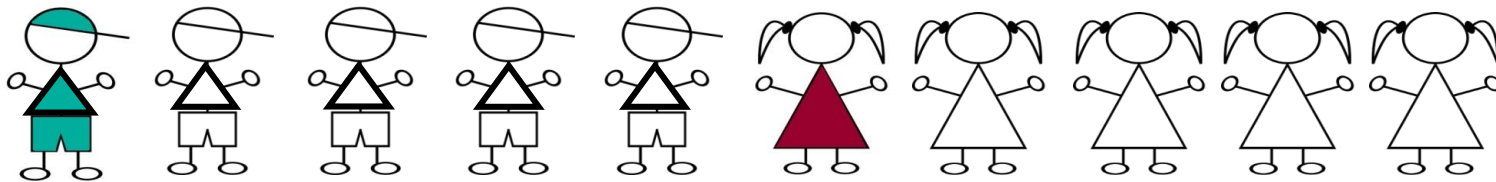




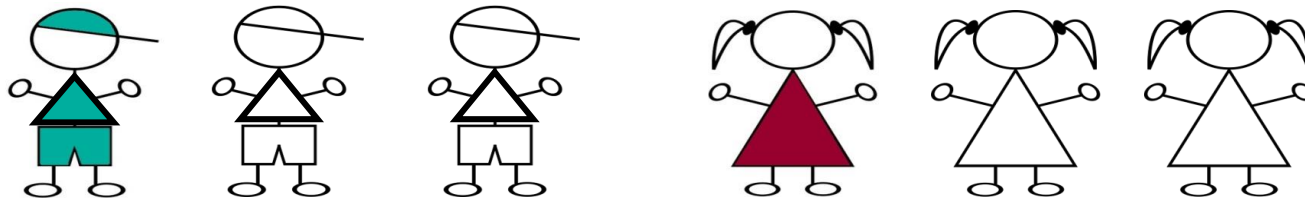
# Causes of OSA:



**One in five children in Reception is overweight or obese**



**One in three children in Year 6 is overweight or obese**



- OSA risk 16-36% for obese children

# Causes of OSA: cranio-facial anatomy/tone

- Small chin or mid-face
- Large tongue
- Low muscle tone
- Children with Down syndrome – perfect storm of multiple risk factors





