# A Primary Care Randomised Controlled Trial of Steam inhalation and Nasal Irrigation For recurrent or chronic Sinus symptoms (SNIFS trial)

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**Background.** Systematic reviews support saline nasal irrigation for chronic/recurrent sinus symptoms but the trials are small, and few in typical primary care settings. Steam inhalation is poorly evidence-based. Our aim was to estimate the impact of brief pragmatic interventions to use steam and nasal irrigation.

**Methods** Adults with a history of recurrent/chronic sinusitis and reporting significant impact on quality-of-life from 72 UK general practices, were randomised to four advice strategies by a practice nurse, using numbered opaque sealed envelopes: 1) usual care 2) steam inhalation daily 3) saline nasal irrigation daily supported by a demonstration video 4) Irrigation and steam inhalation.

**Results.**  961 individuals consented. 871 returned baseline questionnaires (respectively n=210,n=219,n=232,n=210) and 671/871 (77%) participants self-reported Rhinosinusitis Disability Index (RSDI) scores at 3 months (the primary outcome). Multiple imputation avoided assuming data was missing completely at random. RSDI scores improved with both nasal irrigation and no irrigation (-7.4 and -5.2 respectively; adjusted estimate of the difference -2.51, 95% confidence intervals -4.65 to -0.37, p=0.021). By 6 months, significantly more patients maintained a 10 point clinically important improvement in the RSDI (44.1%, 36.6% respectively); fewer used over-the-counter (OTC) medications (59.4%, 68%) or intended to consult the doctor. Steam inhalation reduced headache but no other outcomes. There was no evidence of harms with either intervention.

**Interpretation.** Steam inhalation for chronic sinus symptoms in primary care is not effective. A brief pragmatic intervention to encourage nasal irrigation is less effective than prior evidence suggests, but provides some symptomatic benefit, and empowers self- management.

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**Background.**

Rhinosinusitis probably affects more than 25 million US citizens and 2.5 million Canadians1. Quality of life in CRS is similar to congestive heart disease and chronic pulmonary disease2. Alternatives to using antibiotics are sorely needed: antibiotics are prescribed for nearly all patients3 but the evidence is modest 4 and an international priority is to contain antibiotic resistance5. Steam inhalation is widely advocated in rhinosinusitis, but a Cochrane review of steam for the ‘common cold’ found equivocal evidence6, and a recent primary care trial found no benefit and some harm (mild thermal injury) for pragmatic advice to inhale with steam twice daily for a range of respiratory tract infections7. The Cochrane review of nasal irrigation8 has reported benefit. However most of the trials were small, mainly from secondary care settings and the review documented symptom data from only 129 participants, with high heterogeneity. Two small trials have included some participants from primary care: Rabago et al9 (n=76) assessed a gravity based nasal irrigation device compared to routine care among mainly primary care participants, and Pynnonen et al.10 (n=121) published since the Cochrane review) assessed a positive pressure squeeze bottle compared to saline nasal spray among volunteers from a variety of sources.

We report a large pragmatic study which aimed to estimate the effectiveness of brief advice to use nasal irrigation and or steam inhalations in routine primary care for chronic or recurrent sinus symptoms.

**Methods.**

**Design**

This was a parallel group individually randomised controlled trial with equal allocation ratio.

**Setting**

Practices around the study centre in Southampton, England, were invited to participate. There were no exclusion criteria for practices. Adults identified from the computerised registers from 72 primary care practices were sent invitation letters to attend a recruitment clinic run by practice nurses only if they reported ‘moderate to severe impact of sinus symptoms on their quality of life’(QOL). Nurses assessed eligibility, consented and randomised individuals (see Fig. 1).

**Participant eligibility.**

**Inclusion criteria.** Our pragmatic inclusion criteria matched the Cochrane review: a) aged 18-65 b) 2 episodes of acute sinusitis, or 1 episode of chronic sinusitis recorded as the reason for encounter recorded in the medical records within the last 3 years, and c) who currently reported ‘moderate to severe impact of sinus symptoms on their quality of life’(QOL) (as above).

## Exclusions: inability to complete outcomes; head/neck cancer; HIV; immune-suppressive treatment; cystic fibrosis; pregnancy/breast feeding; other nasal disorders e.g. polyps; poor gag/swallow reflexes.

**Intervention.**

**Usual Care.**

Participants were randomised to four groups defined by 2 interventions (a 2x2 factorial design):

**1) Ususal Care.** All study participants had access to usual care; medication or referral was at the discretion of the doctor according to the normal practice of that doctor (i.e. not standardised).

**2) Advice to use nasal irrigation** (either: a) Daily Nasal Irrigation or b) No Nasal Irrigation)

Participants were given verbal instructions and shown a video clip (uploaded on YouTube) demonstrating how to perform irrigation. They were asked to irrigate the nose (150 ml through each nostril) daily for 6 months, and a SinuCleanse 19 nasal cup was provided to each subject. Patients made their own buffered 2.0% saline irrigation solution every 1 to 2 days comprising: 1 heaped teaspoon salt, one half teaspoon baking soda and 1 pint (473 ml) tap water; how to do this was also demonstrated on the video clip. We chose this particular intervention based on the provisional evidence from a previous randomised controlled trial in primary care9. Each of the above nasal irrigation groups were also randomised to:

**3) Advice to perform steam inhalation** (either a) Daily Steam inhalation or b) No Steam inhalation). Patients were asked to inhale steam for 5 minutes per day by placing a towel over the head over a bowl of recently boiled water. This intervention was chosen for its wide availability, and ease of use; we did not encourage nor discuss use of a particular device such as rhinotherm.

