The effect of ventilation tube insertion on quality of life in children with persistent otitis media with effusion

Abstract

Objectives
To determine the effect of ventilation tube (VT) surgery on quality of life (QoL) in children with persistent otitis media with effusion (OME).

Design
Secondary analysis of trial data (oral steroids versus placebo for persistent OME), comparing QoL by history of VT surgery performed between 5 weeks and 12 months post randomisation. Multilevel regression models were used to identify the association between VT surgery and QoL scores at 12 months, controlling for pre-exposure risk factors associated with surgery, including pre-surgery hearing level.

Setting
Ear, nose and throat (ENT), paediatric audiology and audiovestibular medicine (AVM) departments in Wales and England.

Participants
327 children aged 2 to 8 years old with OME symptoms for at least three months and audiometry proven bi-lateral hearing loss with VT surgery status.

Main outcome measures
Otitis Media questionnaire (OM8-30) and Paediatric Quality of Life Inventory (PedsQL) total and subscale scores, and the Health Utilities Index Mark 3 (HUI3) at 12 months post randomisation.

Results
Participants who had VT surgery had no significant difference in OM8-30, PedsQL or HUI total scores. OM8-30 hearing difficulty (HD) subscale scores at 12 months were better in those who had VT surgery (adjusted mean difference (aMD)=-0.46 (95% confidence interval -0.69 to -0.23), $p<0.001$), and this varied by when the surgery occurred (aMD for surgery between 5 weeks and 6 months = -0.4 (-0.67 to -0.13), $p=0.004$ and between 6 and 12 months =-0.54, (-0.87 to-0.22),$p=0.001$)).

Conclusion
VT surgery was associated with an improvement in HD related functional health status but no change in overall QoL.

Introduction

Otitis media with effusion (OME) is a common condition in children, defined as fluid accumulation within the middle ear space. By the age of four years, 80% of children will have had an episode of OME, but the majority resolve spontaneously within three months [1-6]. Despite the high probability of resolution, 5% of preschool children under the age of 5 years will develop bilateral, persistent disease leading to hearing loss [5, 6] with a potentially detrimental effect on early development in terms of language and social development, behaviour, IQ and reading [1-4, 6]. Evidence-based management options for persistent OME, after a 3 month period of 'watchful waiting', are hearing aids or the surgical insertion of ventilation tubes (VT) [5, 7]. VT surgery has been the mainstay of treatment for persistent OME. However, the number of operations in England has declined principally due to the introduction of the 'watchful waiting' approach which allows longer for spontaneous resolution [2, 5-7]. Despite this, VT insertion remains the most common operation performed within the UK. However, there is considerable variation both between countries and within the UK, unlikely to be representative of regional population variations [2, 5, 8].

VT surgery has been shown to have a modest effect on hearing in the first 6 months, with an improvement of between 4-10dB, however this improvement decreases with time resulting in no benefit at 12 months [6, 8]. Despite this, studies demonstrating a positive impact on quality of life (QoL) have been limited [8-12]. Several uncontrolled before and after studies have shown an improvement in QoL following surgery, with a number including a mixed cohort of children with both recurrent acute otitis media and OME [13-17]. We therefore set out to assess the effect of VT insertion on functional health status and quality of life in a secondary analysis of the 12-month follow-up of a randomised controlled trial of oral steroids for OME in children with persistent OME. A secondary objective was to identify factors associated with undergoing VT surgery. This may be helpful in targeting potential overuse of this surgical procedure.

Materials and methods

This was a secondary analysis of data from the Oral STteroids for the Resolution of OME In CHildren (OSTRICH) trial, a double-blind randomised controlled trial of the effect of a one-week course oral steroids on hearing at five weeks [18]. Trial participants were aged 2 to 8 years old with at least three months of hearing loss secondary to bilateral OME and were recruited from ear, nose and throat (ENT) outpatients or paediatric audiology and audiovestibular medicine (AVM) departments across Wales and England. For further details of the OSTRICH trial study design, see the published study protocol [5].

A total of 380 children were included in the OSTRICH trial. Baseline demographics and medical history were collected from eligible participants including audiology, tympanometry and otoscopy assessments. These were repeated at 5 weeks, 6 and 12 months post-randomisation. In current practice, the recommended standard methods to assess hearing thresholds are ear-specific pure-tone audiometry (PTA) at 0.5, 1, 2 and 4 kHz in children aged three years or older and soundfield VRA in children aged less than three years. However, equally, those over three years of age may not comply with PTA. Therefore, it was recommended that the audiologist or clinician use their judgement on the most appropriate method of assessment for the child and, when possible, maintain that method for the subsequent follow-ups.

