

Appendix 1: Supplementary information [posted as supplied by author]

Details of Interventions

Medication Advice. Advice was one of:

- 1) Paracetamol. Participants will be advised to use paracetamol as their only antipyretic medication.
- 2) Ibuprofen. Participants will be advised to use ibuprofen as their only antipyretic medication.
- or 3) Combined paracetamol and ibuprofen. Participants will be advised to use paracetamol and ibuprofen.

Dosing Advice. Advice was either:

- 1) Regular dosing. Advice to take the medication(s) four times per day (irrespective of whether symptoms or fever have returned)
- or 2) As required dosing. Advice to take medication(s) as required by symptoms up to a maximum of four doses per day

Steam Advice. Advice was either:

- 1) Steam. Subjects will be asked to inhale steam for 5 minutes, three times per day. Adults will be instructed to place a towel over their head over a bowl of recently boiled water. Children will be instructed to sit in a steamy room (made steamy by running a hot shower, or boiling a kettle in the room). Participants will receive written and verbal instructions at the beginning of the study
- or 2) No Steam. Subjects will be asked not to use steam inhalation

Rationale for steam advice

A Cochrane review of heated humidified air for the common cold identified 6 trials. All used a “Rhinotherm” or similar device to deliver the steam¹³. There have been some reports of burns following steam inhalation (for example Murphy et al¹⁴). Major injury is probably rare and have occurred exclusively in children using boiling water after poor instruction. Authors of these reports have therefore recommended advising parents to “sit in the bathroom with a hot shower running” and this advice is also given in textbooks and the NHS Direct website. There were no significant reported problems with this advice and hence this is the advice we used for young children.

Total duration. A Cochrane review of heated humidified air for the common cold identified 6 trials. All used a “Rhinotherm” or similar device to deliver the steam¹³. The most common duration of steam inhalation was 20 minutes (3 studies) but was half 30 minutes in one trial and 60 minutes in another. The review concluded that there was a difference in effectiveness with the duration of warm vapour inhalation, with a longer period (30 minutes) being associated with no benefit and increased resistance of the nasal passage.

Method of steaming. A rhinotherm or similar device is not widely advocated. Usual guidance is to use a bowl of water and a towel. For example, the NHS direct website recommended “a towel is placed over the head over a bowl of very hot water”. In this context 20 minutes of treatment would not be feasible as the water would not remain hot enough. We decided on advising 5 minutes of treatment three times per day as this was practical and would approximate the total of 20 minutes used in some of the previous trials.

Delayed or No Prescription. Advice was either:

- 1) Patient led. The patient is given antibiotics and asked to wait to use them
- 2) Post-dating. The patient is given antibiotics, but post dated.
- 3) Collection. Instructions to wait but can request antibiotics from front desk¹⁵
- 4) Recontact/phone. Patient is asked to contact/phone the surgery to leave message for doctor/nurse re request antibiotics, and able to come to reception
- 5) No offer of prescription but a clinical review for worsening symptoms

For each type of respiratory infection the advice was tailored to the natural history of the disease¹⁹

- **Ear infections:** a further 3 days
- **Sore throat:** a further 5 days
- **Cold symptoms:** a further 5 days
- **Acute rhinosinusitis: a further 10-12 days**
- **Acute cough/ acute bronchitis :** a further 10 days

We advised Penicillin V (for sore throat), Amoxycillin (for otitis media, rhinosinusitis, acute cold, flu-like illness and chest infections) using dosaging according to BNF guidelines for age.

Interactions and per protocol analysis

Interaction between interventions

For symptom severity in the first few days (days 2 to 4) there was no evidence of a significant interaction between Analgesia use and steam (ibuprofen interaction term -0.11, 95% CI -0.41 to 0.19; combined 0.17 (-0.14 to 0.47)), or Analgesia and Dosing (ibuprofen interaction term -0.27,-0.57 to 0.03; combined 0.08,-0.22 to 0.38))

Symptom severity: Subgroup analysis

Among pre-specified subgroups there was no evidence for a significant interaction between analgesic group and:

- longer prior duration of symptoms (more than 5 days: interaction term for ibuprofen 0.2 (-0.1 to 0.5) combined 0.1(-0.40 to 0.2));
- higher baseline temperature (≥ 37.5) (interaction term for ibuprofen -0.1 (-0.4 to 0.2), combined 0.0(-0.40 to 0.3));
- higher baseline severity of symptoms (higher than the median: interaction term for ibuprofen 0.3 , -0.04 to 0.6; combined 0.1 -0.2 to 0.4))
- Diagnosis of otitis media (interaction term for ibuprofen 0.02, -0.01 to 0.21; interaction term for combined group -0.33, -0.86 to 0.21)

