Clinical trial results:
Nasal Airway Obstruction Study (NAIROS)

Summary

EudraCT number	2017-000893-12
Trial protocol	GB
Global end of trial date	17 December 2020

Results information

Result version number	v1 (current)
This version publication date	17 December 2021
First version publication date	17 December 2021

Trial information

Trial identification

Sponsor protocol code	8302

Additional study identifiers

ISRCTN number	ISRCTN16168569
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	ISRCTN: 16168569, REC Reference: 17/NE/0239

Notes:

Sponsors

Sponsor organisation name	The Newcastle upon Tyne Hospitals NHS Foundation Trust
Sponsor organisation address	Freeman Hospital, Freeman Road, Newcastle upon Tyne, United Kingdom, NE7 7DN
Public contact	Mr Sean Carrie, The Newcastle upon Tyne Hospitals NHS Foundation Trust, 44 01912137635, sean.carrie@nhs.net
Scientific contact	Mr Sean Carrie, The Newcastle upon Tyne Hospitals NHS Foundation Trust, 44 01912137635, sean.carrie@nhs.net

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	29 January 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 December 2020
Global end of trial reached?	Yes
Global end of trial date	17 December 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To establish, and inform guidance for, the best management strategy for participants with nasal obstruction associated with a deviated septum via a randomised controlled trial:
a. To compare clinical and cost effectiveness over 6 months in adults with nasal septal deviation between nasal septoplasty +/- contralateral turbinate reduction and medical management.
b. To apply NAIROS level I evidence to inform NHS guidance.

NAIROS is a pragmatic trial, and as such the analysis data provided in this report is from the Intention-To-Treat (ITT) population.

Protection of trial subjects:

An Independent Data Monitoring Committee (IDMC) was convened at least annually to undertake an independent review of data, including safety data. The IDMC reported to the Trial Steering Committee, who made recommendations to the Trial Management Group. No other specific action was required to protect trial subjects.

Background therapy:

Prior to the clinical examination (nasal endoscopy), the use of topical local anaesthetic was left to investigator discretion.
All participants received a topical decongestant (Xylometazoline Hydrochloride Nasal Spray) prior to administration of the Double Ordinal Airway Subjective Scale (DOASS).

Evidence for comparator:

Mometasone furoate spray is licensed in dosage and form for use in patients with reduced nasal airway in the UK and is standard care for this indication.

Actual start date of recruitment	18 January 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 378
Worldwide total number of subjects	378
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	358
From 65 to 84 years	20
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Adult participants, who had the capacity to give written informed consent, were recruited from patients referred to secondary care rhinology clinics at 17 sites across Scotland, England and Wales. Participants were recruited between 18 January 2018 and 05 December 2019.

Pre-assignment

Screening details:

Prior to randomisation, the participant's medical history was documented and a clinical examination of the nasal passages conducted to determine that all of the inclusion criteria and none of the exclusion criteria, were met.

Period 1

Period 1 title	Randomisation
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Randomisation was administered centrally by the Newcastle Clinical Trials Unit (NCTU) secure web-based system on a 1:1 basis using permuted blocks of variable length, stratified by gender and three recognised NOSE-derived categories of baseline severity (30-50 = Moderate, 55-75 = Severe, 80-100 = Extreme). Assignment to either the surgical intervention (septoplasty) or medical management (mometasone furoate spray) was open label.

Arms

Are arms mutually exclusive?	Yes
Arm title	Septoplasty

Arm description:

The surgical intervention under investigation was septoplasty, plus/minus unilateral turbinate reduction.

Arm type	surgical

No investigational medicinal product assigned in this arm

Arm title	Medical Management

Arm description:

Mometasone furoate spray, taken twice daily at 100 microgram (2 sprays in each nostril twice daily) for 6 weeks followed by 2 sprays in each nostril once daily or 1 spray in each nostril twice daily for the remainder of the 6 month intervention period.

Arm type	Active comparator
Investigational medicinal product name	Mometasone furoate spray suspension (50 micrograms/actuation)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray, suspension
Routes of administration	Nasal use

Dosage and administration details:

 100mcg (2 sprays) into each nostril twice daily for 6 weeks followed by 100mcg (2 sprays into each nostril) once daily or 50mcg (1 spray) into each nostril twice daily for the remainder of the 6 month period.