**4) Advice to perform both daily steam inhalation and daily nasal irrigation** (as above).

**Randomisation method.**

Patients were randomised using computer generated random numbers to one of four pragmatic advice strategies contained in opaque sealed numbered envelopes. Sealed envelopes were used for two reasons: a) the complex factorial design made group differentiation more difficult to guarantee: envelopes facilitated immediate access to the correct structured advice sheets for each group, ensuring robust group differentiation, and greater logistic simplicity for recruiters, and b) with attention to equipoise this method has resulted in robust randomisation in several studies7 11-13. In the current study there was no evidence of selective use of numbered envelopes, nor of meaningful difference in group characteristics.

**Outcomes.**

Blinding of patients to intervention group was impossible, and the key outcomes related to symptoms and impact must also be reported by patients.

**Primary outcome**: The validated RhinoSinusitis Disability Index14 (RSDI) was chosen, as it permitted comparison with the previous trial in USA primary care9. 3 months was the primary time point specified in the funding application; 6 months was included to document longer term effects.

**Secondary outcomes:**

SNOT-2015(Sino-nasal Outcome test-20); Single Item Sinus Severity Assessment (SIA); severity of respiratory symptoms16 (number of days feeling unwell with RTIs) or sinusitis; reported use of over the counter medication, reported headaches, and harms (nasal burning or stinging; scalding); EQ5D (European-Quality-of-life-5-dimensions); antibiotic prescription and GP visits; belief in antibiotics and the belief in the need to see the doctor in future episodes; cost-effectiveness will be reported elsewhere.

**Statistics**

**Sample size.** We estimated that to detect an interaction of 10 points in the RSDI between intervention groups we would need to power the study to detect a 5 point main effect (approximately 0.36 SD) which would require a minimum of 125 per group or 316 in total, allowing for four trial subgroups, 80% power, alpha of 0.05, and 80% follow-up. Early pilot work suggested that compliance and attrition might both be important issues. To have sufficient power to assess those with higher compliance assuming 30% complied and we achieved 70% follow-up at 6 months, we needed to recruit  250/(0.3\*0.7)=1192 (rounded); assuming 40% complied 250/(0.4\*0.7)=894, and assuming 50% 250/(0.5\*0.7)=716. So our minimum target was 716 participants. Large samples also provided power for key exploratory secondary analyses (more severely affected individuals; subscales of the RSDI; other clinically defined subgroups detailed below).

**Analysis.** There were no interim analyses, nor stopping rules. Multiple imputation (100 imputations) were done in Stata using a chained equation model, using participant baseline characteristics, the outcome variables and the randomisation group. Analyses controlled for baseline values in the multivariate linear regression model analyses. Since the interaction term between the two interventions were not significant for any outcome, the main effects of each intervention are reported mutually controlled for the other intervention. Models were backwards fitted, retaining the variables that were associated with the outcome at p<=0.20. Key secondary analyses were specified in advance:

* The number of individual achieving a 10 point reduction in RSDI which was estimated to be the MCID (minimal clinical important difference) in the context of surgical trials; 17
* Physical symptom scale of the RSDI (where we anticipated most impact) and the number achieving a clinically important 3.8 point reduction in the physical subscale;
* Other subgroups specified in advance : above the median RSDI score; a history of hay fever; higher deprivation scores; older age (above the median); longer prior illness duration (more than 15 years); use of topical nasal steroids, and gender.

**Changes to the protocol**. We increased the planned sample size to assess the impact of non-compliance, and also modified the randomisation methods (see above). We originally did not have ethical permission to collect the RSDI by phone, but gained approval half-way through the trial since follow-up rates were too low. The primary analysis was initially intended for complete cases, but due to lower follow-up (< 80%) multiple imputation was used to avoid the unlikely assumption that data was missing completely at random. Following peer review, a post-hoc secondary analysis estimated the differential effectiveness among nasal corticosteroids users; the rationale for this analysis was because we did not specify the timing of nasal irrigation, so irrigation following corticosteroids could have lessened the net benefit of irrigation.

**Results:**

961 participants were consented and randomised between 11/02/09 and 30/6/2014, but only 871 completed baseline data (see Figure 1). Groups were well balanced (Table1). 671 completed the RSDI at 3 months and 623 at 6 months. There was no evidence of a significant interaction between intervention groups for either RSDI or SNOT-20 so the main results are presented by factorial groups (nasal irrigation vs no nasal irrigation; steam inhalation vs no steam inhalation).

**Adherence**

At 3 months, the nasal irrigation group reported a median of 20 days (IQR 5, 30) doing nasal irrigation in the preceding month. The steam inhalation group also reported inhaling for a median of 20 days in the preceding month (IQR 6, 30).

**Main results**

The RSDI improved more with nasal irrigation than no nasal irrigation (at 3 months: crude change of -7.42 and -5.23 points respectively). Using multiple imputation the estimated adjusted mean difference between groups was -2.51, 95% confidence intervals -4.65 to -0.37, p=0.021; by 6 months: -2.41, -4.66 to -0.16 p=0.036) (See Table6). The adjusted estimate differs slightly from the unadjusted estimate due to better control of the small differences in confounding variables between groups. 44.1% and 36.6% respectively maintained a 10 point clinically important improvement in the RSDI by 6 months (Table 7 appendix 1), mostly in the physical subscale of the RSDI (Tables 8-9, Appendix 1). There was no effect of steam inhalation (see Table 3). The analysis of complete cases was similar to the imputed analysis, although the imputed analysis was slightly more conservative. Although there were no significant interactions between interventions, most benefit of nasal irrigation at 3 and 6 months occurred in the combined irrigation/steam subgroup (see Appendix 1).