The child's parent or guardian was asked to complete the Otitis Media questionnaire (OM8-30), the Paediatric Quality of Life Inventory (PedsQL) and Health Utilities Index Mark 3 (HUI3) quality of life assessment tools at baseline and at 5 weeks, 6 and 12 months. The OM8-30 questionnaire is a specific functional health assessment tool that assesses the impact of chronic otitis media on three facets of development: physical developmental, general development and hearing difficulties [19]. Better functional health is indicated by a negative or low score. The HUI3 is multi attribute measure of health status, where a higher score indicates a better quality of life, with a maximum score of 1.00 [20]. The mean score of the eight attributes was used during this study. The PedsQL is a generic paediatric health-related quality of life assessment tool, based on five domains consisting of physical health, emotional functioning, social functioning, school functioning, and psychosocial functioning. These can be combined to create an overall score. A higher score indicates a better QoL, with a maximum score of 100 [21]. For the purposes of this study we will refer to these instruments collectively as measuring 'quality of life'. The outcomes of this study will be the aforementioned quality of life measures, collected at 12 months follow-up.

Exposure

Participating children were asked not to undergo VT surgery within the first five weeks of follow-up (from randomisation). Thereafter, decisions about surgery or other re-interventions were made according to usual care processes. At six- and 12-months follow-up parents were asked whether their child had undergone VT surgery.

Children who had missing responses at both time-points or one of the time points and had not had ventilation tube surgery at the other were classified as having missing VT surgery data.

Statistical Analysis
Exposure (VT surgery or not) was characterised using baseline and five-week follow-up data with the time-point closest to the exposure period used (i.e. where risk factors are measured at both time points, the five-weeks data has been used in the model). These factors were described using appropriate summary statistics (mean alongside standard deviation, median alongside inter quartile range, n (%)). To identify risk factors associated with undergoing VT surgery 5 weeks post randomisation (and subsequently adjust for them in the QoL at 12-month models) we used multilevel logistic regression models controlling for clustering of outcomes by recruitment site. After examining associations between factors and VT surgery at a univariable level, candidate predictors were identified using a 10% significance cut off to take forward to identify factors independently predictive of VT surgery in a multivariable model. Estimates are presented as odds ratios (ORs) alongside 95% and p-values.

To examine the associations between VT surgery and the quality of life outcomes at 12 months follow-up, multilevel regression models that controlled for factors associated with having VT surgery, including pre-surgery hearing threshold, were used. For the OM8-30 assessment tool at 12 months, a linear regression model was used, and estimates reported as mean differences. HUI3 outcomes was examined as a binary variable (score=1-perfect health, <1 non-perfect health) due to skewedness and estimates presented as odds ratios (ORs). PedsQL at 12 months was compared between the VT and non-surgical groups using a hurdle regression model used to reflect the skewedness and upper bounded (ceiling) nature of the scores. Two estimates are reported for the hurdle model; first a log-odds (perfect quality of life score=100 or non-perfect score<100) and second a mean difference in QoL between groups in those with a non-perfect score (<100). The impact of timing of surgery was also analysed where QoL, using the three assessment tools, was compared between participants having no surgery, surgery between 5 weeks and 6 months post recruitment, versus patients undergoing surgery between 6- and 12-months post recruitment. Two participants were removed at this stage as the timing of their VT surgery was unclear. All estimates here are presented unadjusted and adjusted (for the risk factors associated with VT surgery) and reported alongside 95% confidence intervals (95% CI) and p-values.

Univariable Cox regression models were performed to identify variables associated with time to VT surgery. The variables that were significantly associated at the 10% level were then analysed using a multivariable Cox regression model. Estimates from this analysis are presented as hazard ratios (HRs) with 95% CIs and p-values.

Stata version 16 [22] and SPSS version 23 [23] were used for statistical analysis.

Ethical Considerations
Ethical approval for the OSTRICH trial [18] was obtained from an NHS research ethics committee, recognised by the UK Ethics Committee Authority (UKECA), the National Research Ethics Service Research Ethics Committee for Wales on Feb 28, 2013 (reference number 13/WA/0004). The trial protocol was reviewed and approved by the Wales Research Ethics Committee 3, recognised by the UKECA. All hospital sites received research and development approval from the respective NHS Health Boards and Trusts in England and Wales. Clinical trial authorisation was obtained from the Medicines and Healthcare products Regulatory Agency (MHRA). The trial was overseen by independent trial steering and data monitoring committees.

Results
Of the 380 participants recruited to the OSTRICH trial, 327 had complete data on VT surgery status over the 12-month follow up period and therefore were included in this study (see figure 1). Of these, 123 (38%) had VT surgery during the course of the study. Fifty-three participants did not have data on VT surgery and were therefore excluded from the analysis. Comparing these patients to those included in the study demonstrated that household smoking was more common (51% vs 25% respectively, p<0.001), as was a history of eczema (32% vs 20% respectively, p=0.045), although overall atopy rate was comparable. The other baseline characteristics were comparable, including socioeconomic status.

Risk factors for VT surgery

After adjustment for recruitment site, children who underwent VT surgery were more likely to report being of Asian ethnicity (and less likely to report being white) than those who did not undergo VT surgery, and were

more likely to have had OME for a longer duration (Table 1). They were also more likely to have worse hearing levels at 5 weeks post-randomisation, and worse quality of life outcomes (specifically in the overall OM8-30 score, the OM8-30 physical health and reported hearing difficulties facets, and the PedsQL psychosocial and social functioning domains). When entered into the multivariable model, only hearing level remained independently associated with VT surgery.

