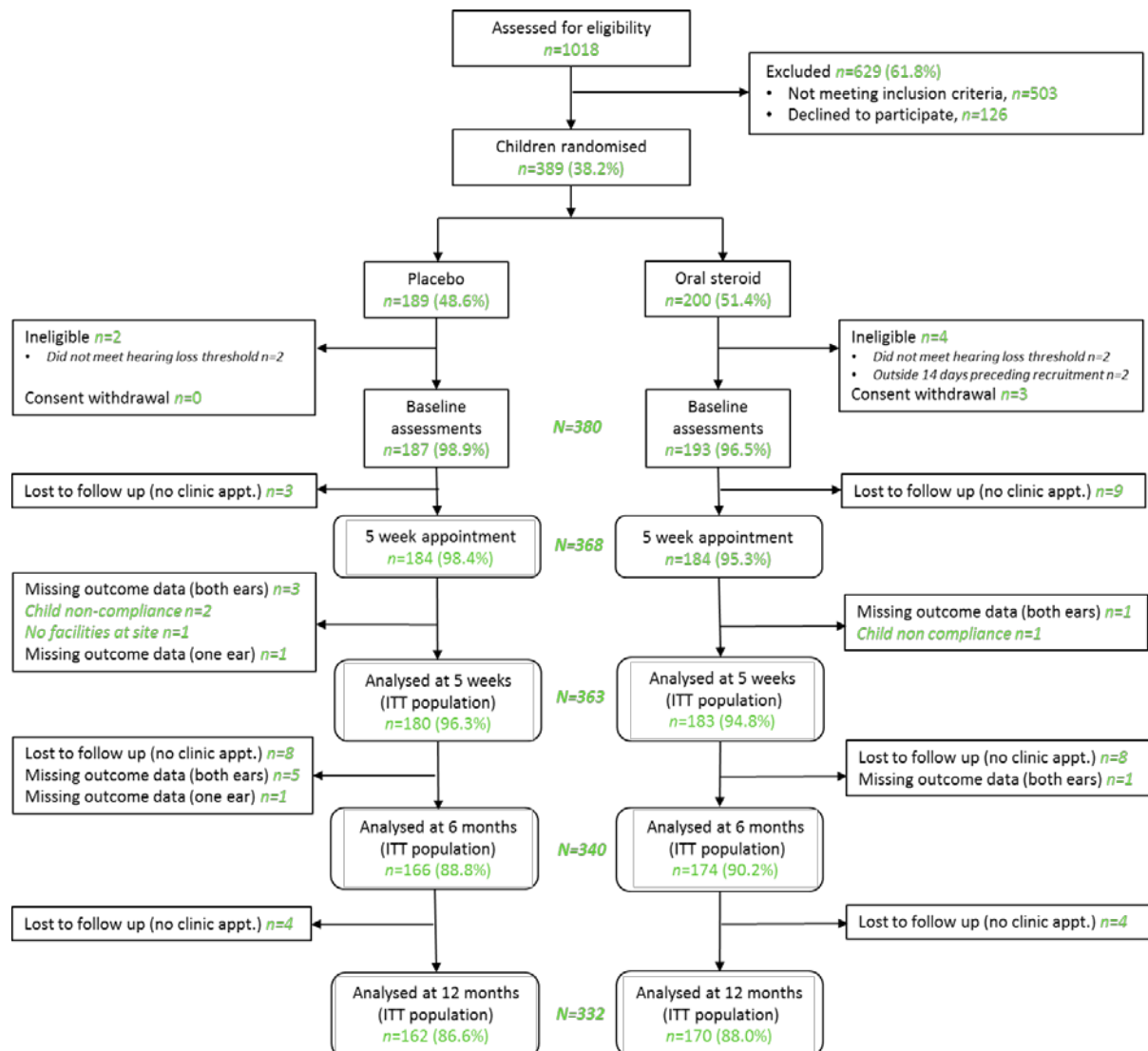


Basic Results Summary 15.08.2018

## Participant Flow:



**Baseline Characteristics:**

**Table 1 Baseline characteristics of randomised children by treatment group**

<b>Variables</b>	<b>Placebo N=187</b>	<b>Oral steroid N=193</b>
<b>Child demographics</b>		
Age at recruitment (years) <i>mean (SD)</i>	5.08 (1.60)	5.30 (1.60)
2-5 years <i>N (%)</i>	133 (71.1)	131 (67.9)
6-8 years <i>N (%)</i>	54 (28.9)	62 (32.1)
Gender <i>N (% Male)</i>	102 (54.5)	109 (56.5)
Townsend deprivation quintile		
1 – least deprived	32 (17.1)	25 (13.0)
2	16 (8.6)	23 (11.9)
3	48 (25.7)	45 (23.3)
4	46 (24.6)	48 (24.9)
5 – most deprived	45 (24.1)	52 (26.9)
Ethnicity <i>N (%)</i>		
White	134 (82.7)	143 (82.2)
Mixed/multiple ethnic	10 (6.2)	10 (5.2)
Asian/Asian British	13 (8.0)	18 (10.3)
Black/African/Caribbean/Black British	3 (1.9)	3 (1.7)
Other ethnic	2 (1.2)	0 (0.0)
<i>Missing</i>	25	19
Season randomised <i>N (%)</i>		
Spring (March to May)	64 (34.2)	70 (36.3)
Summer (June to August)	32 (17.1)	33 (17.1)
Autumn (September to November)	31 (16.6)	34 (17.6)
Winter (December to February)	60 (32.1)	56 (29.0)
Height measured <i>N (%)</i>	62 (33.2)	74 (38.3)
Height (cm) <i>mean (SD)</i>	112.22 (11.34)	115.08 (10.59)
Weight measured <i>N (%)</i>	70 (37.4)	75 (38.9)
Weight (kg) <i>mean (SD)</i>	20.24 (5.49)	21.77 (5.95)
Body Mass Index (BMI) centile <i>N (%)</i>	60 (32.1)	69 (35.8)
<i>Median (25<sup>th</sup> to 75<sup>th</sup> centiles)</i>	18.5 (16.4 to 23.1)	21.0 (18.7 to 24.6)
Relation of carer to child <i>N (%)</i>		
Mother	159 (85.5)	171 (88.6)
Father	24 (12.9)	20 (10.4)
Other	3 (1.6)	2 (1.0)
<i>Missing</i>	1	0