Patients with uncomplicated lower respiratory infections (LRTI) were significantly more likely to benefit from advice to use ibuprofen (interaction term -0.50, -0.93 to -0.07,

p=0.022) or the combined strategy (-0.57, -1.00 to -0.14, p=0.009). Those aged 16 or under were also more likely to benefit from advice to use ibuprofen (interaction term for ibuprofen: -0.67, -1.02 to -0.32) but not the combined strategy (interaction term -0.19, -0.52 to 0.15). There was no significant difference for the effect of analgesics on temperature either for those with temperature ≥ 37.5 (interaction term for ibuprofen 0.16 -0.14 to 0.47; interaction term for combined group 0.15, -0.16 to 0.46) or with fever reported in the previous 24 hours (interaction term for ibuprofen 0.03, -0.22 to 0.29; interaction term for combined group -0.01, 0.00 to 0.24).

Other outcomes. There was no interaction between interventions and no effect of any intervention on mean temperature readings the duration of symptoms rated moderately bad or worse, antibiotic use, beliefs or satisfaction, nor was there any significant interaction for any of the pre-defined subgroups.

Per protocol analysis.

The results were similar for the per protocol analysis for analgesic group in the whole cohort with no evidence of benefit for ibuprofen for symptom severity (+0.003, -0.18 to 0.19) or nor combined ibuprofen and paracetamol (+0.17, -0.002 to 0.34). Similarly for the Steam inhalation per protocol analysis there was minimal impact of steam on symptom severity (+0.07, -0.09 to 0.22).

Table A. Effectiveness of advice to use a regular dose of dose of analgesics

	Crude figures		*Adjusted estimates: (95% CI)	
	As required	Regular		p
			Mean Difference	
Mean (sd) symptom severity days 2-4	1.72 (0.93)	1.72 (0.89)	-0.02 (-0.14 to 0.10)	0.748
Mean (sd) temperature days 2-4	36.6 (0.55)	36.6 (0.63)	0.02 (0.09 to 0.12)	0.722
			Hazard ratio	
Median (IQR) symptom duration (rated moderately bad or worse)	4 (3 to 7)	4 (3 to 7)	0.95 (0.81 to 1.12)	0.539
			Risk ratio	
Number using antibiotics (%)	229/379 (60%)	201/365 (55%)	0.92 (0.77 to 1.07)	0.312
Number returning with new or unresolving symptoms or complications within 1 month	63/444 (14%)	78/436 (18%)	1.22 (0.90 to 1.66)	0.194
Very Satisfied with the consultation	134/151 (89%)	108/130 (83%)	0.95 (0.83 to 1.03)	0.326

*Models all controlled for baseline symptom severity, dosing, steam, antibiotic prescribing and smoking. The duration model also controlled for prior duration of illness. The temperature model also controlled for baseline temperature.

Return with non-resolving symptoms controlled for initial diagnosis.

Table B Baseline table for those with symptom severity recorded at follow-up (for comparison with Table1)

	Paracetamol	Ibuprofen	Both	As required	Regular	No Steam	Steam
Prior Duration (days)	8.0 (7.5)	7.4 (6.7)	7.1 (6.5)	7.5 (6.2)	7.5 (7.6)	7.4 (7.3)	7.5 (6.6)
Mean Baseline severity (all symptoms)	1.0 (0.45)	1.0 (0.45)	1.0 (0.44)	1.0 (0.44)	1.1 (0.46)	1.1 (0.44)	1.0 (0.45)
Fever in previous 24 hours	145/254 (57%)	156/249 (63%)	144/241 (60%)	223/375 (60%)	222/369 (60%)	245/392 (63%)	200/352 (57%)
Lower Respiratory Infection (LRTI)	31/254 (12%)	40/250 (16%)	42/239 (18%)	58/374 (16%)	55/369 (15%)	54/393 (14%)	59/350 (17%)
Otitis media	20/253 (8%)	24/249 (10%)	22/239 (9%)	32/374 (9%)	34/367 (9%)	38/392 (10%)	28/349 (8%)
Prior lung problems	45/249 (18%)	41/251 (16%)	37/240 (15%)	65/374 (17%)	58/366 (16%)	59/391 (15%)	64/349 (18%)
Sex (Female)	162/254 (64%)	155/249 (62%)	141/241 (59%)	225 /375 (60%)	233/369 (63%)	250/392 (64%)	208/352 (59%)
Current Smoker	35/254 (14%)	44/248 (18%)	44/241 (18%)	58/374 (16%)	65/369 (18%)	64/391 (16%)	59/352 (17%)
Age (years)	35 (22)	35 (22)	33 (23)	35 (22)	33 (22)	35 (22)	33 (23)

Data are means (SD) or numbers (%) for those with baseline data. Denominators vary due to missing data. LRTI and otitis media were based on the diagnosis/symptom problem recorded by the GP in the CRF.