**Secondary outcomes.** There were no significant differences for either intervention at 3 or 6 months using the SNOT-20 scale. The nasal irrigation group were more likely to agree by 6 months that they would not visit a doctor for subsequent sinus symptoms - on a 7 point scale + 0.30 (0.08 to 0.53, p=0.009) (Table 4), and at 3 months less likely to report headache (72% versus 81.7%) (Table 5). Nasal irrigation resulted in less use of OTC medication (60% versus 67.4%) (Table 5). There was no difference in the number of respiratory infections reported in the last month (median 1 for all groups at 3 and 6 months). Nasal irrigation did not significantly reduce the number of days unwell with RTIs at 3 or 6 months (respectively 2 vs 1 days, and 3 vs 2 days). The number of days with sinus infections was reduced at 3 months, and significantly at 6 months by 3 days (4 vs 7) (Table 6). There was no effect of steam inhalation on any secondary outcome except headache.

**Harms.** There was no difference in the proportions experiencing nose bleeds, soreness or burning in either intervention group (Table 5).

**Pre-specified subgroups.** There was no evidence of a differential effect of either intervention in the clinical subgroups defined prior to analysis (Appendix 1 Tables 11, 12a and 12b).

Following peer review we assessed interaction for nasal irrigation among individuals using nasal corticosteroids: the interaction terms for in the imputed dataset for the RSDI at 3 months was -2.90 (-10.54, 4.75; p=0.457) and at 6 months: 0.37 (-7.88, 8.61; p=0.931) i.e. no evidence of a lesser effect. Furthermore only a minority used nasal steroids (irrigation groups 9.5% (42/442); no irrigation groups 10% (43/429).

**Discussion**

**Brief Summary.** This is one of the few studies to address the effectiveness of brief advice to use nasal irrigation or steam inhalation for chronic or recurrent sinus symptoms, and the largest trial in any setting. Nasal irrigation resulted in modest improvement in the primary outcome RSDI which was significant at both 3 and 6 months, and evidence of improvement in several secondary outcomes.

**Explanation of findings in the context of previous literature.** The RSDI improved with irrigation but the control group also improved. The 2-3 point difference between groups, and a number needed to treat of approximately 13, was smaller than prior US trials (Rabago et al9; Pynnonen et al10) who enrolled primary care, secondary care, and community volunteer patients9 10. In the latter studies nasal irrigation and control participants reported changes on 100 point scales of 14 and 1 points; and 15 and 8.5 points respectively. Several factors may contribute to the differences: Rabago allowed participants to know their previous ratings which may have anchored the control group responses, and provided individualised training (including video, live demonstration and coached practice to ensure proficiency) which was valued18; Pynnonen also allowed coached practice and both studies had more follow-up contacts and diary monitoring. These more intensive approaches may have increased treatment effect through adherence. However, participants in the current study used irrigation on most days, and the impact was the same in participants irrigating more often. Although the number of irrigations may not explain the discrepancies, the quality or duration of irrigation may still be relevant. Rabago assessed a more severely affected sample, but there was no evidence of greater effectiveness for those higher baseline RSDI in the current study. Rabago and Pynnonen both studied younger populations (10 and 6 years younger respectively) with a much shorter history of sinus complaints, so symptoms may have been more amenable to change. Culturally, nasal irrigation is popular in the USA and expectations about benefit are higher.

We found potentially important changes in other outcomes – particularly reduced headaches, reduced use of over the counter (OTC) medication, and reduced medicalisation i.e. belief in the need to see the doctor in future episodes. Although as might be expected over only 6 months follow-up there were no significant differences in either GP consultations nor antibiotic use, the evidence of reduced medicalisation is important in the longer term given most consultations result in an antibiotic prescription3 and the attendant dangers of antibiotic resistance.

Apart from for headaches, steam inhalation was ineffective, which is matched by the limited impact for acute coryzal illness6, or in acute RTIs more generally7. However the benefit for nasal irrigation was mostly in the combined steam/irrigation group which suggests there may be a role for steam inhalation in supporting nasal irrigation. There was no evidence of the modest harm previously observed for acute RTIs (minor thermal injury7). We chose a pragmatic target of inhalations once a day since intrusive interventions with high ‘work‘ and limited benefit are not maintained. Whether a more intensive approach to inhalations might be beneficial is unclear

**Limitations.** Nine percent of consented participants did not provide baseline RSDI scores - much higher than our previous studies. This likely reflects suboptimal engagement for individuals when consenting, and despite feedback to practices this did not improve during the trial. However, the sample who did return the questionnaire were almost identical to the sample who consented (Table1).Slightly under 80%follow-up was achieved but there was little evidence of attrition bias using multiple imputation. The primary outcome is self-reported, but symptomatic impact can only be documented by self-report, and the ineffectiveness of steam inhalation suggests generalised reporting bias is unlikely. Furthermore, meaningful changes also occurred in other outcomes. The rate of uptake to the baseline appointment was more than 40%, which is good for a cold-calling invitation, and the participants were our intended target i.e. sufficiently concerned about their symptoms to be motivated for self-management. Randomisation envelopes were chosen for good logistic reasons, but equally they can be used to undermine randomisation. However there was no evidence either of selective use of envelopes nor differential group characteristics, suggesting randomisation worked, and we also controlled for a range of baseline characteristics. We chose chronic or recurrent acute sinus symptoms so the sample was heterogeneous (e.g. some having hay fever; variable prior illness duration), but these criteria were similar to prior studies and to the Cochrane review, and there was no evidence of significant selective treatment effects in any clinical subgroup. The inclusion criteria were based on the clinical diagnosis recorded by the doctor, and participants reported significant impact on their quality of life, but it is possible that a more tightly defined group could benefit more. The timing of nasal irrigation was not specified, but we found no evidence of a lesser effect among nasal corticosteroid users.