<b>Variables</b>	<b>Placebo N=187</b>	<b>Oral steroid N=193</b>
<b>Medical history of children</b>		
First episodes of OME <i>N (% Yes)</i>	135 (72.2)	128 (66.3)
Length of time had problems due to this episode of OME <i>N (%)</i>		
<6 months (m)	26 (13.9)	19 (9.9)
6 to <9 m	28 (15.0)	22 (11.5)
9 to <12 m	18 (9.6)	20 (10.4)
12 m or more	115 (61.5)	131 (68.2)
Missing	0	1
Previous ventilation tubes (grommet surgery) <i>N (% Yes)</i>	19 (10.2)	14 (7.3)
On waiting list for ventilation tubes <i>N (% Yes)</i>	52 (27.8)	55 (28.6)
Fitted with hearing aids <i>N (% Yes)</i>	31 (16.6)	27 (14.0)
if yes, frequency of use:		
Not at all	5 (16.1)	2 (7.4)
Occasionally	2 (6.5)	2 (7.4)
Most of the time	8 (25.8)	15 (55.6)
All of the time	16 (51.6)	8 (29.6)
Previous tonsillectomy <i>N (% Yes)</i>	8 (4.3)	9 (4.7)
Previous adenoidectomy <i>N (% Yes)</i>	8 (4.3)	8 (4.1)
<b>Family history of OME</b>		
Has a brother or sister? <i>N (% Yes)</i>	147 (78.6)	156 (80.8)
If yes, at least one currently has or has had OME	34 (23.3)	44 (28.4)
Missing	1	1
Atopy <i>N (%)</i>		
None	131 (70.1)	125 (64.8)
At least one:	56 (29.9)	68 (35.2)
Asthma	22 (11.9)	21 (11.2)
Eczema	41 (22.2)	41 (21.6)
Hay fever	16 (8.7)	21 (11.1)
Missing	0	3
<b>Medications</b>		
Presently using medication regularly longer than one week <i>N (% Yes)</i>	25 (13.4)	32 (16.7)
Asthma ( $\beta$ -agonist or Corticosteroid inhaler, Corticosteroid inhaler in combination)	20	23
Leukotriene receptor antagonists	1	2

<b>Variables</b>	<b>Placebo N=187</b>	<b>Oral steroid N=193</b>
Antihistamine	4	2
Nasal steroids	3	1
Antibiotics	0	0
Pain relief (Ibuprofen, Paracetamol)	2	2
Other	8	17
Antibiotics for an ear infection in last month <i>N (%) Yes)</i>	13 (7.0)	19 (9.9)
<i>Missing</i>	0	1
Smoking in house (> 5 hours a week) <i>N (%) Yes)</i>	56 (29.9)	51 (26.4)

**Table 2 Baseline clinical hearing assessments by treatment group**

	<b>Placebo N=187</b>	<b>Oral steroid N=193</b>
<b>Audiometry</b>		
Method of audiometry <i>N (%)</i>		
PTA	94 (50.3)	108 (56.0)
Ear specific VRA	3 (1.6)	2 (1.0)
Ear specific play audiometry	61 (32.6)	61 (31.6)
Soundfield VRA	17 (9.1)	16 (8.3)
Soundfield performance/play audiometry	12 (6.4)	6 (3.1)
Average decibel (dBHL) that is audible <i>Mean (SD)</i>		
PTA, Ear specific VRA/play audiometry	N=158	N=171
Right ear	37.07 (7.49)	35.94 (8.59)
Left ear	37.39 (8.00)	35.89 (8.83)
Best hearing ear	34.24 (7.21)	32.69 (8.21)
Worst hearing ear	40.22 (7.10)	39.25 (7.94)
Average of the two ears	37.23 (6.53)	35.97 (7.51)
Soundfield average decibel (dBHL) <i>Mean (SD)</i>	N=29 41.13 (8.12)	N=22 38.35 (9.30)
Overall (Average of the two ears and soundfield)	37.83 (6.93)	36.25 (7.74)
<b>Degree of hearing loss (dBHL range) <i>N (%)</i></b> <i>(based on Overall dBHL)</i>		
Slight (16-25)	8 (4.3)	13 (6.7)
Mild (26-40)	116 (62.0)	134 (69.4)
Moderate (41-55)	63 (33.7)	44 (22.8)
Moderate severe (56-70)	0 (0.0)	2 (1.0)
Severe (71-90)	0 (0.0)	0 (0.0)
Profound (>90)	0 (0.0)	0 (0.0)