Number of subjects in period 1	Septoplasty	Medical Management
Started	188	190
Completed	188	190

Period 2	
Period 2 title	Randomisation to 2 week assessment (MM)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms	
Are arms mutually exclusive?	Yes
Arm title	Septoplasty

Arm description:

The surgical intervention under investigation was septoplasty, plus/minus unilateral turbinate reduction.

Arm type	surgical

No investigational medicinal product assigned in this arm

Arm title	Medical Management

Arm description:

Mometasone furoate spray, taken twice daily at 100micrograms (2 sprays in each nostril twice daily) for 6 weeks followed by 2 sprays in each nostril once daily or 1 spray in each nostril twice daily for the remainder of the 6 month intervention period.

Arm type	Active comparator
Investigational medicinal product name	Mometasone furoate spray suspension (50 micrograms/actuation)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray, suspension
Routes of administration	Nasal use

Dosage and administration details:

100mcg (2 sprays) into each nostril twice daily for 6 weeks followed by 100mcg (2 sprays into each nostril) once daily or 50mcg (1 spray) into each nostril twice daily for the remainder of the 6 month period.

Number of subjects in period 2	Septoplasty	Medical Management
Started	188	190
Completed	188	185
Not completed	0	5
Consent withdrawn by subject	-	5

Period 3

Period 3 title	2 week assessment to 6 month assessment
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Septoplasty

Arm description:

The surgical intervention under investigation was septoplasty, plus/minus unilateral turbinate reduction.

Arm type	surgical

No investigational medicinal product assigned in this arm

Arm title	Medical Management

Arm description:

Mometasone furoate spray, taken twice daily at 100micrograms (2 sprays in each nostril twice daily) for 6 weeks followed by 2 sprays into each nostril once daily or 1 spray in each nostril twice daily for the remainder of the 6 month intervention period.

Arm type	Active comparator
Investigational medicinal product name	Mometasone furoate spray suspension (50 micrograms/actuation)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray, suspension
Routes of administration	Nasal use

Dosage and administration details:

100mcg (2 sprays) into each nostril twice daily for 6 weeks followed by 100mcg (2 sprays into each nostril) once daily or 50mcg (1 spray) into each nostril twice daily for the remainder of the 6 month period.

Number of subjects in period 3	Septoplasty	Medical Management
Started	188	185
Completed	173	175
Not completed	15	10
Consent withdrawn by subject	15	10

Period 4

Period 4 title	6 month assessmen to 12 month assessment
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms	
Are arms mutually exclusive?	Yes
Arm title	Septoplasty

Arm description:

The surgical intervention under investigation was septoplasty, plus/minus unilateral turbinate reduction.

Arm type	surgical

No investigational medicinal product assigned in this arm

Arm title	Medical Management

Arm description:

Mometasone furoate spray, taken twice daily at 100micrograms (2 sprays in each nostril twice daily) for 6 weeks followed by 2 sprays once daily into each nostril or 1 spray in each nostril twice daily for the remainder of the 6 month intervention period.

Arm type	Active comparator
Investigational medicinal product name	Mometasone furoate nasal spray suspension (50 micrograms/actuation)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray, suspension
Routes of administration	Nasal use

Dosage and administration details:

100mcg (2 sprays) into each nostril twice daily for 6 weeks followed by 100mcg (2 sprays into each nostril) once daily or 50mcg (1 spray) into each nostril twice daily for the remainder of the 6 month period.

Number of subjects in period 4	Septoplasty	Medical Management
Started	173	175
Completed	122	132
Not completed	51	43
Consent withdrawn by subject	10	10
Lost to follow-up	41	33

Baseline characteristics

Reporting groups	
Reporting group title	Septoplasty
Reporting group description:	
The surgical intervention under investigation was septoplasty, plus/minus unilateral turbinate reduction.	
Reporting group title	Medical Management
Reporting group description:	
Mometasone furoate spray, taken twice daily at 100 microgram (2 sprays in each nostril twice daily) for 6 weeks followed by 2 sprays in each nostril once daily or 1 spray in each nostril twice daily for the remainder of the 6 month intervention period.	