**Conclusion.** A brief pragmatic nasal irrigation intervention in primary care results in less impact than in prior efficacy studies, but reduced overall symptom burden, headache, OTC medication use and the perceived need to consult GPs. Steam inhalation has no consistent benefits. Future research on nasal irrigation should address how much coaching is needed, the role of expectations, and its place in acute sinusitis.

**Acknowledgement**

SNIFS Study team: Paul Little; Beth Stuart; Mark Mullee; Tammy Thomas; Sophie Johnson; Gerry Leydon; David Rabago; Samantha Hall; Ian Williamson ; Lily Yao; Shihua Zhu; James Raftery;Mike Moore; Chris Smith, Stephen Petley, Ben Holdstock-Brown. PL affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained

**Competing Interests.** All authors have completed the Unified Competing Interest form at <http://www.icmje.org/coi_disclosure.pdf> (available on request from the corresponding author) and declare: no support from any organisation for the submitted work ; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years, no other relationships or activities that could appear to have influenced the submitted work. Data sharing: the analysis of complete cases is available on request.

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**Data sharing.** The data set we used for this analysis is available to others on request to PL with details of the analysis proposed; this will be reviewed by the authors and access granted if the request is scientifically sound.

**Ethics:** The study was given ethical approval by the Hampshire Rec B Research Ethics Committee

(number 07/Q1704/69).

**Contributorship:** Paul Little (GP and Professor of Primary Care Research, University of Southampton) had the original idea for the protocol, led protocol development and the funding application, supervised the running of the study centre,contributed to the analysis, led the drafting of the paper. Tammy Thomas (trial manager, University of Southampton) developed the protocol, provided day to day overall management of the study, coordinated recruitment and commented on drafts of the paper. Sophie Johnson provided coordination and data management for the Southampton study centre. Guiqing Yao (Health Economist) and Shihua Zhu with James Raftery developed the protocol for analysis of the notes review data and contributed to the drafting of the paper. Michael Moore (GP and Professor in Primary Care, University of Southampton), developed the protocol for funding, contributed to the management of the study, contributed to the analysis and to the drafting of the paper. Ian Williamson (GP and Senior Lecturer in Primary Care, University of Southampton), developed the protocol for funding, contributed to the management of the study, contributed to the analysis and to the drafting of the paper. James Raftery (Professor of Health Economics, University of Southampton), developed the protocol for funding, contributed to the management of the study, supervised the analysis of resource use data, contributed to the drafting of the paper. Beth Stuart. (Study Statistician, University of Southampton) with input from Mark Mullee (RDS study statistician) developed the analysis protocol, performed the quantitative analysis, and contributed to drafting of the paper. Gerry Leydon (Associate Professor, University of Southampton), David Rabago, Samantha Richards-Hall, Chris Smith, Stephen Petley, and Ben Holdstock-Brown (CS, SP and BH-B were all medical students at the time) were full members of the SNIFS study team and all contributed to developing or refining the protocol; the management of the study; agreeing the analysis, and commenting on drafts of the paper.

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**Table 1a. Baseline characteristics by factorial group (mean (SD) unless specified)**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Participants who returned baseline primary outcomes | | | | All randomised participants | | | |
|  | No nasal irrigation | Nasal irrigation | No steam inhalation | Steam inhalation | No nasal irrigation | Nasal irrigation | No steam inhalation | Steam inhalation |
| Female | 299/428 (69.9%) | 317/442 (71.7%) | 311/442 (70.4%) | 305/428 (71.3%) | 324/465 (69.7%) | 358/494 (72.5%) | 337/478 (70.5%) | 345/481 (71.7%) |
| Age | 52.46 (13.91) | 52.46 (14.31) | 52.21 (13.72) | 52.71 (14.50) | 51.88 (13.95) | 51.60 (14.48) | 51.70 (13.68) | 51.77 (14.73) |
| Age left school | 17.90 (2.89) | 17.89 (3.02) | 18.03 (3.08) | 17.76 (2.82) | 17.91 (2.89) | 17.89 (3.02) | 18.03 (3.08) | 17.75 (2.81) |
| History of hay fever or allergy | 219/414 (52.9%) | 223/431 (51.7%) | 211/430 (49.1%) | 231/415 (55.7%) | 231/441 (52.4%) | 241/470 (51.3%) | 221/ 456 (48.5%) | 251/455 (55.2%) |
| Never smoked | 195/384 (50.8%) | 189/393 (48.1%) | 204/393 (51.9%) | 180/384 (46.9%) | 206/413 (49.9%) | 206/432 (47.7%) | 216/419 (51.6%) | 196/426 (46.0%) |
| IMD score | 21.29 (13.02) | 21.63 (13.31) | 21.54 (13.25) | 21.37 (13.08) | 22.34 (12.96) | 22.97 (13.16) | 22.52 (13.16) | 22.80 (12.96) |
| Baseline severity (single item question) | 2.77 (0.96) | 2.76 (0.90) | 2.73 (0.94) | 2.81 (0.91) | 2.77 (0.95) | 2.77  (0.90) | 2.74 (0.94) | 2.81 (0.90) |
| Years sinus problems | 19.36 (16.21) | 18.70 (15.62) | 19.55 (16.47) | 18.48 (15.32) | 19.22 (16.26) | 18.01 (15.43) | 19.10 (16.28) | 18.12 (15.42) |