	<b>Placebo N=187</b>	<b>Oral steroid N=193</b>
<b>Tympanometry</b>		
Tympanometry performed <i>N</i> (% <i>Yes</i> )	187 (100.0)	192 (99.5)
Type: Right ear <i>N</i> (% <i>Yes</i> )		
B (Flat)	181 (96.8)	184 (96.8)
C (Retracted/negative)	6 (3.2)	6 (3.2)
<i>Missing</i>	0	3
Type: Left ear <i>N</i> (% <i>Yes</i> )		
B (Flat)	181 (97.8)	182 (95.8)
C (Retracted/negative)	4 (2.2)	8 (4.2)
<i>Missing</i>	1	1
No type B ears	1 (0.5)	3 (1.6)
One type B ear	8 (4.3)	10 (5.2)
Two type B ears	177 (95.2)	178 (93.2)
<b>Otoscopy</b>		
Visualise the Tympanic Membrane: Right ear <i>N</i> (%)	180 (96.3)	192 (99.5)
If yes:		
Perforation present	0	0
Appearance suggests presence of middle ear effusion	180 (100.0)	190 (99.0)
Bubbles behind the ear drum	20 (11.1)	22 (11.6)
Visualise the Tympanic Membrane: Left ear <i>N</i> (%)	178 (95.2)	189 (97.9)
If yes:		
Perforation present	2 (1.1)	2 (1.1)
Appearance suggests presence of middle ear effusion	177 (99.4)	187 (98.9)
Bubbles behind the ear drum	20 (11.2)	19 (10.1)

**Table 3 Baseline functional health status and health related quality of life scores**

	<b>Placebo N=187</b>	<b>Oral steroid N=193</b>
<b>HUI-3 Score<sup>a</sup> Median (25<sup>th</sup> to 75<sup>th</sup> centiles)</b>	0.80 (0.63 to 0.93)	0.79 (0.66 to 0.92)
Range (Min, Max)	-0.16 to 1.00	0.10 to 1.00
<i>Missing</i>	28	29
<b>PedsQL<sup>b</sup> Median (25<sup>th</sup> to 75<sup>th</sup> centiles)</b>	<b>187</b>	<b>189</b>
Physical Functioning	90.6 (78.1 to 100.0)	90.6 (79.7 to 98.4)
Emotional Functioning	70.0 (60.0 to 85.0)	75.0 (55.0 to 85.0)
Social Functioning	90.0 (75.0 to 100.0)	90.0 (72.5 to 100.0)
Psychosocial Health Summary Score	78.8 (63.54 to 87.5)	78.3 (63.4 to 87.1)
Total Summary Score	82.1 (69.0 to 90.5)	82.6 (68.0 to 90.7)
<i>Missing</i>	0	4
School Functioning	75.0 (58.3 to 90.0)	70.0 (58.3 to 85.0)
<i>Missing</i>	8	10
<b>OM8-30<sup>c</sup> Mean (sd)</b>	<b>187</b>	<b>190</b>
Infection-related physical health factor score	-0.31 (1.03)	-0.17 (0.99)
General development impact factor score	0.52 (1.24)	0.48 (1.20)
Reported hearing difficulties factor score	0.74 (0.78)	0.87 (0.82)
Total Summary Score	0.47 (1.04)	0.60 (1.03)
<b>Parent reported overall child's health N(%)</b>		
Poor	4 (2.2)	6 (3.2)
Fair	28 (15.1)	29 (15.5)
Good	61 (33.0)	54 (28.9)
Very good	56 (30.3)	55 (29.4)
Excellent	36 (19.5)	43 (23.0)
<i>Missing</i>	2	6

a HUI3 (eight attributes) comprises a family of multi-attribute preference-based utility measures. High scores indicate better health related quality of life (max =1.00)

b PedsQL = High scores indicate better quality of life (max=100)

c OM8-30 = Low/more negative scores indicates better otitis media related quality of life

## Outcome Measures:

### Primary outcome measure

Acceptable hearing at five weeks from randomisation (four weeks after conclusion of treatment), where acceptable hearing is defined as less than 20 dB averaged at 0.5, 1, 2 and 4 kHz in at least one ear in children aged 3-8 years, and less than 25 dB averaged at 0.5, 1, 2 and 4 KHz by sound field VRA in children aged under 3 years. These thresholds are based on national guidelines.

**Table 4 Acceptable hearing by treatment group**

	<b>Placebo N=180</b>	<b>Oral steroid N=183</b>	<b>Adjusted<sup>a</sup> OR (95% CI)</b>	<b>p-value</b>
<b>ITT population</b>				
Acceptable hearing N(%)				
No	121 (67.2)	110 (60.1)	Reference	
Yes	59 (32.8)	73 (39.9)	1.36 (0.88 to 2.11)	0.164
<b>Per-protocol population</b>				
Acceptable hearing N(%)				
No	76 (65.5)	75 (59.1)	Reference	
Yes	40 (34.5)	52 (40.9)	1.27 (0.75 to 2.17)	0.378
<b>CACE</b>				
Primary analysis			0.07 <sup>b</sup> (-0.02 to 0.16)	0.109
Full adherence to oral steroid (vs. none/some)			0.08 <sup>b</sup> (-0.03 to 0.20)	0.103

- a Adjusted for site, child's age group at recruitment (2-5 years, 6-8 years), and time since recruitment to 5-week assessment (days)
- b Adjusted difference in proportions (95% CI)

### Secondary analysis of primary outcome

Two secondary analyses of the primary outcome were proposed in the SAP at 5 weeks, using the outcome as a continuous measure. This enabled an examination of any improvements or deterioration in dBHL over time. This outcome was modelled in two-ways:

1. as a child level analysis using the average, best or worst hearing levels from children assessed via PTA (where two ears were assessed), and the only assessment of hearing in those using ear specific insert VRA or ear specific play audiometry.
2. as an ear-level analysis to account for both ears being tested using the ear specific VRA.