	No VT surgery (n=204)	VT surgery (n=123)	Unadjusted* OR† (95% CI), p-value	Adjusted** OR† (95% CI), p-value
Characteristics at recruitment				
Age (years) Mean (SD)	5.15 (1.62)	5.15 (1.54)	0.96 (0.80 to 1.14), 0.62	-
Gender				
Female	93 (45.6)	53 (43.1)	Reference group	
Male	111 (54.4)	70 (56.9)	1.00 (0.58 to 1.70), 0.99	-
Ethnicity			**Overall p-value=0.022**	Overall p-value=0.059
White	169 (88.9)	84 (73.0)	Reference group	Reference group
Mixed/multiple	7 (3.7)	10 (8.7)	2.89 (0.91 to 9.15), 0.072	2.66 (0.69 to 10.30), 0.16
Asian/Asian British	9 (4.7)	19 (16.5)	4.03 (1.49 to 10.88), 0.006	4.02 (1.31 to 12.31), 0.015
Black/African/Caribbean/Black British	3 (1.6)	2 (1.7)	1.36 (0.18 to 10.61), 0.77	2.20 (0.22 to 22.06), 0.50
Other	2 (1.1)	0 (0.0)	-	-
Missing data	*14*	*8*		
Socioeconomic status			Overall p-value=0.78	-
1 - least deprived	31 (15.2)	22 (17.9)	Reference group	
2	18 (8.8)	15 (12.2)	0.99 (0.35 to 2.82), 0.98	
3	60 (29.4)	22 (17.9)	0.65 (0.28 to 1.54), 0.33	
4	44 (21.6)	35 (28.5)	1.05 (0.45 to 2.46), 0.91	
5 - most deprived	51 (25.0)	29 (23.6)	0.87 (0.35 to 2.14), 0.76	
Season recruited			Overall p-value=0.15	
Spring (March to May)	61 (29.9)	50 (40.7)	Reference group	
Summer (June to August)	41 (20.1)	15 (12.2)	0.40 (0.18 to 0.91), 0.028	
Autumn (September to November)	35 (17.2)	21 (17.1)	0.90 (0.42 to 1.94), 0.79	
Winter (December to February)	67 (32.8)	37 (30.1)	0.67 (0.35 to 1.29), 0.23	
First episode of OME?				

	No VT surgery (n=204)	VT surgery (n=123)	Unadjusted* OR† (95% CI), p-value	Adjusted** OR† (95% CI), p-value
No	58 (28.4)	43 (35.0)	Reference group	
Yes	146 (71.6)	80 (65.0)	1.01 (0.56 to 1.81), 0.98	
Duration of current episode of OME*			**Overall p-value=0.009**	Overall p-value=0.091
<6 months	29 (14.2)	9 (7.3)	**Reference group**	Reference group
6 to <9 months	25 (12.3)	20 (16.3)	2.69 (0.88 to 8.21), 0.082	2.78 (0.68 to 11.34), 0.16
9 to <12 months	15 (7.4)	18 (14.6)	7.86 (2.30 to 26.9), 0.001	7.00 (1.54 to 31.76), 0.012
≥12 months	135 (66.2)	76 (61.8)	3.91 (1.49 to 10.3), 0.006	3.37 (0.97 to 11.69), 0.056
Relatives with glue ear			Overall p-value=0.64	
No	114 (55.9)	74 (60.2)	Reference group	
Yes	49 (24.0)	19 (15.4)	0.72 (0.36 to 1.44), 0.36	
N/A - no siblings	41 (20.1)	28 (22.8)	1.09 (0.56 to 2.13), 0.80	
Missing data	*0*	*2*	-	
Household smoking N (%) Yes* **	50 (24.5)	30 (24.4)	1.29 (0.69 to 2.42), 0.42	
Atopy N (%) Yes	69 (33.8)	35 (28.5)	0.86 (0.49 to 1.54), 0.62	
Previous Adeno-tonsillectomy N (%) Yes	10 (4.9)	9 (7.3)	1.54 (0.52 to 4.56), 0.43	
Previous grommet surgery N (%) Yes	12 (5.9)	17 (13.8)	1.88 (0.76 to 4.65), 0.17	
Use of hearing aids N (%) Yes	37 (18.1)	11 (8.9)	0.725 (0.31 to 1.69), 0.46	
Trial arm				
Placebo	98 (48.0)	61 (49.6)	Reference group	
Steroids	106 (52.0)	62 (50.4)	0.99 (0.59 to 1.66), 0.97	
5-week follow-up characteristics				
Average decibel (dBHL) that is audible, Mean (SD) of the average of the two ears	28.3 (11.2)	31.4 (9.2)	**1.04 (1.01 to 1.07), 0.003**	**1.03 (1.01 to 1.06), 0.044**
Tympanogram				
No type B ears	3 (1.5)	1(0.8)	Reference group	
At least one Type B ear	7 (3.4)	8 (6.5)	0.43 (0.11 to 1.65), 0.22	
Missing data	*0*	*1*	-	