**Table 1b. Baseline characteristics by individual groups (mean (SD) unless specified)**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Participants who returned baseline primary outcomes | | | | All randomised participants | | | |
|  | Control | Nasal irrigation | Steam inhalation | Both nasal irrigation and steam inhalation | Control | Nasal irrigation | Steam inhalation | Both nasal irrigation and steam inhalation |
| Female | 151/210 (71.9%) | 160/232 (69.0%) | 148/218 (67.9%) | 157/210 (74.8%) | 160/225 (71.1%) | 177/253 (70.0%) | 164/240 (68.3%) | 181/241 (75.1%) |
| Age | 52.60 (13.66) | 51.85 (13.80) | 52.31 (14.18) | 53.13 (14.85) | 52.10 (13.61) | 51.35 (13.77) | 51.67 (14.29) | 51.87 (15.20) |
| Age left school | 18.01 (2.95) | 18.05 (3.20) | 17.80 (2.83) | 17.71 (2.81) | 18.00 (2.95) | 18.05 (3.20) | 17.81 (2.82) | 17.70 (2.80) |
| History of hay fever or allergy | 107/203 (52.7%) | 104/227 (45.8%) | 112/211 (53.1%) | 119/204 (58.3%) | 111/212 (52.4%) | 110/244 (45.1%) | 120/229 (52.4%) | 131/226 (58.0%) |
| Never smoked | 98/187 (52.4%) | 106/206 (51.5%) | 97/197 (49.2%) | 83/187 (44.4%) | 102/196 (52.0%) | 114/223 (51.1%) | 104/217 (47.9%) | 92/209 (44.0%) |
| IMD score | 21.15 (13.32) | 21.90 (13.20) | 21.42 (12.74) | 21.32 (13.46) | 22.05 (13.27) | 22.95 (13.07) | 22.62 (12.68) | 22.98 (13.27) |
| Baseline severity (single item question) | 2.72 (0.95) | 2.74 (0.93) | 2.82 (0.96) | 2.78 (0.86) | N/A | N/A | N/A | N/A |
| Years sinus problems | 20.01 (17.05) | 19.14 (15.95) | 18.75 (15.39) | 18.20 (15.27) | 19.72 (16.92) | 18.55 (15.70) | 18.78 (15.68) | 17.43 (15.14) |

**Table 2. Mean (s.d.) at baseline, and estimates using multiple imputation at 3 months and 6 months on RSDI and SNOT-20 for factorial groups**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | No Nasal irrigation | Nasal Irrigation | No steam inhalation | Steam inhalation |
| RSDI at baseline | 44.18  (19.29) | 43.02  (20.61) | 43.60  (20.59) | 43.58  (19.32) |
| RSDI at 3 months | 38.95 (19.65) | 35.60 (21.13) | 37.60 (20.59) | 36.89 (20.37) |
| RSDI at 6 months | 38.26 (20.05) | 35.06 (22.33) | 36.83 (21.87) | 36.43 (20.69) |
| SNOT-20 at baseline | 2.45 (1.00) | 2.37 (0.95) | 2.40 (0.99) | 2.41 (0.97) |
| SNOT-20 at 3 months | 2.14 (1.02) | 1.97 (1.07) | 2.07 (1.04) | 2.04 (1.05) |
| SNOT-20 at 6 months | 2.16 (1.07) | 2.01 (1.11) | 2.10 (1.09) | 2.07 (1.10) |

**Table 2b. Mean (s.d.) at baseline, and estimates using multiple imputation at 3 months and 6 months on RSDI and SNOT-20 for individuals groups**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Control | Nasal irrigation | Steam inhalation | Both nasal irrigation and steam inhalation |
| RSDI at baseline | 44.26 (20.02) | 43.01 (21.11) | 44.11 (18.60) | 43.02 (20.09)s |
| RSDI at 3 months | 39.27 (19.72) | 36.09 (21.22) | 38.66 (19.57) | 35.05 (21.01) |
| RSDI at 6 months | 38.05 (20.61) | 35.72 (22.88) | 38.45 (19.58) | 34.33 (21.68) |
| SNOT-20 at baseline | 2.45 (1.02) | 2.36 (0.85) | 2.44 (0.98) | 2.37 (0.95) |
| SNOT-20 at 3 months | 2.17 (1.00) | 1.98 (1.07) | 2.11 (1.03) | 1.96 (1.06) |
| SNOT-20 at 6 months | 2.17 (1.06) | 2.03 (1.11) | 2.15 (1.08) | 1.99 (1.12) |

**Table 3. Estimated differences in RSDI and SNOT-20 at 3 and 6 months**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | RSDI @ 3 months | | RSDI @ 6 months | | SNOT-20 @ 3 months | | SNOT-20 @ 6 months | |
| Nasal irrigation |  |  |  |  |  |  |  |  |
| * Crude mean difference |  | -2.53 (-4.68, -0.39) |  | -2.34 (-4.49, -0.07) |  | -0.12 (-0.25, 0.01) |  | -0.10 (-0.24, 0.03) |
| * Adjusted mean difference |  | -2.51 (-4.65, -0.37) |  | -2.41 (-4.66, -0.16) |  | -0.12 (-0.25, 0.004) |  | -0.11 (-0.25, 0.03) |
| Steam inhalation |  |  |  |  |  |  |  |  |
| * Crude mean difference |  | -0.78 (-2.92, 1.36) |  | -0.46 (-2.75, 1.84) |  | -0.04 (-0.17, 0.09) |  | -0.03 (-0.17, 0.10) |
| * Adjusted mean difference |  | -0.73 (-2.85, 1.39) |  | -0.60 (-2.87, 1.68) |  | -0.05 (-0.17, 0.08) |  | -0.04 (-0.17, 0.10) |
| Interaction term |  | -0.53 (-4.81, 3.65) |  | -1.91 (-6.34, 2.52) |  | 0.02 (-0.22, 0.27) |  | -0.03 (-0.30, 0.23) |