**Table 5 Child and ear level analysis of hearing level (dBHL) at 5 weeks by treatment group**

	Treatment group	Baseline		5 weeks		Change (5 weeks – baseline)	
		N	Mean (SD) <i>Weighted Mean (SD)</i>	N	Mean (SD) <i>Weighted Mean (SD)</i>	Mean (SD)	Difference in adjusted <sup>a</sup> means (95% CI)
Child level analysis							
Average hearing level	Placebo	181	37.79 (6.92) <i>37.68 (6.93)</i>	181	30.99 (11.00) <i>30.84 (10.95)</i>	-6.80 (10.67)	-0.56 (-2.56 to 1.44)
	Oral steroid	183	36.25 (7.72) <i>36.18 (7.67)</i>	183	29.32 (10.38) <i>29.22 (10.34)</i>	-6.93 (9.57)	
Best hearing level	Placebo	181	35.24 (7.74) <i>35.17 (7.74)</i>	181	28.02 (11.55) <i>27.82 (11.46)</i>	-7.23 (11.59 )	-0.96 (-3.07 to 1.16)
	Oral steroid	183	33.30 (8.46) <i>33.24 (8.43)</i>	183	25.82 (10.80) <i>25.71 (10.74)</i>	-7.48 (10.57)	
Worst hearing level	Placebo	181	40.33 (7.26) <i>40.20 (7.26)</i>	181	33.96 (11.33) <i>33.85 (11.29)</i>	-6.37 (11.12)	-0.37 (-2.52 to 1.78)
	Oral steroid	183	39.19 (8.11) <i>39.12 (8.03)</i>	183	32.82 (11.37) <i>32.72 (11.36)</i>	-6.37 (10.52)	
Ear level analysis							
	Placebo	361	37.81 (7.91)	361	31.01 (11.82)	-6.80 (11.79)	-0.78 <sup>b</sup> (-2.79 to 1.23)
	Oral steroid	364	36.20 (8.79)	364	29.38 (11.54)	-6.82 (10.98)	

a Adjusted for baseline hearing, site, child's age group at recruitment (2-5 years, 6-8 years), and time since recruitment to 5 week assessment (days)

b Adjusted for baseline hearing, age at recruitment, time since recruitment to 5-week assessment (days), site, and participant.



## Secondary outcome measures

1. Satisfactory hearing at 6 and 12 months, measured as above,
2. Tympanometry (using calibrated standardised tympanometers and modified Jeger classification Types B and C2)

**Table 6 Proportion of children with evidence of (a) acceptable hearing at audiology and (b) tympanometric resolution of OME at 5 weeks, 6 and 12 months by treatment group**

		Placebo	Oral steroid	Time effect		Treatment effect <sup>a</sup>		Treatment x Time effect
		n /N (%)	n /N (%)	Adjusted <sup>b</sup> OR (95% CI)	<i>p</i> -value	Adjusted <sup>b</sup> OR (95% CI)	<i>p</i> -value	<i>p</i> -value
(a) Acceptable hearing at audiometry	5 weeks	59/180 (32.8)	73/183 (39.9)	Reference		1.42 (0.91 to 2.21)	0.121	0.975
	6 months	86/166 (51.8)	105/174 (60.3)	2.30 (1.47 to 3.60)	<0.001			
	12 months	99/162 (61.1)	118/170 (69.4)	3.46 (2.19 to 5.46)	<0.001			
(b) Tymp. resolution of OME	5 weeks	13/178 (7.3)	7/182 (3.8)	Reference		0.51 (0.20 to 1.30)	0.159	0.007
	6 months	17/147 (11.6)	26/152 (17.1)	1.69 (0.79 to 3.61)	0.179			
	12 months	9/144 (6.3)	31/159 (19.5)	0.85 (0.35 to 2.06)	0.724			

a Treatment effect is oral steroids compared to placebo averaged across all follow-up time points

b Adjusted for site and child's age group at recruitment (2-5 years, 6-8 years)