# Why worry about OSA?

## IN otherwise healthy typically developing children:

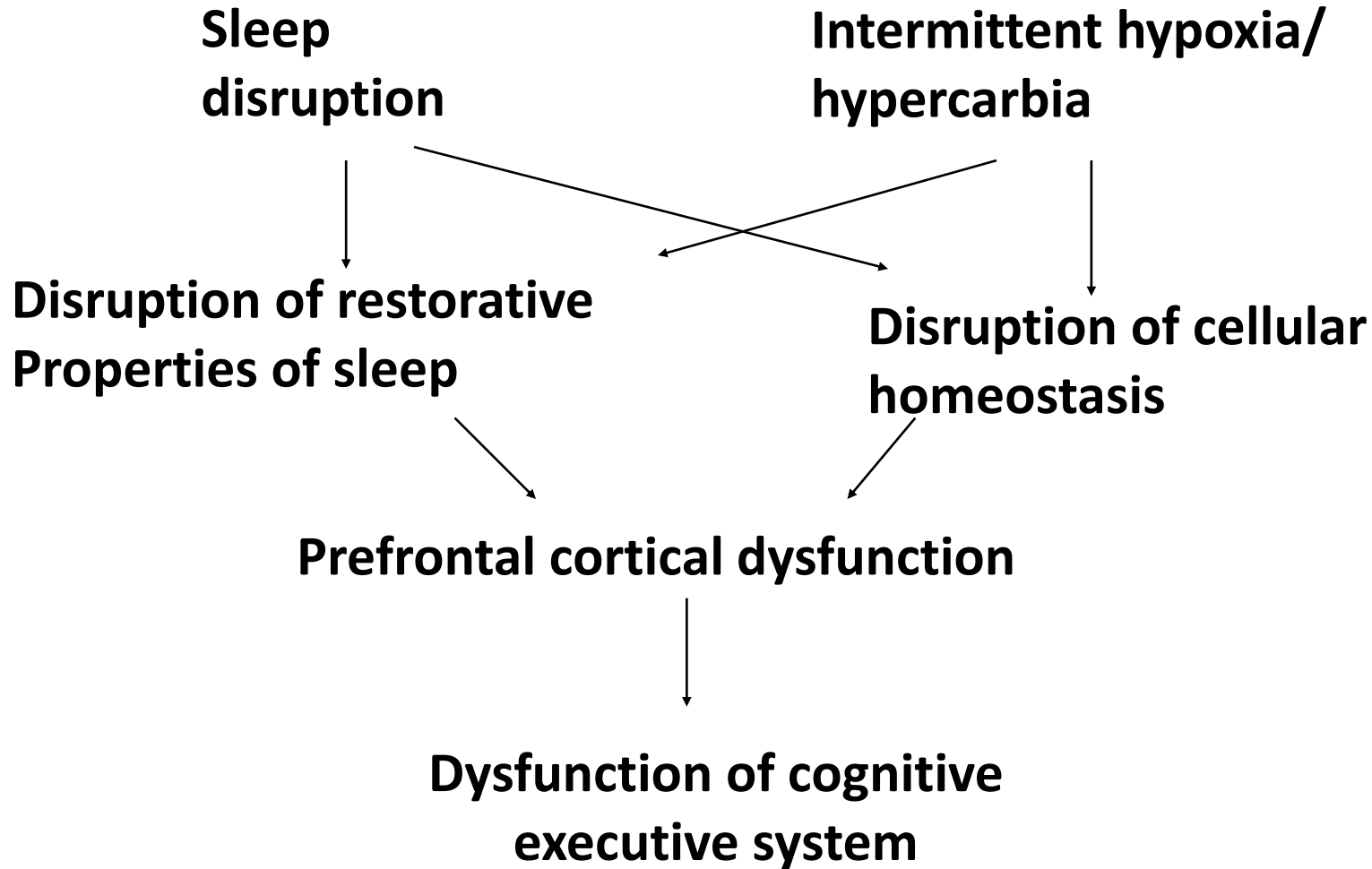
- Impairment of daytime attention<sup>1</sup>
- Worse school performance<sup>2</sup>
- Behavioural problems
- High blood pressure<sup>3</sup>
- Faltering growth<sup>4,5</sup>
- Reduced quality of life<sup>6</sup>
- Increased health care utilization<sup>7</sup>

## IN children with Down syndrome:

- Poverty of research data (more on this later!)


# Why does OSA affect the brain?

## Pre-frontal model for neurocognitive deficit in Sleep Disordered Breathing<sup>8</sup>



# How do we diagnose OSA?

# 1. Symptoms

- During sleep
    - snoring
    - pauses in breathing followed by gasp
    - restless sleep
    - enuresis
    - sweating
    - unusual sleeping positions
    - Headache and dry mouth on waking
  - In the day
    - Learning and development
    - Behavioural problems
- 
- non-specific!

# Questionnaire tools

- Only one fulfils psychometric quality criteria (Pediatric sleep questionnaire<sup>9</sup>) but includes questions about BEHAVIOUR so poor specificity in a DS population:

*My child often...*

- *does not seem to listen when spoken to directly*
- *has difficulty organising tasks and activities*
- *is easily distracted by extraneous stimuli*
- *fidgets with hands or feet or squirms in seat*
- *is “on the go” or often acts as if “driven by a motor”*
- *interrupts or intrudes on others (e.g. butts into conversation)*

# The development of a screening questionnaire for obstructive sleep apnea in children with Down syndrome

*Emma Sanders<sup>1</sup>, Catherine Mary Hill<sup>1,2</sup>, Hazel Jean Evans<sup>1,2†</sup> and Catherine Tuffrey<sup>1,3\*†</sup>*

- 14 item questionnaire
- Question items developed using expert consensus to generate a content validity index and parent cognitive interviews confirmed readability and relevance of questions<sup>10</sup>
- Psychometric properties evaluation underway



# Physical examination

- BMI
  - Dysmorphic features
  - ENT exam
  - Chest wall deformity
  - Disorders affecting muscle tone
  - Evidence of pulmonary hypertension
- A systematic review of in 2004 concluded that clinical history and examination are poor at predicting OSA in children and have limited utility<sup>11</sup>.