**Table 4. Impact on single item sinus severity assessment, attitudes to antibiotics and consulting**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Impact of on sinus severity assessment (3 months)** | | **Impact of on sinus severity assessment (6 months)** | | **\*Belief in antibiotics** | | **\*Would not visit doctor next time (3 months)** | | **\*Would not visit doctor next time (6 months)** | |
| **Nasal irrigation** |  |  |  |  |  |  |  |  |  |  |
| * Crude mean difference |  | 0.07 (-0.17, 0.30) |  | 0.23 (-0.03, 0.49) |  | 0.08 (-0.14, 0.30) |  | 0.19 (-0.04, 0.42) |  | 0.30 (0.08, 0.53) |
| * Adjusted mean difference |  | 0.07 (-0.17, 0.31) |  | 0.22 (-0.04, 0.48) |  | 0.09 (-0.13, 0.30) |  | 0.22 (-0.01, 0.45) |  | 0.32 (0.09, 0.54) |
| **Steam irrigation** |  |  |  |  |  |  |  |  |  |  |
| * Crude mean difference |  | 0.05 (-0.20, 0.30) |  | 0.11 (-0.15, 0.37) |  | -0.11 (-0.34, 0.11) |  | -0.04 (-0.26, 0.20) |  | 0.08 (-0.16, 0.31) |
| * Adjusted mean difference |  | 0.06 (-0.18, 0.31) |  | 0.11 (-0.15, 0.37) |  | -0.12 (-0.34, 0.10) |  | -0.01 (-0.24, 0.22) |  | 0.08 (-0.15, 0.31) |

*\*Agreeing with statement on a 7 point Likert scale*

***Table 5. Headache, nose bleeds, OTC use during the last month reported at 3 and 6 months\****

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | No nasal irrigation | | Nasal irrigation | | No steam inhalation | | Steam inhalation | |
| **3 months** | | | | | | | | |
| **Headache** |  | 81.7% |  | 72.0% |  | 80.4% |  | 73.1% |
| Univariate risk ratio |  | 1.00 |  | 0.88 (0.81, 0.95) |  | 1.00 |  | 0.90 (0.83, 0.98) |
| Adjusted risk ratio |  | 1.00 |  | 0.88 (0.81, 0.96) |  | 1.00 |  | 0.91 (0.84, 0.99) |
|  |  |  |  |  |  |  |  |  |
| **Harms: Nose bleeds, soreness or burning** |  | 65.6% |  | 64.2% |  | 66.8% |  | 62.9% |
| Univariate risk ratio |  | 1.00 |  | 0.98 (0.88, 1.10) |  | 1.00 |  | 0.94 (0.83, 1.05) |
| Adjusted risk ratio |  | 1.00 |  | 0.98 (0.88, 1.09) |  | 1.00 |  | 0.92 (0.82, 1.03) |
|  |  |  |  |  |  |  |  |  |
| **OTC treatments used in the last month** |  | 67.4% |  | 60.0% |  | 64.3% |  | 62.9% |
| Univariate risk ratio |  | 1.00 |  | 0.89 (0.80, 1.00) |  | 1.00 |  | 0.98 (0.87, 1.10) |
| Adjusted risk ratio |  | 1.00 |  | 0.90 (0.81, 1.00) |  | 1.00 |  | 0.99 (0.89, 1.11) |
| **6 months** | | | | | | | | |
| **Headache** |  | 79.8% |  | 73.9% |  | 77.3% |  | 76.2% |
| Univariate risk ratio |  | 1.00 |  | 0.93 (0.85, 1.01) |  | 1.00 |  | 0.98 (0.90, 1.07) |
| Adjusted risk ratio |  | 1.00 |  | 0.93 (0.85, 1.01) |  | 1.00 |  | 0.99 (0.91, 1.08) |
|  |  |  |  |  |  |  |  |  |
| **Harms: Nose bleeds, soreness or burning** |  | 66.7% |  | 60.6% |  | 63.9% |  | 63.3% |
| Univariate risk ratio |  | 1.00 |  | 0.91 (0.81, 1.02) |  | 1.00 |  | 0.99 (0.87, 1.13) |
| Adjusted risk ratio |  | 1.00 |  | 0.90 (0.80, 1.01) |  | 1.00 |  | 0.98 (0.86, 1.12) |
|  |  |  |  |  |  |  |  |  |
| **OTC treatments used in the last month** |  | 68.0% |  | 59.4% |  | 64.8% |  | 62.4% |
| Univariate risk ratio |  | 1.00 |  | 0.87 (0.78, 0.98) |  | 1.00 |  | 0.96 (0.85, 1.08) |
| Adjusted risk ratio |  | 1.00 |  | 0.87 (0.78, 0.97) |  | 1.00 |  | 0.95 (0.85, 1.07) |

\* Participants were asked at 3 months whether they had used aspirin gargles, difflam gargles, cough medicine, vicks vapour rubs, echinacea, lozenges or nasal sprays in the preceding month