### 3. Otoscopic findings

**Table 7 Otoscopy findings by treatment group over time**

		Placebo	Oral steroid	Time effect		Treatment effect <sup>a</sup>		Treatment x Time effect
		n /N (%)	n /N (%)	Adjusted <sup>b</sup> OR (95% CI)	p-value	Adjusted <sup>b</sup> OR (95% CI)	p-value	p-value
Perforation present in at least one ear	Baseline	2/184 (1.1)	2/192 (1.0)			0.78 (0.37 to 1.66)	0.520	0.623
	5 weeks	2/169 (1.2)	0/171 (0.0)	Reference				
	6 months	9/152 (5.9)	6/155 (3.9)	12.43 (2.77 to 55.76)	0.001			
	12 months	7/134 (5.2)	6/151(4.0)	9.21 (2.00 to 42.98)	0.004			
Presence of a middle ear effusion in at least one ear	Baseline	183/184 (99.4)	192/192 (100.0)			0.70 <sup>c</sup> (0.35 to 1.39)	0.312	0.950
	5 weeks	152/168 (90.5)	150/172 (87.2)	Reference				
	6 months	96/151 (63.6)	90/154 (58.4)	0.18 (0.10 to 0.33)	<0.001			
	12 months	80/138 (58.0)	80/151 (53.0)	0.14 (0.08 to 0.26)	<0.001			
Bubbles present behind ear drum in at least one ear	Baseline	23/183 (12.6)	25/190 (13.2)			1.57 (0.76 to 3.26)	0.222	0.165
	5 weeks	15/164 (9.1)	23/169 (13.6)	Reference				
	6 months	19/147 (12.9)	13/152 (8.6)	1.54 (0.73 to 3.25)	0.260			
	12 months	4/135 (3.0)	8/149 (5.4)	0.30 (0.10 to 0.96)	0.042			

4. a Treatment effect is oral steroids compared to placebo averaged across all follow-up time-points

5. b Adjusting for baseline, site and child's age group at recruitment (2-5 years, 6-8 years)

6. c Adjusting for site and child's age group at recruitment (2-5 years, 6-8 years). Model would not converge with baseline measures.

4. Healthcare consultations related to OME, and other resource use

**Table 8 Healthcare consultations relating to OME and other resource use**

	Placebo N=170	Oral steroid N=179	Adjusted <sup>a</sup> IRR <sup>b</sup> (95% CI)	p-value
<b>Healthcare consultations relating to OME</b>				
No consultations <i>N (%)</i>	146 (85.9)	162 (90.5)	Reference	
At least one consultation <i>N (%)</i>	24 (14.1)	17 (9.5)	0.64 <sup>c</sup> (0.33 to 1.25)	0.188
1 consultation	16 (9.4)	13 (7.3)		
2 consultations	5 (2.9)	2 (1.1)		
3 consultations	3 (1.8)	2 (1.1)		
			Adjusted <sup>a</sup> OR (95% CI)	p-value
<b>Time off school/nursery/work for ear problems</b>				
No time off taken <i>N (%)</i>	162 (95.3)	173 (96.6)	Reference	
Time off taken <i>N (%)</i>	8 (4.7)	6 (3.4)	0.71 (0.14 to 4.08)	0.697
Min to Max (days)	0.1 to 6.0	0.1 to 7.0		
<b>Time off school/nursery/work for non-ear problems</b>				
No time off taken <i>N (%)</i>	155 (91.2)	171 (95.5)	Reference	
Time off taken <i>N (%)</i>	15 (8.8)	8 (4.5)	0.49 (0.14 to 1.66)	0.249
Min to Max (days)	0.3 to 8.0	1.0 to 7.0		

a Adjusted for site, and child's age group at recruitment (2-5, 6-8 years)

b Incidence rate ratio (IRR) of the oral steroid compared to placebo, An IRR< 1 indicating more events in placebo and an IRR>1 indicating more events in the oral steroid group.

c Negative binomial model used due to overdispersion and is a better fitting model (determined by Akaike Information Criterion (AIC)).

## 5. Grommet surgery at 6, and 12 months

**Table 9 Proportion of children planning or having operations for ventilation tubes at 6 and 12 months by treatment group (over past 6 months)**

	Placebo	Oral steroid	Time effect		Treatment effect <sup>a</sup>		Treatment x Time effect
	n/N (%)	n/N (%)	Adjusted <sup>b</sup> OR (95% CI)	p-value	Adjusted <sup>b</sup> OR (95% CI)	p-value	p-value
<b>5 weeks</b>	*	*					
<b>6 months</b>	38/170 (22.4)	39/173 (22.5)	Reference		Reference		
<b>12 months</b>	23/162 (14.2)	23/172 (13.4)	0.54 (0.30 to 0.98)	0.042	1.10 (0.64 to 1.89)	0.728	0.762

a Treatment effect is oral steroids compared to placebo averaged across all follow-up time- points

b Adjusted for site and child's age group at recruitment (2-5 years, 6-8 years)

\* Children were not permitted to have ventilation tubes within the first 5 weeks post randomisation.

## 6. Adverse effects

Only one adverse event (AE)/ Serious Adverse event (SAE) was reported during the trial in the placebo group, where the child had an asthma attack. No between treatment group comparison was made.