	No VT surgery (n=204)	VT surgery (n=123)	Unadjusted* OR† (95% CI), p-value	Adjusted** OR† (95% CI), p-value
Quality of Life measures				
OM8-30 ***Mean (SD)***				
Infection related physical health	-0.39 (0.97)	-0.28 (1.04)	**1.28 (0.98 to 1.68), 0.075**	1.10 (0.72 to 1.67), 0.66
General development	0.50 (1.20)	0.55 (1.21)	1.13 (0.90 to 1.42), 0.28	
Reported hearing difficulties	0.55 (0.90)	0.76 (0.79)	**1.67 (1.19 to 2.33), 0.003**	1.48 (0.93 to 2.35), 0.098
Overall	0.32 (1.09)	0.52 (1.12)	**1.44 (1.12 to 1.85), 0.005**	1.08 (0.64 to 1.83), 0.76
Missing	*1*	*0*		
HUI3 binary ***N (%)***				
Non perfect health (<1)	*142 (78.0)*	*82 (78.9)*	Reference group	
Perfect health (=1)	*40 (22.0)*	*22 (21.2)*	0.68 (0.34 to 1.37), 0.28	
Missing	*22*	*19*		
PedsQL ***Mean (SD)***				
Physical health	86.25 (17.4)	82.93 (21.6)	0.99 (0.98 to 1.01), 0.27	
Emotional functioning	74.36 (20.3)	69.61 (23.0)	0.99 (0.98 to 1.00), 0.17	
Psychosocial health	78.87 (16.9)	75.42 (19.7)	**0.99 (0.97 to 1.00), 0.086**	1.00 (0.96 to 1.04), 0.92
Social functioning	85.56 (19.6)	82.44 (22.7)	**0.99 (0.98 to 1.00), 0.096**	0.99 (0.97 to 1.02), 0.72
School functioning	76.60 (19.1)	75.74 (18.6)	0.99 (0.98 to 1.01), 0.27	
Total score	81.57 (15.6)	78.49 (18.1)	0.99 (0.97 to 1.00), 0.14	

Table 1. Pre-exposure sociodemographics and characteristics in each exposure group (VT surgery)
* adjusted for site; ** adjusted for site and all other risk factors in multivariable model; *** household smoking of approximately 5 hours per week or more, † OR predicting VT surgery.
OM8-30: a negative or low score indicates a better quality of life (11).
Health Utilities Index mark 3 (HUI3): a higher score indicates a better quality of life, with a maximum score of 1.00(12).
PedsQL: a higher score indicates a better QoL, with a maximum score of 100(13).
VT - Ventilation tube, SD - standard deviation, IQR - interquartile range. P values in bold statistically significant.

Association between VT surgery and Quality of Life at 12 months

For almost all outcomes the point estimates for quality of life at 12 months follow-up suggested better QoL for participants who underwent VT surgery between 5 weeks and 12 months follow-up compared to those who did not, but the difference was only statistically significant for the OM8-30 reported hearing difficulties facet (Table 2). This association remained after adjusting for factors significantly associated with VT surgery and recruitment site. There was no significant difference in the other OM8-30 facets, HUI3 score, or any of the five domains of the PedsQL.

	No VT surgery (n= 204)	**VT surgery (n=123)**	**Unadjusted* difference in means (95% CI), p-value**	**Adjusted** difference in means, p-value**
OM8-30 ***Mean (SD)***				
Infection related physical health	-0.69 (0.94)	-0.52 (1.04)	0.19 (-0.05 to 0.43), 0.11	
General development	0.30 (1.21)	0.26 (1.10)	-0.004 (-0.29 to 0.29), 0.98	
Reported hearing difficulties	0.08 (0.93)	-0.25 (0.97)	**-0.27 (-0.50 to -0.03), 0.026**	**-0.46 (-0.69 to -0.23), <0.001**
Overall	-0.22 (1.22)	-0.29 (1.13)	0.03 (-0.26 to 0.33), 0.82	
Missing	*12*	*21*		
HUI3 binary ***N (%)***			**Unadjusted* Odds ratio (95% CI), p-value**	
Non perfect health (score<1)	127 (69.8)	63 (63.0)	Reference	
Perfect health (score=1)	55 (30.2)	37 (37.0)	1.24 (0.70 to 2.22), 0.46	
Missing	*22*	*23*		
PedsQL ***median (IQR)***			**Unadjusted* mean difference/log-odds ratio (95% CI), p-value**	
Physical health	93.8 (84.4 to 100.0)	93.8 (86.6 to 100.0)	28.38 (-15.49 to 72.24), 0.21 -0.13 (-0.44 to 0.18), 0.41	
Emotional functioning	75.0 (60.0 to 95.0)	80.0 (60.0 to 90.0)	4.70 (-2.09 to 11.49), 0.18 -0.27 (-0.62 to 0.08), 0.13	
Psychosocial health	82.7 (70.0 to 93.2)	82.7 (71.2 to 92.0)	5.25 (-3.42 to 13.92), 0.24 -0.25 (-0.69 to 0.19), 0.26	
Total score	85.9 (75.0 to 94.6)	85.9 (78.3 to 93.3)	7.20 (-2.50 to 16.90), 0.15 -0.33 (-0.79 to 0.13), 0.16	
Missing	12	22		
Social functioning	95.0 (75.0 to 100.0)	95.0 (80.0 to 100.0)	16.03 (-6.72 to 38.78), 0.17 0.19 (-0.11 to 0.50), 0.21	
Missing	*13*	*22*		
School functioning	83.3 (65.0 to 95.0)	80.0 (61.9 to 91.7)	-1.91 (-9.14 to 5.32), 0.61 -0.22 (-0.58 to 0.13), 0.22	
Missing	*22*	*25*		