Reporting group values	Septoplasty	Medical Management	Total
Number of subjects	188	190	378
Age categorical			
Patients who have attended a rhinology clinic and consented to screening assessments			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	175	183	358
From 65-84 years	13	7	20
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	62	63	125
Male	126	127	253
Ethnic Group			
Units: Subjects			
White	169	165	334
Asian (Indian/Pakistani/Bangladeshi ancestry)	13	14	27
Other Asian	1	2	3
Other ethnic origin	3	9	12
Not Recorded	2	0	2
NOSE score category			
Randomisation stratification - NOSE score expressed as a category			
Units: Subjects			
moderate	30	32	62
severe	89	89	178
extreme	69	69	138
not recorded	0	0	0

End points

End points reporting groups

Reporting group title	Septoplasty
Reporting group description:	
The surgical intervention under investigation was septoplasty, plus/minus unilateral turbinate reduction.	
Reporting group title	Medical Management
Reporting group description:	
Mometasone furoate spray, taken twice daily at 100 microgram (2 sprays in each nostril twice daily) for 6 weeks followed by 2 sprays in each nostril once daily or 1 spray in each nostril twice daily for the remainder of the 6 month intervention period.	
Reporting group title	Septoplasty
Reporting group description:	
The surgical intervention under investigation was septoplasty, plus/minus unilateral turbinate reduction.	
Reporting group title	Medical Management
Reporting group description:	
Mometasone furoate spray, taken twice daily at 100micrograms (2 sprays in each nostril twice daily) for 6 weeks followed by 2 sprays in each nostril once daily or 1 spray in each nostril twice daily for the remainder of the 6 month intervention period.	
Reporting group title	Septoplasty
Reporting group description:	
The surgical intervention under investigation was septoplasty, plus/minus unilateral turbinate reduction.	
Reporting group title	Medical Management
Reporting group description:	
Mometasone furoate spray, taken twice daily at 100micrograms (2 sprays in each nostril twice daily) for 6 weeks followed by 2 sprays into each nostril once daily or 1 spray in each nostril twice daily for the remainder of the 6 month intervention period.	
Reporting group title	Septoplasty
Reporting group description:	
The surgical intervention under investigation was septoplasty, plus/minus unilateral turbinate reduction.	
Reporting group title	Medical Management
Reporting group description:	
Mometasone furoate spray, taken twice daily at 100micrograms (2 sprays in each nostril twice daily) for 6 weeks followed by 2 sprays once daily into each nostril or 1 spray in each nostril twice daily for the remainder of the 6 month intervention period.	

Primary: SNOT-22 score at 6 months

End point title	SNOT-22 score at 6 months
End point description:	
The 22-item Sinonasal outcome test (SNOT-22) is a validated patient reported questionnaire, used to assess general sinonasal symptoms. SNOT-22 consists of 22 questions that are answered on a scale from "0" (no problem) up to "5" (problem as bad as it can be). The total score is generated by adding all item values. The total can range from 0 (no problem) to 110 (problem as severe as it can be).	
End point type	Primary
End point timeframe:	
SNOT-22 score at 6 months post-randomisation	

End point values	Septoplasty	Medical Management		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	152[1]	155[2]		
Units: total score				
arithmetic mean (confidence interval 95%)	19.9 (17.0 to 22.7)	39.5 (36.1 to 42.9)		

Notes:

[1] - ITT analysis group

[2] - ITT population

Statistical analyses

Statistical analysis title	Primary Analysis - Regression model

Statistical analysis description:

The ITT population includes all participants who provided primary endpoint data (SNOT-22 at 6 months). The ITT primary analysis adjusts for baseline stratification factors (NOSE severity category and gender) and SNOT-22 score.