## 7. Symptoms (reported by parent and/or child)

**Table 1 Summary statistics for weekly overall symptom score, nausea and behaviour change by treatment group**

		Placebo	Oral steroid	Time effect		Treatment <sup>a</sup> effect		Treatment x Time effect
	Week	n /N (%)	n /N (%)	Adjusted <sup>b</sup> OR (95% CI)	p-value	Adjusted <sup>b</sup> OR (95% CI)	p-value	p-value
<b>No problem with any symptom<sup>c</sup> (score of 0)</b>	1	19 (13.6)	13 (8.7)	Reference		0.59 (0.28 to 1.27)	0.178	0.801
	2	20 (13.4)	18 (11.6)	1.00 (0.50 to 1.99)	0.990			
	3	22 (14.7)	19 (12.3)	1.09 (0.55 to 2.15)	0.807			
	4	17 (11.4)	21 (13.2)	0.83 (0.40 to 1.69)	0.600			
	5	21 (14.7)	22 (13.8)	1.10 (0.55 to 2.19)	0.789			
<b>No symptoms of nausea, vomiting or indigestion</b>	1	132 (79.5)	124 (72.5)	Reference		0.67 (0.40 to 1.11)	0.116	0.806
	2	136 (83.4)	138 (81.2)	1.30 (0.74 to 2.28)	0.355			
	3	145 (87.3)	142 (83.5)	1.78 (0.98 to 3.23)	0.057			
	4	138 (84.1)	144 (84.7)	1.37 (0.78 to 2.41)	0.278			
	5	136 (85.0)	143 (84.6)	1.46 (0.82 to 2.59)	0.201			
<b>No symptoms of changes in</b>	1	96 (58.2)	90 (52.9)	Reference		0.76 (0.49 to 1.19)	0.231	0.779
	2	97 (59.9)	105 (61.4)	1.09 (0.69 to 1.70)	0.723			

<b>behaviour and mood</b>	3	102 (62.6)	113 (66.9)	1.20 (0.76 to 1.89)	0.425			
	4	105 (65.2)	111 (66.1)	1.35 (0.85 to 2.13)	0.201			
	5	106 (67.1)	113 (67.7)	1.47 (0.92 to 2.34)	0.104			

a Treatment effect is oral steroids compared to placebo averaged across all follow-up time-points

b Adjusting for site and child's age group at recruitment (2-5 years, 6-8 years)

c Hearing, ear pain, speech, energy levels, sleep, attention span, balance and being generally unwell

## 8. Functional health status (OM8-30)

**Table 2 Mean (sd) OM8-30 score<sup>a</sup> and by each facet by treatment group**

		Placebo		Oral steroid		Time effect		Treatment effect <sup>b</sup>		Treatment x Time effect
		N	Mean (SD)	N	Mean (SD)	Adjusted <sup>c</sup> mean difference (95% CI)	<i>p</i> -value	Adjusted <sup>c</sup> mean difference (95% CI)	<i>p</i> -value	<i>p</i> -value
Total OM8-30 score	Baseline	187	0.47 (1.04)	190	0.60 (1.03)			0.05 (-0.12 to 0.22)	0.539	0.301
	5 weeks	177	0.33 (1.08)	182	0.49 (1.11)	Reference				
	6 months	158	-0.13 (1.13)	163	-0.14 (1.19)	-0.44 (-0.62 to -0.27)	<0.001			
	12 months	150	-0.29 (1.20)	154	-0.22 (1.18)	-0.56 (-0.74 to -0.38)	<0.001			
Infection related physical health facet	Baseline	187	-0.31 (1.03)	190	-0.17 (0.99)			0.04 (-0.12 to 0.20)	0.666	0.591
	5 weeks	177	-0.44 (0.98)	182	-0.30 (1.00)	Reference				
	6 months	158	-0.67 (0.90)	163	-0.68 (0.95)	-0.25 (-0.42 to -0.09)	0.003			
	12 months	150	-0.69 (0.90)	154	-0.57 (1.04)	-0.25 (-0.41 to -0.08)	0.004			
General	Baseline	187	0.52 (1.24)	190	0.48 (1.20)			0.08 (-0.07 to	0.314	0.292

<b>development impact facet</b>	5 weeks	177	0.54 (1.24)	182	0.58 (1.18)	Reference		0.23)		
	6 months	158	0.44 (1.19)	163	0.43 (1.18)	-0.04 (-0.20 to 0.12)	0.630			
	12 months	150	0.29 (1.19)	154	0.25 (1.16)	-0.18 (-0.34 to -0.02)	0.024			
<b>Reported hearing difficulties facet</b>	Baseline	187	0.74 (0.78)	190	0.87 (0.82)			0.03 (-0.13 to 0.20)	0.692	0.866
	5 weeks	177	0.58 (0.88)	182	0.67 (0.87)	Reference				
	6 months	158	0.04 (0.88)	163	0.06 (0.99)	-0.54 (-0.72 to -0.37)	<0.001			
	12 months	150	-0.05 (0.91)	154	-0.04 (0.99)	-0.63 (-0.81 to -0.45)	<0.001			

a OM8-30 = Low/more negative scores indicates better otitis media related quality of life

b Treatment effect is oral steroids compared to placebo averaged across all follow-up time-points

c Adjusting for site, child's age group at recruitment (2-5 years, 6-8 years), and baseline OM8-30 score

9. Health related quality of life (PedsQL and HUI3)

**Table 3 Median (25<sup>th</sup> to 75<sup>th</sup> centiles) total PedsQL score<sup>a</sup> and each domain by treatment group**