# European respiratory taskforce guideline on investigation and management of OSA in 2-18 y olds<sup>12</sup>

- Defines child at risk of OSA as having  $\geq 1$  of following:
  - Symptoms
  - Clinical findings OR neuromuscular disorders and syndromes known to be at risk e.g. Down syndrome
  - Diagnostic findings e.g. lateral neck XR/MRI
- Recommended investigation
  - Polysomnography
  - Polygraphy
- IF not available
  - Home PSG or polygraphy
  - Pulse oximetry

# International diagnostic standards

- Based on the number of EVENTS per hour of sleep : the **apnoea/hypopnoea index (OAHl)**
- **Hypopnoea** = reduced airflow by >30% from baseline ONLY scored if assoc. with >3% desat. OR EEG arousal
- **Apnoea** – cessation of airflow
- Each event must last at least 2 breath cycles
- ALWAYS with continued effort to breathe
- OAHl  $\geq 2$  events per hour = OSA
- OAHl  $\geq 5$  events per hour = risk of morbidity treatment indicated

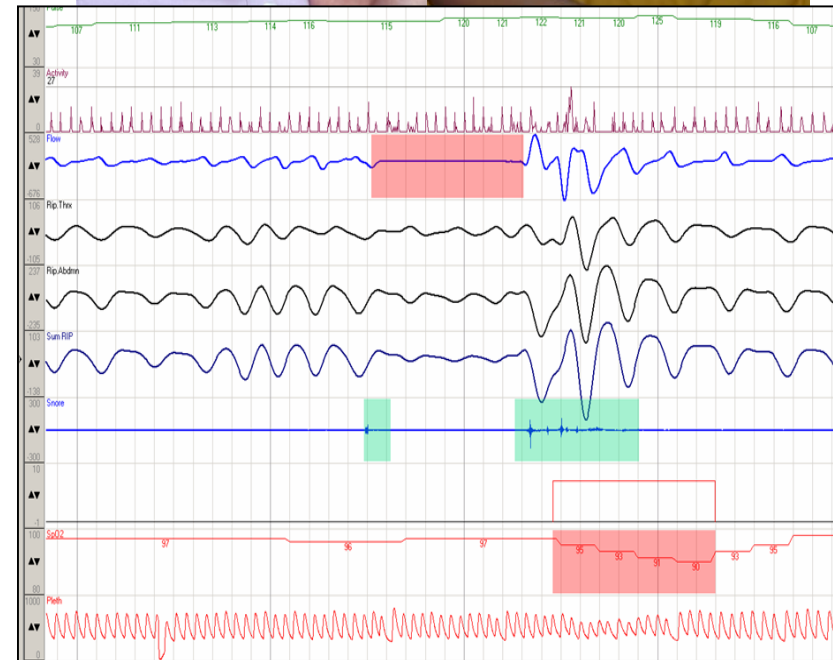
# Full polysomnography (gold standard)

- Measures sleep and wake and identifies stage of sleep
- EEG ( min.3 leads), EOG, EMG (chin)
- Respiration – movements (RIP)
- Respiration – airflow
- ECG
- Gas exchange – SpO<sub>2</sub> and CO<sub>2</sub>
- Snoring
- Body position
- +/- limb EMG



# Commonest test in the UK: respiratory polygraphy

- Respiration – movements
- Respiration – airflow
- ECG
- Gas exchange – O<sub>2</sub> and CO<sub>2</sub>
- Snoring
- Body position
- Sensitivity of 90.9% and a specificity of 94.1% to detect obstructive apnoea/hypopnoea index  $\geq 5.6$ /hr compared to a gold standard = polysomnography



# European Consensus Guidelines for the Management of OSA<sup>12</sup>

Children who benefit from treatment include those with:

- AHI >5/hr OR AHI 1–5/hr + other factors predicting persistence
- Complex conditions (e.g. **Down syndrome**)

## Stepwise treatment approach

- Weight loss if overweight or obese
- Nasal anti-inflammatory treatment
- Adenotonsillectomy
- Rapid maxillary expansion or orthodontic appliances
- CPAP therapy