Comparison groups	Septoplasty v Medical Management
Number of subjects included in analysis	307
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	< 0.0001 [4]
Method	Regression, Linear
Parameter estimate	Median difference (final values)
Point estimate	-20.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.63
upper limit	-16.4
Variability estimate	Standard error of the mean
Dispersion value	1.836

Notes:

[3] - The analysis compares SNOT-22 scores at 6 months, by arm, adjusted for stratification variables (NOSE severity and gender) and baseline SNOT-22 scores, for the ITT population. The minimal clinically important difference (MCID) is a difference of 9 points for the SNOT-22 score between the 2 arms.
[4] - Highly statistically significant effect of septoplasty, with scores on average 20 units less than those in the medical management arm (while holding all other variables the same). Lower 95% CI limit is -16.4, below the MCID of 9 points (superiority).

Secondary: NOSE score at 6 months

End point title	NOSE score at 6 months

End point description:

The Nasal Obstruction Symptom Evaluation (NOSE) score is a patient reported outcome measure of nasal obstruction symptoms.
NOSE consists of five questions that are answered on a scale from "0" (not a problem) up to "4" (severe problems). The total score is generated by adding all item values and multiplying the raw score with 5. The final score is within a range from 0 to 100. A score of 0 indicates no obstructive nasal problems and a score of 100 implies severe problems.

End point type	Secondary

End point timeframe:

NOSE score at 6 months post-randomisation

End point values	Septoplasty	Medical Management		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	145[5]	144[6]		
Units: total score				
arithmetic mean (confidence interval 95%)	29.0 (24.9 to 33.1)	62.2 (58.3 to 66.2)		

Notes:

[5] - ITT population

[6] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: SNOT-22 score at 12 months

End point title	SNOT-22 score at 12 months

End point description:

The 22-item Sinonasal outcome test (SNOT-22) is a validated patient reported questionnaire, used to assess general sinonasal symptoms.
SNOT-22 consists of 22 questions that are answered on a scale from "0" (no problem) up to "5" (problem as bad as it can be). The total score is generated by adding all item values. The total can range from 0 (no problem) to 110 (problem as severe as it can be).

End point type	Secondary

End point timeframe:

12 months post-randomisation

End point values	Septoplasty	Medical Management		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119[7]	125[8]		
Units: total score				
arithmetic mean (confidence interval 95%)	21.2 (17.7 to 24.6)	30.4 (26.6 to 34.3)		

Notes:

[7] - ITT population

[8] - ITT population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All adverse events (AEs) and adverse reactions (ARs) occurring from randomisation (baseline) through to the end of trial participation at 12 months (Visit 3).

Adverse event reporting additional description:

Adverse events were coded using the MedDRA dictionary and are presented by preferred term, grouped by system organ class.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20

Reporting groups

Reporting group title	Septoplasty

Reporting group description:

The surgical intervention under investigation was septoplasty, plus/minus unilateral turbinate reduction.

Reporting group title	Medical Management

Reporting group description:

Mometasone fuorate spray, taken twice daily at 100mcg (2 sprays in each nostril twice daily) for 6 weeks followed by 2 sprays in each nostril once daily or 1 spray in each nostril twice daily for the remainder of the 6 month intervention period.

Serious adverse events	Septoplasty	Medical Management	
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 166 (6.63%)	5 / 186 (2.69%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Abdominal trauma			
subjects affected / exposed	0 / 166 (0.00%)	1 / 186 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Anaesthetic complication			
subjects affected / exposed	3 / 166 (1.81%)	2 / 186 (1.08%)	
occurrences causally related to treatment / all	3 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative bleeding			

subjects affected / exposed	5 / 166 (3.01%)	1 / 186 (0.54%)	
occurrences causally related to treatment / all	5 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vasovagal episode			
subjects affected / exposed	2 / 166 (1.20%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inappropriate hospital admission	Additional description: 2 participants in the surgical arm were admitted to hospital overnight after receiving the surgical intervention. These admissions were an administrative oversight by the hospital; the surgical intervention is planned as a day case.		
subjects affected / exposed	2 / 166 (1.20%)	0 / 186 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Polypharmacy overdose			
subjects affected / exposed	0 / 166 (0.00%)	1 / 186 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Infection			
subjects affected / exposed	2 / 166 (1.20%)	2 / 186 (1.08%)	
occurrences causally related to treatment / all	2 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Septoplasty	Medical Management	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	112 / 166 (67.47%)	77 / 186 (41.40%)	
Surgical and medical procedures			
Nose deformity	Additional description: Nose shape/asymmetry		
subjects affected / exposed	4 / 166 (2.41%)	0 / 186 (0.00%)	
occurrences (all)	4	0	
Varicose vein operation			
subjects affected / exposed	0 / 166 (0.00%)	1 / 186 (0.54%)	
occurrences (all)	0	1	