Table 2. Results for Quality of life outcomes at 12 months by VT surgery status
* adjusted for site; ** adjusted for site and ethnicity, duration of OME, and hearing and OM8-30 reported hearing difficulties at 5 weeks follow-up (pre-exposure).
OM8-30: a negative or low score indicates a better quality of life (11).
Health Utilities Index mark 3 (HUI3): a higher score indicates a better quality of life, with a maximum score of 1.00(12).
PedsQL: a higher score indicates a better QoL, with a maximum score of 100(13).
VT - Ventilation tube, SD - standard deviation, IQR - interquartile range. P values in bold statistically significant.

Timing of VT surgery initially appeared to impact the degree of improvement in OM8-30 hearing related functional health whereby children undergoing VT surgery 6 to 12 months after recruitment had the greatest improvement compared to the non-surgical group. However, after adjusting for hearing and OM8-30 hearing difficulties at 5 weeks, both children undergoing VT surgery earlier in the study at 5 weeks to 6 months (adjusted mean difference -0.40, (95% CI -0.67 to -0.13), p=0.004) and those who had surgery later, 6-12 months (adjusted mean difference -0.54, (95% CI -0.87 to -0.22), p=0.001), had similar improvement in OM8-30 hearing related functional health compared to the non-surgical group (Table 3). Surgical timing did not appear to affect the other facets of OM8-30, or the PedsQL or HUI3 (Table 3).

	No VT surgery (n= 204)	VT surgery 5 weeks to 6 months (n=87)	VT surgery 6 to 12 months (n=36)	No surgery (ref) vs surgery 5 weeks to 6 months	No surgery (ref) vs surgery 6 to 12 months
OM8-30 *Mean (SD)*				**Adjusted* difference in means (95% CI), p-value**	
Infection related physical health	-0.69 (0.94)	-0.63 (1.03)	-0.28 (1.02)	0.06 (-0.25 to 0.36), 0.71	0.31 (-0.06 to 0.69), 0.10
General develop-ment	0.30 (1.21)	0.09 (1.12)	0.60 (0.97)	-0.18 (-0.53 to 0.16), 0.29	0.26 (-0.16 to 0.68), 0.22
Reported hearing difficulties	0.08 (0.93)	-0.15 (1.01)	-0.46 (0.84)	**-0.40 (-0.67 to -0.13), 0.004**	**-0.54 (-0.87 to -0.22), 0.001**
Overall	-0.22 (1.22)	-0.42 (1.11)	-0.02 (1.16)	-0.27 (-0.61 to 0.08), 0.13	0.09 (-0.32 to 0.51), 0.66
Missing	*12*	*18*	*3*		
HUI3 binary *N (%)*					
Non per-fect health (score<1)	127 (69.8)	44 (65.7)	19 (57.6)	**Adjusted* odds ratio (OR) (95% CI), p-value**	
Perfect health (score=1)	55 (30.2)	23 (34.3)	14 (42.4)	1.37 (0.61 to 3.08), 0.45	1.91 (0.78 to 4.68), 0.16
Missing	*22*	*20*	*3*		
PedsQL *Median (IQR)*				**Adjusted* mean difference/log-odds ratio (95% CI), p-value**	
Physical health	93.75 (84.4 to 100.0)	93.75 (87.5 to 100.0)	92.19 (84.38 to 96.88)	13.50 (-12.19 to 39.18), 0.30 0.14 (-0.28 to 0.56), 0.52	13.62 (-15.40 to 42.63), 0.36 -0.34 (-0.90 to 0.22), 0.24
Emotional function-ing	75 (60 to 95)	80 (60 to 90)	70 (65 to 86.9)	6.50 (-2.03 to 15.04), 0.14 -0.10 (-0.58 to 0.38), 0.68	3.76 (-6.92 to 14.45), 0.49 -0.06 (-0.64 to 0.53), 0.85
Psychoso-cial health	82.69 (70.0 to 93.2)	84.62 (76.92 to 93.33)	79.55 (66.67 to 86.25)		
Total score	85.87 (75.0 to 94.57)	86.96 (80.48 to 94.57)	82.97 (75.0 to 89.98)	6.50 (-3.02 to 15.97), 0.18 0.31 (-0.31 to 0.92), 0.32	2.31 (-8.4 to 13.1), 0.67 -0.52 (-1.59 to 0.54), 0.34
Missing	*12*	*18*	*4*		