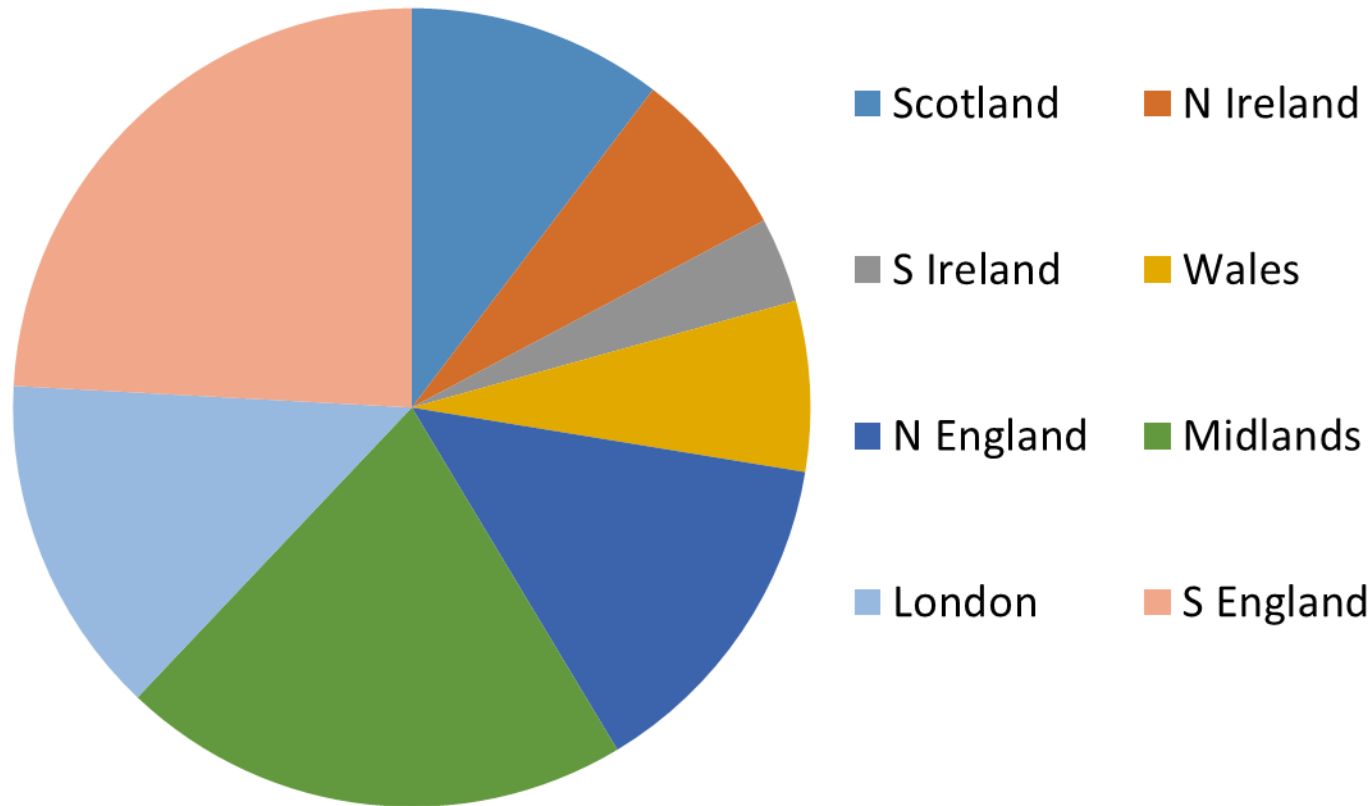
# UK expert consensus report UNIVERSITY OF Southampton in 2009<sup>13</sup>

- Down syndrome: *‘ based on the 197 children reported, sleep related breathing disorders occurs in 58% and between one-third and three-fifths of children with Down syndrome have desaturation below 90% while asleep’.*
- Recommended SCREENING as follows:
- Oximetry once in infancy then annually to 3-5 yrs
- Children with abnormalities on screening, or a clinical suspicion of a false negative screening test, should have respiratory polysomnography
- BUT ACKNOWLEDGED LACK OF EVIDENCE