Tooth extraction			
subjects affected / exposed	1 / 166 (0.60%)	0 / 186 (0.00%)	
occurrences (all)	1	0	
Antibiotic prophylaxis			
subjects affected / exposed	1 / 166 (0.60%)	0 / 186 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Nasal discomfort			
subjects affected / exposed	11 / 166 (6.63%)	5 / 186 (2.69%)	
occurrences (all)	19	5	
Pain			
subjects affected / exposed	9 / 166 (5.42%)	7 / 186 (3.76%)	
occurrences (all)	12	7	
Nasal induced Infection/fever/temperature			
subjects affected / exposed	11 / 166 (6.63%)	7 / 186 (3.76%)	
occurrences (all)	11	7	
Numbness			
subjects affected / exposed	4 / 166 (2.41%)	1 / 186 (0.54%)	
occurrences (all)	4	1	
Swelling	Additional description: Swelling		
subjects affected / exposed	3 / 166 (1.81%)	0 / 186 (0.00%)	
occurrences (all)	3	0	
Nasal septum perforation	Additional description: Perforation		
subjects affected / exposed	2 / 166 (1.20%)	0 / 186 (0.00%)	
occurrences (all)	2	0	
Adhesion	Additional description: Adhesion/synechiae		
subjects affected / exposed	1 / 166 (0.60%)	0 / 186 (0.00%)	
occurrences (all)	1	0	
Fatigue	Additional description: Tiredness/fatigue		
subjects affected / exposed	1 / 166 (0.60%)	0 / 186 (0.00%)	
occurrences (all)	1	0	
other	Additional description: admitted overnight to hospital after surgical intervention due to pre-existing condition		
subjects affected / exposed	1 / 166 (0.60%)	0 / 186 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			

Epistaxis	Additional description: Epistaxis/bleeding/clot		
subjects affected / exposed	10 / 166 (6.02%)	20 / 186 (10.75%)	
occurrences (all)	13	20	
Rhinorrhoea	Additional description: Rhinorrhea/mucus		
subjects affected / exposed	9 / 166 (5.42%)	5 / 186 (2.69%)	
occurrences (all)	9	5	
Nasal dryness	Additional description: Dry nose/itching/crusting		
subjects affected / exposed	1 / 166 (0.60%)	5 / 186 (2.69%)	
occurrences (all)	1	6	
Nasal congestion	Additional description: Blocked nose		
subjects affected / exposed	5 / 166 (3.01%)	0 / 186 (0.00%)	
occurrences (all)	6	0	
Asthma	Additional description: exacerbation		
subjects affected / exposed	0 / 166 (0.00%)	1 / 186 (0.54%)	
occurrences (all)	0	1	
Psychiatric disorders			
Anxiety disorder	Additional description: Anxiety/depression		
subjects affected / exposed	0 / 166 (0.00%)	3 / 186 (1.61%)	
occurrences (all)	0	3	
Injury, poisoning and procedural complications			
Post procedural complication	Additional description: Sense of smell/taste		
subjects affected / exposed	1 / 166 (0.60%)	0 / 186 (0.00%)	
occurrences (all)	2	0	
shoulder injury	Additional description: Muscular strain Right Shoulder following MVA		
subjects affected / exposed	0 / 166 (0.00%)	1 / 186 (0.54%)	
occurrences (all)	0	1	
Cardiac disorders			
ECG changes	Additional description: ECG changes post-induction of anaesthesia		
subjects affected / exposed	1 / 166 (0.60%)	0 / 186 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Headache	Additional description: Headache		
subjects affected / exposed	6 / 166 (3.61%)	2 / 186 (1.08%)	
occurrences (all)	6	2	
Dizziness	Additional description: Dizziness		