		Placebo		Oral steroid		Time effect		Treatment effect <sup>b</sup>		Treatment x Time effect
		N	Median (25 <sup>th</sup> to 75 <sup>th</sup> centile)	N	Median (25 <sup>th</sup> to 75 <sup>th</sup> centile)	Adjusted <sup>c</sup> estimate (95% CI)	<i>p</i> -value	Adjusted <sup>c</sup> estimate (95% CI)	<i>p</i> -value	<i>p</i> -value
Total PedsQL	Baseline	187	82.1 (69.0 to 90.5)	189	84.8 (73.8 to 92.7)			-85.11 <sup>d</sup> (-420.65 to 250.44)	0.619	0.475
	5 weeks	176	84.8 (73.8 to 92.7)	182	84.5 (72.4 to 91.7)	Reference				
	6 months	158	84.5 (75 to 90.7)	162	82.6 (72.6 to 94.6)	-32.11 <sup>d</sup> (-378.89 to 314.67)	0.856			
	12 months	149	85.7 (77.7 to 92.9)	154	86.9 (75.0 to 95.2)	146.53 <sup>d</sup> (-205.89 to 498.94)	0.415			
Physical health	Baseline	187	90.6 (78.1 to 100.0)	189	90.6 (79.7 to 98.4)			0.84 <sup>e</sup> (0.51 to 1.37)	0.480	0.554
	5 weeks	176	90.6 (81.3 to 100.0)	182	90.6 (80.5 to 100.0)	Reference				
	6 months	158	93.8	162	93.8	0.90 <sup>e</sup> (0.54 to 1.49)	0.675			



		Placebo		Oral steroid		Time effect		Treatment effect <sup>b</sup>		Treatment x Time effect
		N	Median (25 <sup>th</sup> to 75 <sup>th</sup> centile)	N	Median (25 <sup>th</sup> to 75 <sup>th</sup> centile)	Adjusted <sup>c</sup> estimate (95% CI)	p-value	Adjusted <sup>c</sup> estimate (95% CI)	p-value	p-value
			(81.3 to 100.0)		(77.3 to 100.0)					
	12 months	149	93.8 (85.0 to 100.0)	154	93.8 (84.4 to 100.0)	1.39 <sup>e</sup> (0.85 to 2.28)	0.195			
Emotional functioning	Baseline	187	70.0 (60.0 to 85.0)	189	75.0 (55.0 to 85.0)			2.02 <sup>f</sup> (-1.85 to 5.89)	0.306	0.778
	5 weeks	175	75.0 (60.0 to 90.0)	182	75.0 (60.0 to 90.0)	Reference				
	6 months	158	70.0 (55.0 to 85.0)	162	75.0 (60.0 to 95.0)	1.17 <sup>f</sup> (-4.46 to 6.79)	0.684			
	12 months	149	75.0 (60.0 to 90.0)	154	80.0 (65.0 to 100.0)	2.05 <sup>f</sup> (-3.67 to 7.77)	0.482			
Social Functioning	Baseline	187	90.0 (75 to 100)	189	90.0 (72.5 to 100.0)			1.20 <sup>e</sup> (0.75 to 1.92)	0.436	0.854
	5 weeks	175	90.0 (80.0 to 100.0)	182	90.0 (73.8 to 100.0)	Reference				

		Placebo		Oral steroid		Time effect		Treatment effect <sup>b</sup>		Treatment x Time effect
		N	Median (25 <sup>th</sup> to 75 <sup>th</sup> centile)	N	Median (25 <sup>th</sup> to 75 <sup>th</sup> centile)	Adjusted <sup>c</sup> estimate (95% CI)	p-value	Adjusted <sup>c</sup> estimate (95% CI)	p-value	p-value
	6 months	158	90.0 (80.0 to 100.0)	162	90.0 (70.0 to 100)	0.81 <sup>e</sup> (0.50 to 1.32)	0.403			
	12 months	148	95.0 (80.0 to 100.0)	154	95.0 (78.8 to 100.0)	1.10 <sup>e</sup> (0.67 to 1.79)	0.717			
School Functioning	Baseline	179	75.0 (58.3 to 90.0)	183	70.0 (58.3 to 85.0)			-240.53 <sup>d</sup> (-718.72 to 237.65)	0.324	0.916
	5 weeks	172	80.0 (65.0 to 91.7)	176	77.5 (60.0 to 90.0)	Reference				
	6 months	154	83.3 (66.3 to 95.0)	156	80.0 (66.67 to 90.0)	184.37 <sup>d</sup> (-308.02 to 676.76)	0.463			
	12 months	143	83.3 (66.67 to 91.7)	147	80.0 (60.0 to 95.0)	217.95 <sup>d</sup> (-286.59 to 722.49)	0.397			
Psychosocial	Baseline	187	78.8 (63.5 to 87.5)	189	78.3 (63.4 to 87.1)					
	5 weeks	175	81.7 (69.2 to 90.0)	182	81.2 (67.3 to 90.0)	Reference		0.71 <sup>e</sup> (0.26 to 2.00)	0.509	0.577

		Placebo		Oral steroid		Time effect		Treatment effect <sup>b</sup>		Treatment x Time effect
		N	Median (25 <sup>th</sup> to 75 <sup>th</sup> centile)	N	Median (25 <sup>th</sup> to 75 <sup>th</sup> centile)	Adjusted <sup>c</sup> estimate (95% CI)	p-value	Adjusted <sup>c</sup> estimate (95% CI)	p-value	p-value
	6 months	158	80.0 (70.0 to 90.0)	162	79.0 (67.5 to 93.3)	1.57 <sup>e</sup> (0.64 to 3.90)	0.327			
	12 months	149	82.7 (71.4 to 91.7)	154	84.0 (69.8 to 93.6)	1.45 <sup>e</sup> (0.57 to 3.66)	0.433			

a PedsQL = High scores indicate better quality of life (max=100)

b Treatment effect is oral steroids compared to placebo averaged across all follow-up time-points

c Adjusted for site, child's age group at recruitment (2-5, 6-8 years), and baseline PedsQL score

d Squared transformation used on the raw scores. Parameter estimate =adjusted difference in squared means;

e Outcome transformed to binary: perfect health (score=100) vs non-perfect health ( <100) . Parameter estimate =adjusted odds ratio;

f No transformation used. Parameter estimate displayed as adjusted difference in mean