# Screening practice DSMIG members

*(Hill CM and Evans HE, 2012)*

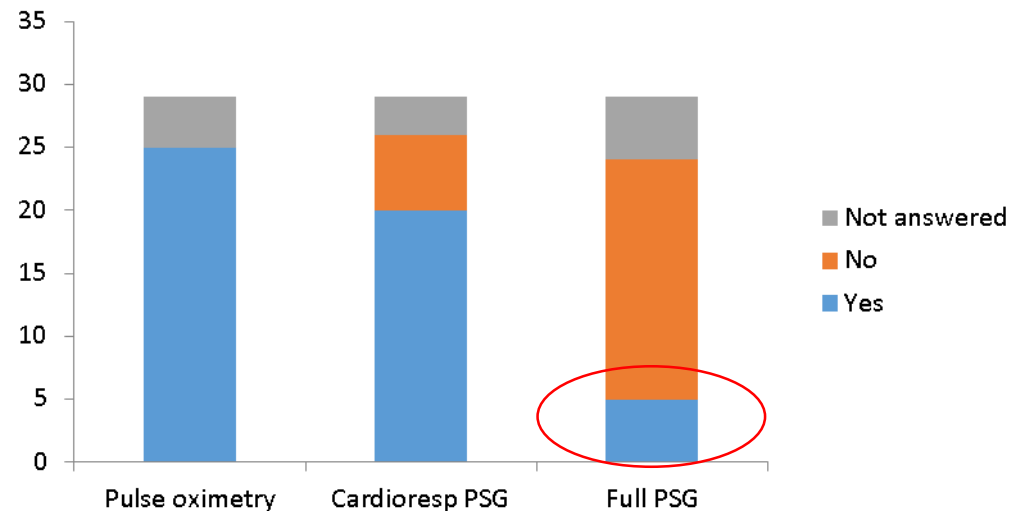
## Location of 29 respondents



## Adherence to RCPCH guidelines

- Only 5 had a screening programme
- 4 followed RCPCH guidelines
- 1 used cardiorespiratory PG as first line

## Availability of technology



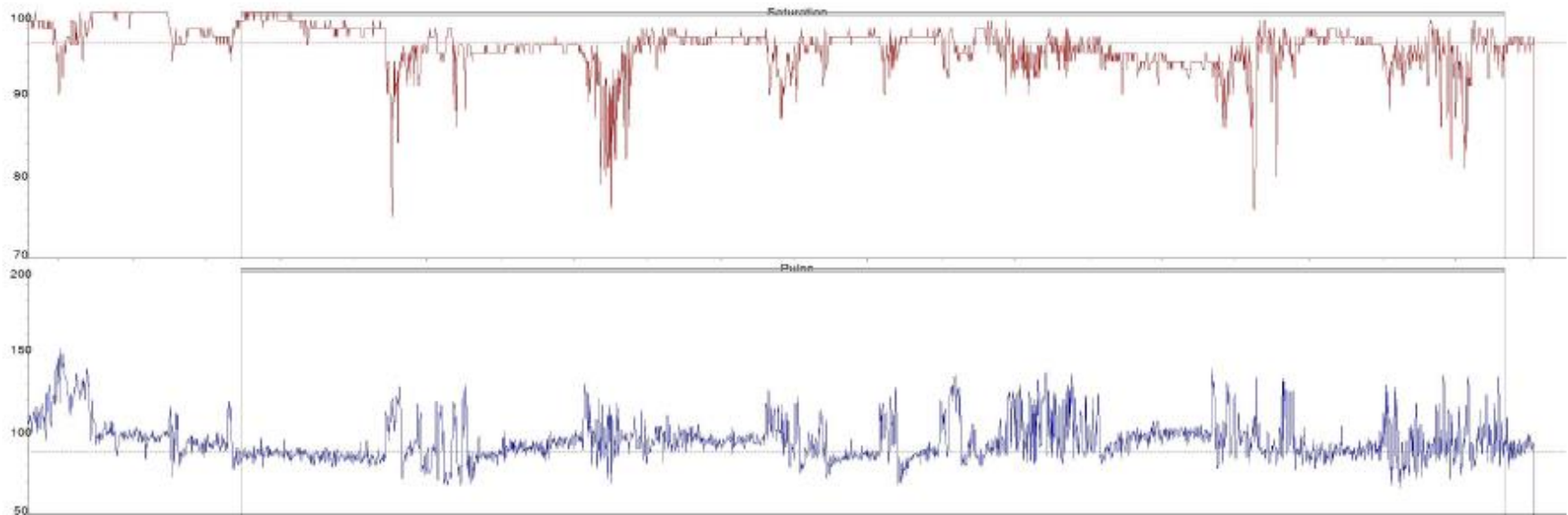
- 19/25 routinely offer pulse oximetry at HOME

## Advantages

- Widely available
- Well tolerated

## Disadvantages

- Sensitivity & specificity unknown
- Child may be awake
- Central apnoea causes dips in oxygen



# Known gaps in research evidence

- Accurate prevalence data – how common is it in DS?
- What is the best way to test for it and how often should children be screened?
- Natural history of condition treated/untreated
- Effects on cognition
- Best way to treat it



## Very limited research on OSA and cognition in children with DS<sup>14</sup>

- 38 children with DS (15 males aged 7–12y).
- Arizona Cognitive Test Battery: psychometric measures designed and validated for this population
- Home polysomnography .
- Mean Verbal IQ score ( $p=0.006$ ) was 9 points lower in those with OSA (AHI >1.5) than in those without OSA
- Performance on measures of cognitive flexibility was poorer ( $p=0.03$ )
- Those with OSA showed increased light-stage sleep ( $p=0.009$ ) at the expense of slow-wave sleep ( $p=0.04$ )