**Table 6. Number of days feeling unwell with respiratory tract infections (RTIs: cough;cold;sore-throat;fever) or sinusitis in the past month**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | No nasal irrigation | Nasal irrigation | No steam inhalation | Steam inhalation |
| **RTIs: Days unwell**  **(at 3 months)** |  |  |  |  |
| Median number of days | 2 (0,7) | 1 (0,7) | 2 (0,7) | 2 (0,8) |
| Univariate risk ratio | 1.00 | 0.93 (0.76, 1.14) | 1.00 | 1.06 (0.86, 1.29) |
| Adjusted risk ratio | 1.00 | 0.95 (0.77, 1.16) | 1.00 | 1.10 (0.89, 1.35) |
| **RTIs: Days unwell**  **(at 6 months)** |  |  |  |  |
| Median number of days | 3 (0,8) | 2 (0,7) | 2 (0,7) | 2 (0,8) |
| Univariate risk ratio | 1.00 | 0.96 (0.78, 1.19) | 1.00 | 1.17 (0.94, 1.45) |
| Adjusted risk ratio | 1.00 | 0.96 (0.77, 1.18) | 1.00 | 1.18 (0.95, 1.46) |
| **Sinusitis: days unwell**  **( 3 months)** |  |  |  |  |
| Median number of days | 6 (1,18) | 5 (0,15) | 6 (1,17) | 6 (0,18) |
| Univariate risk ratio | 1.00 | 0.88 (0.75, 1.03) | 1.00 | 0.97 (0.83, 1.14) |
| Adjusted risk ratio | 1.00 | 0.88 (0.75, 1.03) | 1.00 | 0.95 (0.81, 1.12) |
| **Sinusitis:days unwell**  **(6 months)** |  |  |  |  |
| Median number of days | 7 (0,18) | 4 (0,14) | 5 (0,14) | 6 (0,18) |
| Univariate risk ratio | 1.00 | 0.82 (0.69, 0.98) | 1.00 | 1.02 (0.86, 1.21) |
| Adjusted risk ratio | 1.00 | 0.81 (0.68, 0.96) | 1.00 | 1.02 (0.85, 1.22) |

*Appendix 1*

***Table 7. Proportions achieving at least a 10 point improvement in RSDI score***

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **No nasal irrigation** | | **Nasal irrigation** | | **No steam inhalation** | | **Steam inhalation** | |
|  |  | Imputed |  | Imputed |  | Imputed |  | Imputed |
| **6 months** |  | 36.6% |  | 44.1% |  | 39.4% |  | 41.5% |
| Univariate risk ratio |  | 1.00 |  | 1.37 (1.01, 1.86) |  | 1.00 |  | 1.10 (0.81, 1.51) |
| Adjusted risk ratio |  | 1.00 |  | 1.38 (1.01, 1.88) |  | 1.00 |  | 1.11 (0.81, 1.53) |
|  |  |  |  |  |  |  |  |  |
| **3 months** |  | 32.3% |  | 39.7% |  | 36.8% |  | 35.3% |
| Univariate risk ratio |  | 1.00 |  | 1.37 (1.01, 1.87) |  | 1.00 |  | 0.95 (0.70, 1.29) |
| Adjusted risk ratio |  | 1.00 |  | 1.36 (1.00, 1.85) |  | 1.00 |  | 0.94 (0.68, 1.28) |

***Table 8. Mean differences in subscales of the RSDI at 3 and 6 months***

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **3 months** | |  | |  | | **6 months** | |  | |  | |
|  | **Physical** | | **Functional** | | **Emotional** | | **Physical** | | **Functional** | | **Emotional** | |
| **Nasal irrigation** |  |  |  |  |  |  |  |  |  |  |  |  |
| **Crude** |  | -1.25  (-2.09, -0.41) |  | -0.65  (-1.36, 0.07) |  | -0.77  (-1.57, 0.03) |  | -1.28  (-2.18, -0.39) |  | -0.51  (-1.27, 0.24) |  | -0.69  (-1.51, 0.14) |
| **Adjusted** |  | -1.28  (-2.12, -0.45) |  | -0.63  (-1.34, 0.08) |  | -0.79  (-1.59, 0.01) |  | -1.30  (-2.18, -0.40) |  | -0.55  (-1.29, 0.20) |  | -0.73  (-1.55, 0.10) |
| **Steam inhalation** |  |  |  |  |  |  |  |  |  |  |  |  |
| **Crude** |  | -0.15  (-1.01, 0.70) |  | -0.31  (-1.03, 0.41) |  | -0.34  (-1.12, 0.45) |  | -0.15  (-1.06, 0.76) |  | -0.25  (-1.03, 0.53) |  | -0.04  (-0.88, 0.80) |
| **Adjusted** |  | -0.19  (-1.04, 0.65) |  | -0.30  (-1.01, 0.42) |  | -0.37  (-1.15, 0.41) |  | -0.20  (-1.09, 0.70) |  | -0.32  (-1.10, 0.45) |  | -0.07  (-0.91, 0.77) |

**Table 9 . Proportions achieving a 3.8 point difference or more in the RSDI physical subscale**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | No nasal irrigation | | Nasal irrigation | | No steam inhalation | | Steam inhalation | |
|  |  | Imputed |  | Imputed |  | Imputed |  | Imputed |
| **6 months** |  | 36.7% |  | 45.6% |  | 41.3% |  | 41.1% |
| Univariate odds |  | 1.00 |  | 1.45  (1.06, 1.99) |  | 1.00 |  | 1.01 (0.74, 1.37) |
| Adjusted odds |  | 1.00 |  | 1.45  (1.05, 2.00) |  | 1.00 |  | 1.00 (0.73, 1.38) |
| **3 months** |  | 33.4% |  | 42.1% |  | 39.1% |  | 36.5% |
| Univariate odds |  | 1.00 |  | 1.45  (1.06, 1.97) |  | 1.00 |  | 0.91 (0.67, 1.24) |
| Adjusted odds |  | 1.00 |  | 1.44 (1.05, 1.97) |  | 1.00 |  | 0.91 (0.66, 1.24) |