subjects affected / exposed	2 / 166 (1.20%)	0 / 186 (0.00%)	
occurrences (all)	2	0	
vasovagal episode			
subjects affected / exposed	0 / 166 (0.00%)	1 / 186 (0.54%)	
occurrences (all)	0	1	
Hypoglossal nerve paralysis			
subjects affected / exposed	1 / 166 (0.60%)	0 / 186 (0.00%)	
occurrences (all)	1	0	
Insomnia			
subjects affected / exposed	1 / 166 (0.60%)	0 / 186 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Osteopenia			
subjects affected / exposed	0 / 166 (0.00%)	1 / 186 (0.54%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Ear discomfort	Additional description: Ear blocked/tinnitus/Labyrinthitis		
subjects affected / exposed	3 / 166 (1.81%)	0 / 186 (0.00%)	
occurrences (all)	3	0	
Gastrointestinal disorders			
reflux	Additional description: Reflux/heartburn		
subjects affected / exposed	0 / 166 (0.00%)	4 / 186 (2.15%)	
occurrences (all)	0	4	
Nausea	Additional description: Nausea		
subjects affected / exposed	1 / 166 (0.60%)	1 / 186 (0.54%)	
occurrences (all)	1	1	
Skin and subcutaneous tissue disorders			
mouth sores			
subjects affected / exposed	1 / 166 (0.60%)	0 / 186 (0.00%)	
occurrences (all)	1	0	
Dermatitis			
subjects affected / exposed	0 / 166 (0.00%)	1 / 186 (0.54%)	
occurrences (all)	0	1	
Endocrine disorders			
Fatty Liver			
subjects affected / exposed	0 / 166 (0.00%)	1 / 186 (0.54%)	
occurrences (all)	0	1	

diabetes type 2			
subjects affected / exposed	1 / 166 (0.60%)	1 / 186 (0.54%)	
occurrences (all)	1	1	
Hypertension			
subjects affected / exposed	0 / 166 (0.00%)	1 / 186 (0.54%)	
occurrences (all)	0	1	
Liver function test abnormal			
subjects affected / exposed	0 / 166 (0.00%)	1 / 186 (0.54%)	
occurrences (all)	0	1	
Vitamin D deficiency			
subjects affected / exposed	0 / 166 (0.00%)	1 / 186 (0.54%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Subluxation of left shoulder			
subjects affected / exposed	0 / 166 (0.00%)	1 / 186 (0.54%)	
occurrences (all)	0	1	
shoulder pain			
subjects affected / exposed	0 / 166 (0.00%)	1 / 186 (0.54%)	
occurrences (all)	0	1	
Arthritis	Additional description: left hip		
subjects affected / exposed	0 / 166 (0.00%)	1 / 186 (0.54%)	
occurrences (all)	0	1	
Back injury			
subjects affected / exposed	0 / 166 (0.00%)	1 / 186 (0.54%)	
occurrences (all)	0	1	
Face injury			
subjects affected / exposed	0 / 166 (0.00%)	1 / 186 (0.54%)	
occurrences (all)	0	1	
Muscle injury	Additional description: right hip		
subjects affected / exposed	1 / 166 (0.60%)	0 / 186 (0.00%)	
occurrences (all)	1	0	
Sciatica			
subjects affected / exposed	1 / 166 (0.60%)	0 / 186 (0.00%)	
occurrences (all)	1	0	
Fibula fracture			