The Garfield Weston  
Foundation



## OSA in young children with DS

CI: Cathy Hill. PIs: Heather Elphick, Hazel Evans, Paul Gringras & Michael Farquhar. Sleep technologists: Ruth Kingshott & Johanna Gavlak. Research team: Jane Martin, Janine Reynolds, Anna Ashworth, Carla Rush. Statistician: Ruth Pickering (main data) and Romola Bucks (M-Plus analysis)

## Primary aim

- To determine the diagnostic test accuracy of pulse oximetry to predict OSA in children with DS as measured against respiratory polygraphy

## Secondary aims

- To study the association between OSA and neurobehavioral measures
- To establish a cohort of children to map the natural history of OSA in DS and offer future intervention studies

## Recruitment

- Aimed to recruit 180
- Multi-modal recruitment approach:
  - Regional community paediatricians, respiratory and cardiology services
  - Parent support groups and word of mouth
  - DSMIG

## Inclusion criteria

- Children with Down syndrome aged 6 months to 6<sup>th</sup> birthday
- No cardiorespiratory polygraphy in the past 3 months
- Not using home oxygen or CPAP
- Family able to travel to centre

# Measures: OSA

One night each of home pulse oximetry and respiratory polygraphy



# Measures: Behavior Rating of Executive Function (P)

63 item parent report, validated in children aged 2 yrs - 5 yrs 11mo including in children with developmental disability

## It yields 5 sub-scales:

- **Inhibit**
  - **Shift**
  - **Emotional control (EC)**
  - **Working memory (WM)**
  - **Plan/organise (PO)**
- 3 broader indexes
    - Inhibitory self-control (ISCI)
    - Flexibility (FI)
    - Emergent metacognition (EMI)
  - Global executive composite (GEC)

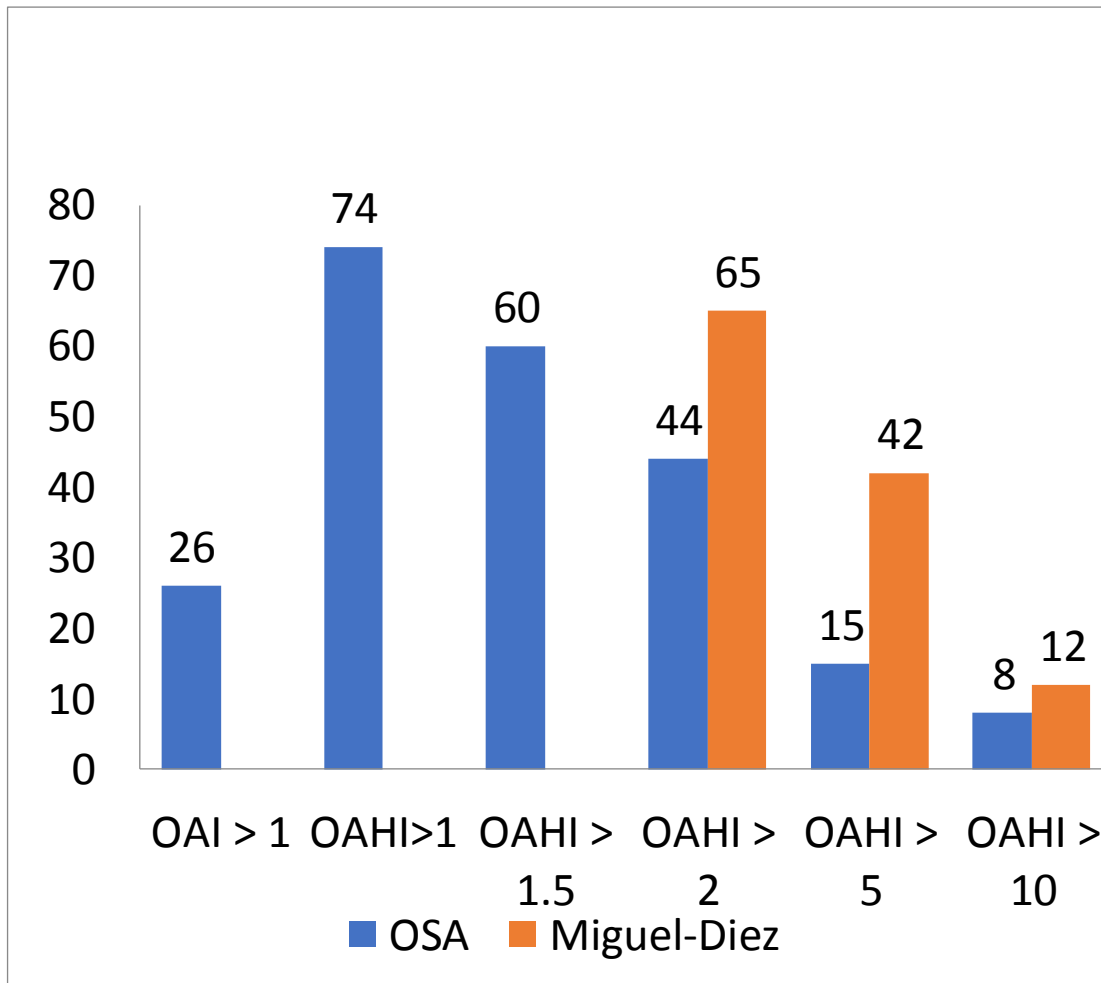
Scores of 65 or more are considered clinically significant