Social function-ing	95 (750 to 100)	100 (90 to 100)	90 (71.25 to 100)	16.92 (-7.07 to 40.91), 0.17 0.43 (0.02 to 0.84), 0.04	11.14 (-12.54 to 34.82), 0.36 -0.15 (-0.67 to 0.37), 0.58
Missing	*13*	*18*	*4*		
School function-ing	83.33 (65.0 to 95.0)	83.33 (62.5 to 91.67)	70 (60 to 85)	0.88 (-8.19 to 9.95), 0.85 0.04 (-0.44 to 0.53), 0.86	-3.16 (-13.54 to 7.21), 0.55 -0.70 (-1.47 to 0.07), 0.08
Missing	*22*	*20*	*5*		

Table 3. Quality of life at 12 months post recruitment by timing of surgery.
* adjusted for site and ethnicity, duration of OME, and hearing and OM8-30 reported hearing difficulties at 5 weeks follow-up (pre-exposure).
OM8-30: a negative or low score indicates a better quality of life[19].
Health Utilities Index mark 3: a higher score indicates a better quality of life, with a maximum score of 1.00[20].
PedsQL: a higher score indicates a better QoL, with a maximum score of 100[21].
SD - standard deviation, IQR - interquartile range. P values in bold statistically significant.

Time to VT Surgery

Multivariable Cox regression analysis, after adjusting for recruitment site, revealed that Asian ethnicity and mixed ethnicity were independently associated with a shorter time to VT surgery.

	Adjusted* HR	95% CI	P value
Ethnicity			
White	reference		
Mixed/multiple	**2.06**	**1.03 to 4.14**	**0.042**
Asian/Asian British	**2.21**	**1.23 to 3.97**	**0.008**
Black/African/Caribbean/ Black British	0.81	0.18 to 3.76	0.79
Other	Too few numbers for analysis		
Previous grommet surgery	1.64	0.92 to 2.94	0.096
Hearing aids	0.81	0.41 to 1.61	0.55
Average hearing loss (both ears, using all methods of assessment)	1.14	0.82 to 1.58	0.45

Table 4. **Cox regression multivariable model**

* adjusted for site and other variables in model. HR – hazard ratio.

Discussion

In this secondary analysis of data from a trial of oral steroids for children with persistent OME, we found no evidence of a significant association between having VT surgery and an improvement in overall health-related quality of life at 12 months post-recruitment, when measured using total OM8-30, PedsQL or HUI3 scores. However, having VT surgery was associated with better OM8-30 'hearing difficulties' facet scores at 12 months, even after adjusting for pre-exposure hearing level. Further analysis revealed that this was a significant association for both those who had undergone their VT surgery earlier in the study (5 weeks to 6 months post requirement) and those who underwent surgery later (6-12 months post recruitment) compared to children not undergoing surgery. We also found that hearing level post randomisation was independently associated with an increased odds of having VT surgery and that being of Asian or mixed/multiple ethnicities was associated with a shorter time to surgery.

Our finding that hearing level pre-exposure was independently associated with an increased odds of VT surgery is not surprising. Children with more profound hearing loss are more likely to have surgery recommend by their responsible clinician, and parents are more likely to accept this recommendation. Interestingly, other baseline factors likely to be related to disease severity such as duration of OME, previous history of OME or VT surgery and QoL measures were not independently associated with having surgery. One possible explanation for the lack of association between hearing related functional health at baseline and VT surgery is the poor correlation that has been demonstrated between objective and subjective (parent reported) hearing loss [15]. It has been suggested that parents often under-estimate the degree of hearing loss their child is experiencing and overestimate their health related QoL and may explain the lack of association we have also found in this regard [15].

Results of studies analysing the QoL effects post VT surgery, compared to a non-surgical group, have been mixed with the majority demonstrating no overall QoL benefit in OME and therefore similar to our results in

terms of overall QoL [8-10, 24]. However, we did demonstrate an improvement in functional health related to hearing difficulties in those who underwent VT surgery compared to those that did not. This improvement in function health remained even after adjusting for pre-exposure hearing level, which was associated with an increased odds of surgery. This result has not been demonstrated previously as previous studies in this area have been observational before and after studies that have not made a comparison with a non-surgical population. Our results therefore add further evidence to suggest VT surgery improves hearing related QoL, at least within the first 12 months post-surgery.

As far as we are aware, this is the first study to demonstrate a shorter time to VT surgery in children with Asian and mixed ethnicity. This association was maintained after controlling for recruitment site and measured baseline characteristics such as socioeconomic status and family history. Cultural and behavioural factors are the most likely explanations for this association, but it warrants further study.