subjects affected / exposed	1 / 166 (0.60%)	0 / 186 (0.00%)	
occurrences (all)	1	0	
Nasal injury	Additional description: Bruising to the nose after a fall		
subjects affected / exposed	1 / 166 (0.60%)	0 / 186 (0.00%)	
occurrences (all)	1	0	
Wrist fracture			
subjects affected / exposed	1 / 166 (0.60%)	0 / 186 (0.00%)	
occurrences (all)	1	0	
Pain	Additional description: Pain in finger bones		
subjects affected / exposed	1 / 166 (0.60%)	0 / 186 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Infection	Additional description: Infection/fever/temperature		
subjects affected / exposed	10 / 166 (6.02%)	8 / 186 (4.30%)	
occurrences (all)	11	8	
Cough	Additional description: Cough/cold/flu		
subjects affected / exposed	6 / 166 (3.61%)	5 / 186 (2.69%)	
occurrences (all)	9	5	
bites to ankles			
subjects affected / exposed	0 / 166 (0.00%)	1 / 186 (0.54%)	
occurrences (all)	0	1	
COVID-19			
subjects affected / exposed	1 / 166 (0.60%)	0 / 186 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 November 2017	- Change of Senior Statistician. - Section 8.2 - updated wording on the frequency of Sterimar dosing to be consistent with the remainder of the protocol. - Section 11.2.1 Analysis of the Primary Outcome Measure. Update to the wording for the range of NOSE values to be consistent with the remainder of the protocol. - Addition of a section to the protocol to state that a NIMP (nasal decongestant spray) will be used at the baseline, 6 month and 12 month follow up visits, and stating the name of the NIMP (Xylometazoline). - Updated exclusion criteria (clarification and addition)
11 June 2018	- Update to the protocol, Patient Identification Card and letter to GP to clarify that sterimar isotonic nasal spray must be taken before mometasone nasal spray - Update to the protocol and PIS to clarify that patients randomised to septoplasty must have their septoplasty anytime within 8 weeks of randomisation. - Update to the protocol to state that patients who request local anaesthetic for nasal endoscopy may have the nasal endoscopy assessment carried out after the other trial assessments have been completed. - Throughout the protocol, update to change the name of the Sterimar nasal spray from isotonic spray to saline spray. - Update to the protocol - clarification of the pregnancy reporting guidelines to state pregnancy of a female partipant or the female partner of a male participant. - Update protocol – update Reference Safety Information - Change the exclusion criteria from any history of intranasal recreational drug use to any history of intranasal recreational drug use within the past 6 months. - Update protocol to add fainting and vasovagal episodes and group with dizziness as an undesirable effect of general anaesthesia. - Throughout protocol – correct the misspelling of xylometazoline.

16 January 2019	PROTOCOL (and PIS and ICF where necessary) - removal of references to internal pilot/pilot phase. Replace 'Safety Monitoring Plan' with 'Sponsor Risk Assessment' and state the RSI for the IMP. - state the risk of septoplasty as the trial intervention compared to standard surgical care. - state the location of the RSI for septoplasty - Remove all references to a pilot phase - widen the window for the 6 month visit – clarify how to securely email consent and eligibility forms to NCTU for monitoring - clarify how participant usage of the nasal sprays will be calculated. Clarify why IMP compliance is not monitored - clarify management of patients between the 6 month and 12 month follow up visits and/or participants who wish to remain in the trial but discontinue allocated treatment. - clarify pregnancy reporting (also in PIS). - removal of all references to arm 'crossover'. - update Data Protection Act to General Data Protection Regulation (2018). PIS - clarification that the patient should be prepared for treatment from whichever arm they are allocated to and that patients randomised to surgical management should be prepared to have surgery within 8 weeks. ICF - Clarify that if a participant withdraws from the study, data collected up to that point will be kept; addition of a clause stating that, for participants randomised to medical management, they agree to inform the trial team if their partner becomes pregnant. Nasal Spray Instruction - Replace spray instructions with an instruction to refer to the product patient information leaflet.
16 October 2019	- Update to the the schedule of events and data collection to add an online platform to the methods of completion for the SNOT-22 questionnaire.
13 February 2020	Change of site PI at the Stockport site
17 December 2020	- Amendment of the primary outcome analysis. The text 'baseline severity SNOT-22 score as a continuous covariate' has been removed from the secondary analysis sentence to the primary analysis sentence. By adjusting for the baseline values of the primary outcome measure, this makes for a more powerful primary analysis. - 'BMI' as a clinical covariate has been deleted. This is a historical typographical error and participant BMI data has never been collected.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

All forms of airway clinical assessment and objective testing of nasal airway function were suspended from March 2020 onwards (COVD-19 pandemic). The resultant lower numbers, may have an impact on the statistical precision of the analysis.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/32054508