# Results 1: demographics

- 202 children recruited of whom 188 had a successful respiratory polygraphy study
- No differences between centres in any of the core variables

<b>Age (months)</b>	mean (SD) min-max	<b>36.3 (20.6)</b> <b>6-71</b>
<b>Gender</b>	male female	<b>100 (53%)</b> <b>88 (47%)</b>
<b>BMI (3 missing)</b>	mean (SD) min-max	<b>16.9 (1.5)</b> <b>13.0-21.2</b>

# Prevalence of OSA<sup>15, 16</sup>



- Male gender and habitual snoring predicted OSA but did not have independent predictive power in the presence of the other factors.
- Age, BMI centile and tonsillar size did not predict OSA.

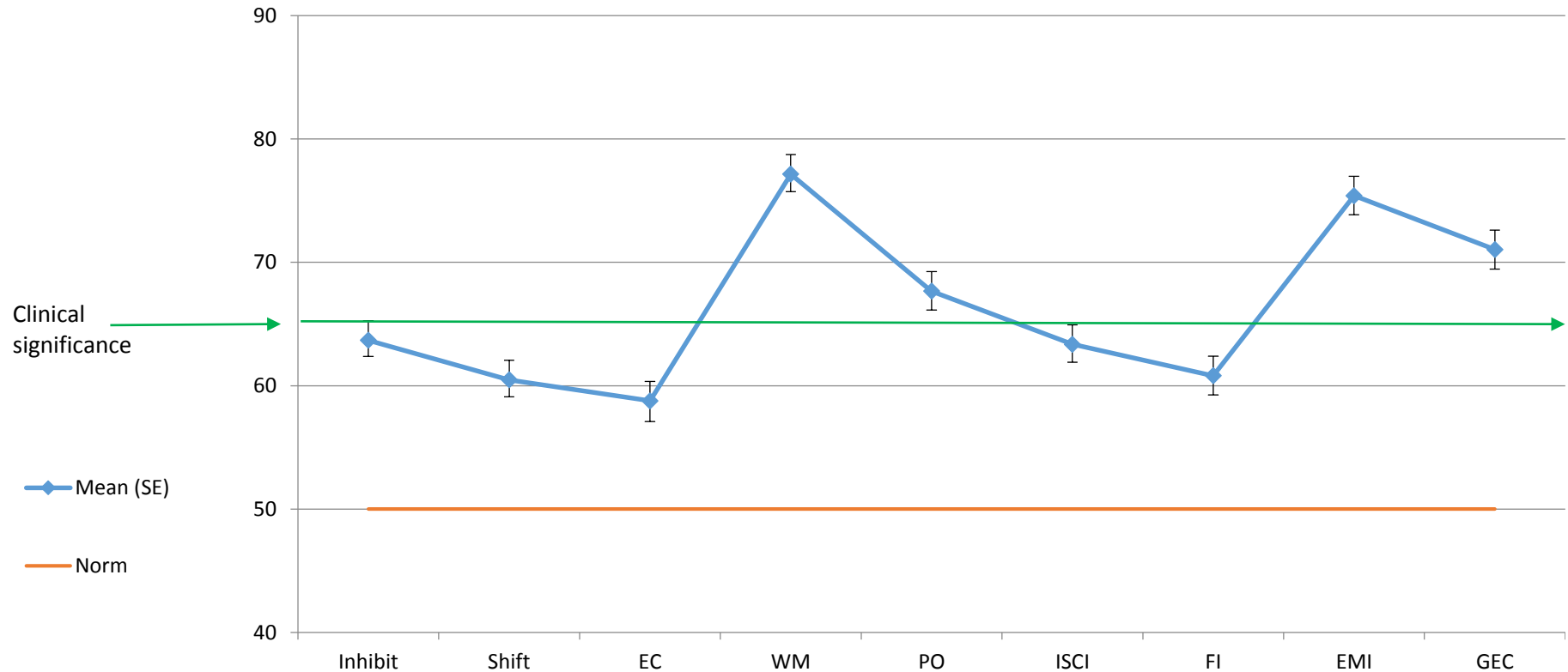


# How did pulse oximetry perform as a screening tool?

- The best OSA predictor was delta 12s index. This is a marker of oxygen saturation variability. In our analysis values  $>0.555$  predicted clinically significant OSA with sensitivity 92% and specificity 65%
- 23/25 TRUE positives were correctly detected
- In a clinical validation sample sensitivity was retained with only slight loss of specificity (63%)
- We recommend that ALL positives are then confirmed with respiratory polygraphy. This approach could HALVE the number of children needing detailed studies

- BRIEF-P were completed for 80/96 children (50 male) aged 3+ yrs.
- 5 were completed inconsistently were excluded.
- 69/75 had successful respiratory polygraphy
- OSA was defined as  $\text{OAHI} \geq 1.5$  ( $n=41$ ) and absent if  $\text{OAHI} \leq 1.49$  ( $n=28$ ) consistent with Arizona data.
- To assess whether OSA predicted poorer executive function behaviours, multivariate regression models with OSA group as the predictor and BRIEF-P T-scores as dependent measures.

# BRIEF-P data (n=75)



Pairwise comparisons: relative to other scales, children performed most poorly on working memory (WM) (all  $p < .005$ ) and plan/organise ( $p < .001$ ).

# Does OSA predict BRIEF-P?

- Children with OSA experienced greater difficulties with Shift ( $B=.21$ ,  $R^2=.04$ ,  $p=.04$ ) and Working Memory ( $B=.27$ ,  $R^2=.07$ ,  $p=.01$ ), indicating deficits in transitioning smoothly between activities or attentional focus, and ability to hold information in mind whilst working on a response