**Table 4 Summary statistics for the HUI3 score<sup>a</sup> by treatment group**

		Placebo	Oral steroid	Time effect		Treatment effect <sup>b</sup>		Treatment x Time effect
		N (%)	N (%)	Adjusted <sup>c</sup> OR (95% CI)	p-value	Adjusted <sup>c</sup> OR (95% CI)	p-value	p-value
N (%) perfect health score=1	Baseline	22 (13.8)	22 (13.4)			1.23 (0.66 to 2.27)	0.511	0.790
	5 weeks	33 (21.3)	37 (22.6)	Reference				
	6 months	49 (32.2)	52 (33.5)	2.36 (1.31 to 4.26)	0.004			
	12 months	44 (31.0)	51 (34.0)	1.99 (1.09 to 3.65)	0.025			

a High scores indicate better health related quality of life (max =1.00)

b Treatment effect is oral steroids compared to placebo averaged across all follow-up time points

c Adjusted for site, child's age group at recruitment (2-5, 6-8 years), and baseline binary HUI3 score

## 10. Short and longer term cost effectiveness

**Table 14 Base and case sensitive analysis for the primary cost effectiveness analysis (incremental cost per acceptable hearing resolution at 5 weeks)**

Parameter	Incremental cost (£)	Incremental effect	ICER (cost (£) per additional resolution)
<b>Base case</b>	39	7.1%	£546 per additional hearing resolution
Upper 95% bound <sup>1</sup> of net cost	71	16.4%	£432 per additional hearing resolution
Upper 95% bound <sup>1</sup> of % successful hearing resolution			
Upper 95% bound <sup>1</sup> of net cost	71	-0.0%	Oral steroid dominated by placebo
Lower 95% bound <sup>1</sup> of % successful hearing resolution			
Lower 95% bound <sup>1</sup> of net cost	6	16.4%	£37 per additional hearing resolution
Upper 95% bound <sup>1</sup> of % successful hearing resolution			
Lower 95% bound <sup>1</sup> of net cost Upper 95% bound <sup>1</sup> of % successful hearing resolution	6	-0.0%	Oral steroid dominated by placebo

<sup>1</sup> Based on the upper and lower confidence intervals from the base case costs and covariate adjusted clinical resolution gain at 5 weeks.

**Table 15 Base case and sensitivity analysis for the primary cost effectiveness analysis (incremental cost per acceptable hearing resolution at 12 months)**

Parameter	Incremental cost (£)	Incremental effect	ICER (cost (£) per additional hearing resolution)
<b>BASE CASE</b>	<b>177</b>	5.8%	£3,052 per additional hearing resolution
Upper 95% bound <sup>1</sup> of net cost	487	17.2%	£2,831 cost per additional hearing resolution
Upper 95% bound <sup>1</sup> of % successful hearing resolution			
Upper 95% bound <sup>1</sup> of net cost	487	-5.5%	Oral steroid dominated by placebo
Lower 95% bound <sup>1</sup> of % successful hearing resolution			
Lower 95% bound <sup>1</sup> of net cost	-132	17.2%	Oral steroid dominates placebo
Upper 95% bound <sup>1</sup> of % successful hearing resolution			
Lower 95% bound <sup>1</sup> of net cost	-132	-5.5%	£2,400 saved per

Lower 95% bound <sup>1</sup> of % successful hearing resolution			reduction in adequate hearing
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<sup>1</sup>Based on the upper and lower confidence intervals from the base case costs and covariate adjusted clinical resolution gain at 12 months.

**Adverse Events:**

Only one Serious Adverse event (SAE) was reported during the trial in the placebo group, where the child had an asthma attack. Adverse events are reported in Table 16.

Table 16 Parent reported adverse events during week 1

	<b>Placebo N=170</b>	<b>Oral steroids N=179</b>
<b>No problems reported</b>	148 (87.1)	154 (86.0)
<b>Children reported with having at least one problem</b>	22 (12.9)	25 (14.0)
<b>Total number of problems</b>	<b>24</b>	<b>27</b>
<b>RTI</b>		
Phlegmy cough/cold/sneezing/ temperature/nosebleed/ conjunctivitis/itchy eyes/generally unwell	2	7
Headache	3	4
Parotitis	1	0
Ear pain on touch/ear ache	1	1
Rash/pox/scarlet fever	2	0
Flushed cheeks	0	1
<b>Digestion</b>		
Increased appetite	4	3
Low appetite	2	0
Diarrhoea	2	2
Constipation	1	1
Nausea	0	1
<b>Behaviour</b>		
Hyperactive	1	3
Tired	1	1
Frustration	1	0
Change in behaviour	0	2
Parent states child not hearing	1	0
Sleep walking	0	1
<b>Other</b>		
Finger infection	1	0
Knee pain	1	0