The major strengths of this study are the breadth of outcome measures and potential confounders measured in the OSTRICH study. To our knowledge, this is the first study to assess the impact of VT on functional health status using the OME disease specific assessment tool OM8-30. We found no association between having VT surgery and any of the three outcome measures used in this study but did find a difference in one of the facet scores of one of the instruments. This was an exploratory analysis and it is possible that it is a type I error. However, our finding is certainly consistent with previously published data on VT surgery and hearing loss. A further limitation of this study is that most of the QoL and functional health status data were collected via parent-reported questionnaires, and as parents were aware of whether their child had had VT surgery there is a risk of response bias. However, we used validated instruments which is likely to have minimised any bias, and it has previously been shown that parent-reported QoL scores are generally congruent with child self-rated QoL with regard to physical functioning or physical symptoms [25]. A final limitation is that as an exploratory observational study, the pre exposure groups were not entirely comparable, in particular hearing thresholds were higher in the group that had VT surgery. However, this was adjusted for within the multilevel regression models, therefore minimising the impact of this potential confounding factor.

In conclusion, to our knowledge this is the first study of the impact of VT surgery on QoL that compares a surgical and non-surgical patient population using an OME disease specific QoL tool. This study found no evidence of a beneficial effect of VT surgery on overall QoL but did find evidence of a beneficial effect on hearing difficulty related health status. We also identified that Asian and mixed ethnicity appears to reduce time to surgery, a finding that has not been previously shown.

References

1. Perera, R., et al., *Autoinflation for hearing loss associated with otitis media with effusion.* Cochrane Database Syst Rev, 2013. **31**(5): p. Cd006285.
2. Williamson, I., *Otitis media with effusion in children.* BMJ Clin Evid, 2011. **2011**: p. 0502.
3. Williamson, I., et al., *Topical intranasal corticosteroids in 4-11 year old children with persistent bilateral otitis media with effusion in primary care: double blind randomised placebo controlled trial.* BMJ, 2009. **339**: p. b4984.
4. Williamson, I., et al., *Effect of nasal balloon autoinflation in children with otitis media with effusion in primary care: an open randomized controlled trial.* CMAJ, 2015. **187**(13): p. 961-969.
5. Waldron, C.A., et al., *Oral steroids for the resolution of otitis media with effusion (OME) in children (OSTRICH): study protocol for a randomised controlled trial.* Trials, 2016. **17**: p. 115.
6. Simpson, S.A., et al., *Oral or topical nasal steroids for hearing loss associated with otitis media with effusion in children.* Cochrane Database Syst Rev, 2011. **11**(5): p. Cd001935.
7. *National Institute for Health and Care Excellence. Otitis media with effusion in under 12s: surgery*. 2008 [cited 2018 8th January]; Available from: https://www.nice.org.uk/guidance/cg60.
8. Browning, G.G., et al., *Grommets (ventilation tubes) for hearing loss associated with otitis media with effusion in children.* Cochrane Database Syst Rev, 2010(10): p. Cd001801.
9. Steele, D.W., et al., *Effectiveness of Tympanostomy Tubes for Otitis Media: A Meta-analysis.* Pediatrics, 2017. **139**(6).
10. Wilks, J., et al., *Randomised controlled trial of early surgery versus watchful waiting for glue ear: the effect on behavioural problems in pre-school children.* Clin Otolaryngol Allied Sci, 2000. **25**(3): p. 209-14.
11. Hellstrom, S., et al., *Ventilation tube treatment: a systematic review of the literature.* Otolaryngol Head Neck Surg, 2011. **145**(3): p. 383-95.
12. Chow, Y., D.A. Wabnitz, and J. Ling, *Quality of life outcomes after ventilating tube insertion for otitis media in an Australian population.* Int J Pediatr Otorhinolaryngol, 2007. **71**(10): p. 1543-7.
13. Rosenfeld, R.M., et al., *Impact of tympanostomy tubes on child quality of life.* Arch Otolaryngol Head Neck Surg, 2000. **126**(5): p. 585-92.
14. Grindler, D.J., et al., *Impact of Otitis Media Severity on Children's Quality of Life.* Otolaryngol Head Neck Surg, 2014. **151**(2): p. 333-40.
15. Timmerman, A.A., L.J. Anteunis, and C.M. Meesters, *Response-shift bias and parent-reported quality of life in children with otitis media.* Arch Otolaryngol Head Neck Surg, 2003. **129**(9): p. 987-91.
16. Heidemann, C.H., et al., *Quality-of-Life Differences among Diagnostic Subgroups of Children Receiving Ventilating Tubes for Otitis Media.* Otolaryngol Head Neck Surg, 2015. **153**(4): p. 636-43.
17. Richards, M. and C. Giannoni, *Quality-of-life outcomes after surgical intervention for otitis media.* Arch Otolaryngol Head Neck Surg, 2002. **128**(7): p. 776-82.
18. Francis, N.A., et al., *Oral steroids for resolution of otitis media with effusion in children (OSTRICH): a double-blinded, placebo-controlled randomised trial.* Lancet, 2018. **392**(10147): p. 557-568.
19. Timmerman, A.A., et al., *Psychometric evaluation of the OM8-30 questionnaire in Dutch children with otitis media.* Eur Arch Otorhinolaryngol, 2008. **265**(9): p. 1047-56.
20. Feeny, D., et al., *Multi-attribute health status classification systems. Health Utilities Index.* Pharmacoeconomics, 1995. **7**(6): p. 490-502.
21. Varni, J.W., M. Seid, and C.A. Rode, *The PedsQL: measurement model for the pediatric quality of life inventory.* Med Care, 1999. **37**(2): p. 126-39.