**Table 10. Results for the four separate intervention groups.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Control | Nasal Irrigation | Steam Inhalation | Combined Treatment |
| RSDI at baseline | 44.26 (19.98) | 43.01 (21.07) | 44.11 (18.56) | 43.02 (20.04) |
| RSDI at 3 months | 39.27 (19.73) | 36.09 (21.22) | 38.66 (19.57) | 35.05 (21.01) |
| RSDI at 6 months | 38.05 (20.61) | 35.72 (22.88) | 38.45 (19.48) | 34.33 (21.68) |
| Univariate difference at 3 months |  | -2.27 (-5.17, 0.63) | -0.51 (-3.40, 2.38) | -3.31 (-6.49, -0.13) |
| Multivariate difference at 3 months |  | -2.26 (-5.15, 0.63) | -0.47 (-3.31, 2.38) | -3.24 (-6.40, -0.09) |
| Univariate difference at 6 months |  | -1.39 (-4.56, 1.78) | 0.50 (-2.49, 3.51) | -2.80 (-6.18, 0.59) |
| Multivariate difference at 6 months |  | -1.29 (-4.42, 1.85) | 0.56 (-2.41, 3.53) | -3.02 (-6.39, 0.35) |

**Table 11. Effect modification in subgroups**

|  |  |  |
| --- | --- | --- |
| Subgroup | Interaction term for nasal irrigation treatment at 6 months | Interaction term for steam inhalation treatment at 6 months |
| History of hay fever | -0.79 (5.38, 3.79) | 2.36 (-2.20, 6.91) |
| Gender | -0.64 (-5.29, 4.00) | -0.86 (-5.79, 4.07) |
| Age above median (age 50) | 2.02 (-2.51, 6.55) | -0.99 (-5.48, 3.50) |
| IMD score above median (score 34) | 0.03 (-4.47, 4.52) | -2.03 (-6.58, 2.52) |
| Prior duration of illness above median (15 years ) | -1.45 (-7.72, 4.83) | 1.78 (-2.69, 6.25) |
| Baseline RSDI above median (score 44) | 1.17 (-4.02, 6.37) | -1.57 (-6.60, 3.46) |
| Complied with intervention (median 20 days or more) | 3.15 (-5.46, 11.75) | -1.73 (-10.68, 7.21) |

**Table 12a Results for factorial groups split below median RSDI at baseline**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | No Nasal irrigation | Nasal irrigation | No steam inhalation | Steam inhalation |
| RSDI at baseline | 27.71 (10.90) | 27.61 (10.86) | 27.08 (11.04) | 28.24 (10.68) |
| RSDI at 3 months | 27.03 (14.86) | 24.14 (15.38) | 25.18 (15.71) | 25.80 (14.67) |
| RSDI at 6 months | 25.96 (15.78) | 23.41 (16.54) | 24.31 (16.66) | 24.90 (15.80) |
| Univariate difference at 3 months |  | -2.83 (-5.52, -0.13) |  | -0.34 (-3.07, 2.39) |
| Multivariate difference at 3 months |  | -2.91 (-5.62, -0.20) |  | -0.32 (-3.02, 2.38) |
| Univariate difference at 6 months |  | -2.49 (-5.59, 0.624) |  | -0.32 (-3.32, 2.69) |
| Multivariate difference at 6 months |  | -2.44 (-5.57, 0.68) |  | -0.51 (-3.53, 2.50) |

**Table 12b. Results for factorial groups above the median RSDI at baseline**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | No Nasal irrigation | Nasal irrigation | No steam inhalation | Steam inhalation |
| RSDI at baseline | 59.55 (10.84) | 60.61 (13,81) | 60.43 (12.99) | 59.73 (11.67) |
| RSDI at 3 months | 50.08 (16.85) | 48.73 (19.08) | 50.25 (16.94) | 48.57 (18.95) |
| RSDI at 6 months | 49.72 (16.48) | 48.40 (20.56) | 49.57 (18.98) | 48.57 (18.11) |
| Univariate difference at 3 months |  | -2.20 (-5.51, 1.11) |  | -1.28 (-4.59 2.04) |
| Multivariate difference at 3 months |  | -2.49 (-5.73, 0.75) |  | -1.34 (-4.61, 1.92) |
| Univariate difference at 6 months |  | -2.22 (-5.61, 1.17) |  | -0.55 (-3.94, 2.85) |
| Multivariate difference at 6 months |  | -2.17 (-5.55, 1.20) |  | -0.46 (-3.85, 2.94) |

**Appendix 2.**

**The rhinosinusitis disability index (RSDI) domains and items**

**Physical**

The pain or pressure in my face makes it difficult for me to concentrate

The pain in my eyes makes it difficult for me to read

I have difficulty stooping over to lift objects because of face pressure

Because of my problem I have difficulty with strenuous yard work and housework

Straining increases or worsens my problem

I am inconvenienced by my chronic runny nose

Food does not taste good because of my change in smell

My frequent sniffing is irritating to my friends and family

Because of my problem I don’t sleep well

I have difficulty with exertion due to my nasal obstruction

My sexual activity is affected by my problem

**Functional**

Because of my problem I feel handicapped

Because of my problem I feel restricted in performance of my routine daily activities

Because of my problem I restrict my recreational activities

Because of my problem I feel frustrated

Because of my problem I feel fatigued

Because of my problem I avoid traveling

Because of my problem I miss work or social activities

My outlook on the world is affected by my problem

Because of my problem I find it difficult to focus my attention away from my

problem and on other things

**Emotional**

Because of my problem I feel stressed in relationships with friends and family

Because of my problem I feel confused

Because of my problem I have difficulty paying attention

Because of my problem I avoid being around people

Because of my problem I am frequently angry

Because of my problem I do not like to socialize

Because of my problem I frequently feel tense

Because of my problem I frequently feel irritable

Because of my problem I am depressed

My problem places stress on my relationships with members of my family or friends

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