- Children with OSA also experienced greater difficulties with Inhibitory self-control ( $B=.20$ ,  $R^2=.04$ ,  $p=.04$ ) and Emergent Metacognition ( $B=.23$ ,  $R^2=.06$ ,  $p=.02$ ), suggesting that OSA contributes to difficulties with self-regulating behaviour and emotions, and active problem solving

- High prevalence of OSA in young children with Down syndrome supporting the need for regular screening
- Pulse oximetry could provide an accessible screening method for OSA and halve the number of children needing detailed studies
- We report for the first time that presence of OSA predicts greater deficits in executive function behaviours in **pre-school children** with Down syndrome
- Greatest deficits observed in working memory and shift sub-scales namely: transitioning smoothly between activities or attentional focus, and ability to hold information in mind whilst working on a response

- Life expectancy in DS has dramatically improved - today's children will live to middle age and beyond
- Children with DS and OSA have limited cognitive reserve to compensate for OSA related neural insult and OSA may be a risk factor for the development of dementia in later life
- Screening programmes should be implemented as recommended in 2009
- Importantly OSA in this population is amenable to treatment
- Treatment trials are urgently needed to evidence benefit from current UK first line practice of adeno-tonsillectomy

# Final acknowledgement

Children and families who supported the study 100%  
of whom have signed to our research registry





# Thank you for listening! Any questions?





# Sleep education

<http://www.piernetwork.org>

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Or [sleeptraining@uhs.nhs.uk](mailto:sleeptraining@uhs.nhs.uk)

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### Feedback from our training courses

'Thank you for a really excellent course last week. The content and clarity of presentations was outstanding and I feel more confident in my clinical work having attended' - consultant paediatrician

'I would not hesitate to recommend this course to any of my colleagues' - health visitor

'Thank you so much for the really excellent training course last week. I really enjoyed it and it has inspired me to 'think sleep' throughout my practice' - consultant child psychiatrist

'Looking forward to putting my newly learned skills into practice' - therapist.

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