22. *StataCorp. 2017. Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC*
23. *IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp. .*
24. Rovers, M.M., et al., *Randomised controlled trial of the effect of ventilation tubes (grommets) on quality of life at age 1-2 years.* Arch Dis Child, 2001. **84**(1): p. 45-49.
25. Eiser, C. and R. Morse, *Can parents rate their child's health-related quality of life? Results of a systematic review.* Qual Life Res, 2001. **10**(4): p. 347-57.

Conflict of Interest

The authors have no conflicts of interest to report.

Data availability statement

All data requests should be submitted to the corresponding author for consideration. Access to anonymised patient-level data may be granted following review.

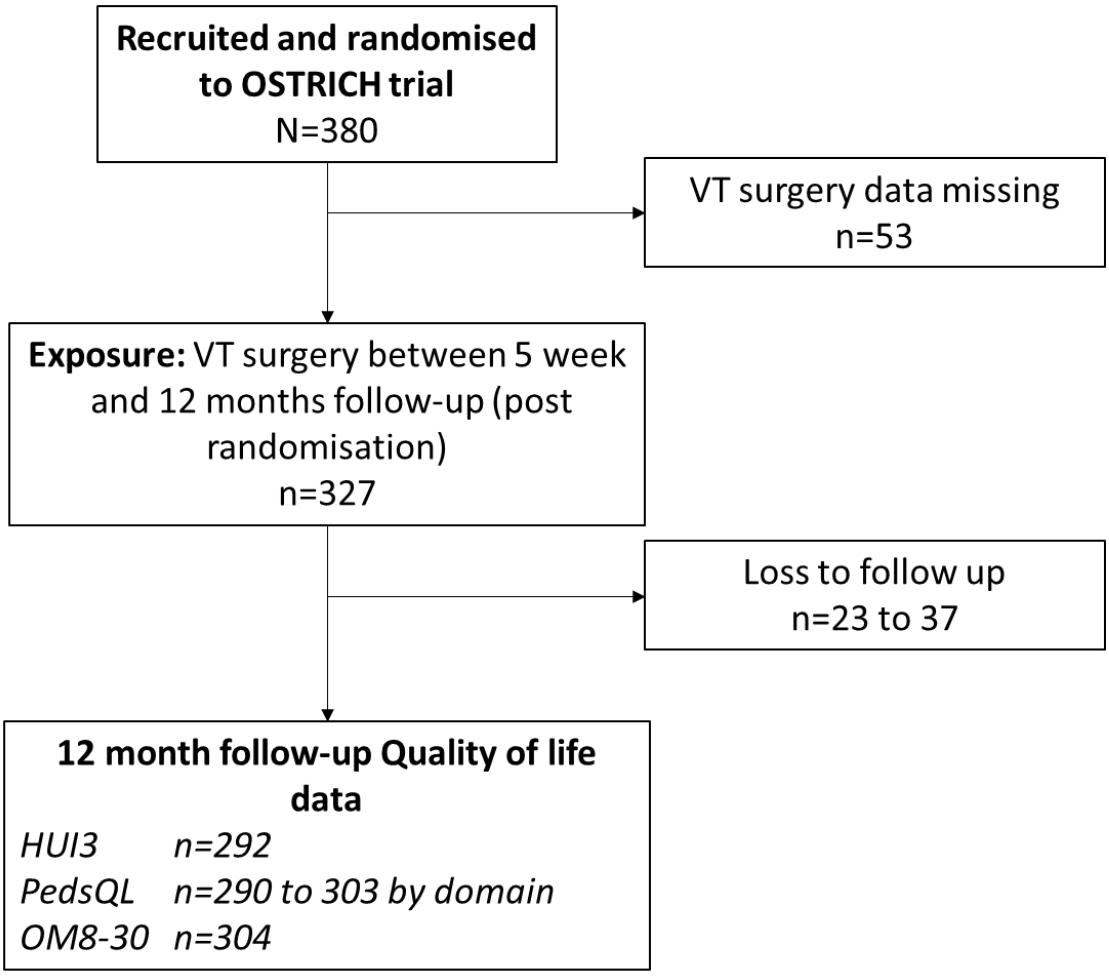

Figure 1. Flow chart demonstrating patient numbers and patient drop out numbers at the various study stages.