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REVIEW

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The role of saline nasal sprays or drops in nasal hygiene: a review of the evidence and clinical perspectives*

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Abstract

Background: This article provides, for the first time, a comprehensive view on everyday practice and evidence-based advice on the regular use of saline nasal sprays or drops to support nasal function and to help protect from airborne pollutants, pollens and viruses.

Method: An extensive literature search was conducted with PubMed, Google Scholar and national healthcare databases to identify and summarise the evidence available to date on the role of saline nasal sprays or drops in nasal hygiene. Clinical perspectives from international respiratory specialists were included.

Results: Following the PubMed searches, twenty-three articles were assessed in adults and children using isotonic or hypertonic saline nasal sprays and drops, including five systematic reviews and 11 randomised controlled trials. Six national clinical guidance documents were included from the other database searches to give a total of 29 articles. The findings support that regular, daily use of saline nasal sprays or drops could provide relief from nasal symptoms in adults and children with upper respiratory tract infections or allergic rhinitis; future studies are expected to demonstrate benefit following air pollutant exposure. No serious adverse events were reported. National guidance recommends daily nasal hygiene with saline sprays and drops, some from infancy.

Conclusion: Regular, daily use of saline nasal spray or drops could reduce the effects of noxious stimuli in the nose, helping to support respiratory health.

Key words: Air pollution, nasal hygiene, pollen, saline nasal sprays or drops, respiratory viruses.

Introduction

Healthy humans are predominantly nose-breathing at rest[(1)]. The nose and nasal mucosa play an essential role in maintaining healthy airways by entrapping inhaled airborne aggressors such as pollutants, pollen and infectious viruses, as well as heating and humidifying inhaled air. This prevents irritation or damage to delicate distal pulmonary tissues and allows the lungs to work efficiently[(2)].

Irritation of nasal mucosa by airborne aggressors can disrupt the functioning of the nose, and result in nasal symptoms such as congestion, rhinorrhoea and sneezing[(3-5)]. Failure to clear noxious stimuli from the upper respiratory system can lead to an increased risk of infection or allergic response, and has been linked to long-term, chronic conditions of the lungs and other organs[(3, 6)]. Thus, it is important to keep the nose functioning effectively to control diseases of the lungs and support overall health[(2)].

The rise in the levels of airborne pollutants, pollen and infectious viruses around the world, as well as increasing numbers of patients seeking advice on nasal symptoms and over-the-counter

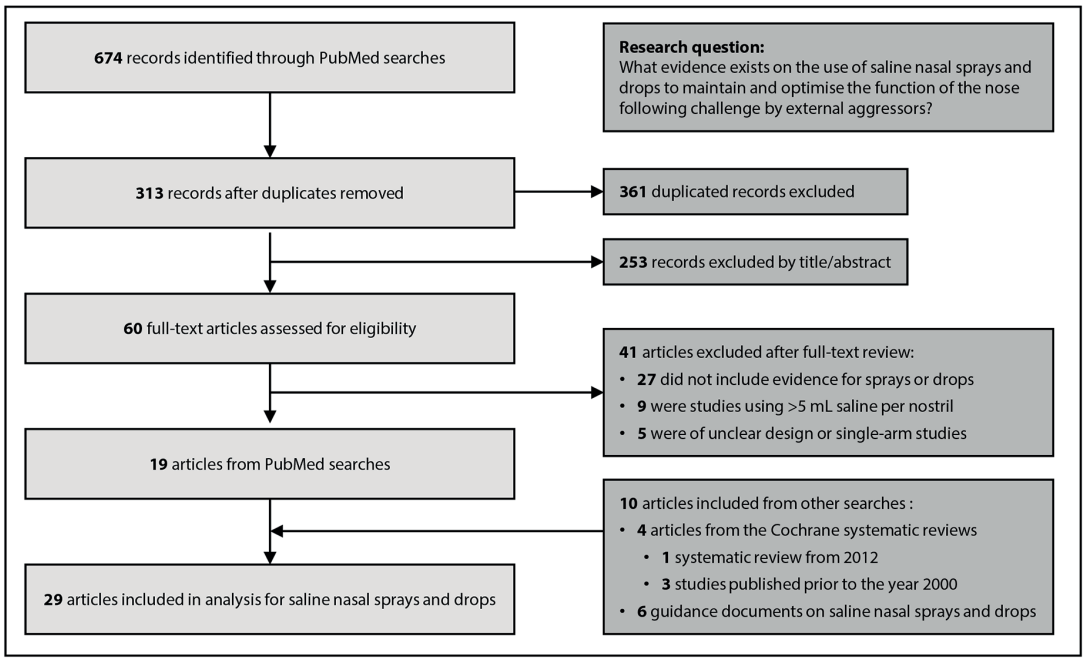

Figure 1. The flow chart of the literature review. The types of articles included systematic reviews, randomised controlled trials (RCTs), non-RCTs, observational studies, prospective and retrospective cohort studies, case control studies, cross-sectional studies and recommendations from respected authorities. Studies involving patients with chronic respiratory infections or chronic diseases with respiratory features, such as cystic fibrosis, bronchiolitis or those recovering from sinus surgery were excluded. Studies using larger volumes of saline nasal solutions (>5 mL) were excluded unless the comparator was a saline nasal spray or drops. In addition to PubMed, the following sources were searched for relevant references: World Health Organization reports, NICE Clinical Knowledge Summaries, the Cochrane Library, The Lancet Commissions, and guidelines for use of devices designed to reduce nasal congestion. Non-systematic searches of Google Scholar were conducted to retrieve grey literature and other sources of potential evidence. The full text of each potentially relevant study was evaluated to determine whether it met the inclusion and exclusion criteria for this review. Data from relevant studies were extracted and included year and country of study, sample size, study population, methodological quality, type of saline solution and device used as well as efficacy and safety outcomes.

treatments in community pharmacies, requires that healthcare professionals possess the most recent and relevant knowledge to make appropriate recommendations. Here, saline nasal sprays and drops are evaluated as they offer convenience and ease of use, which may increase patient acceptability and compliance compared with high-volume nasal washes.

This review aims to:

- Provide state-of-the-art information for healthcare professionals on the important, but often overlooked role that the nose plays in protecting against the negative health impacts of exposure to airborne pollutants, pollen and viruses
- Provide an evidence-based overview of the effective use of saline nasal sprays and drops in adults and children
- Share clinical perspectives and practical advice from respiratory specialists on the use of saline nasal sprays and drops to support nasal health
- Identify remaining knowledge gaps and research directions

Search strategy and selection criteria

A literature search was conducted to identify evidence on the role that saline nasal sprays and drops can play in nasal health to inform expert advice for providers and patients. PubMed and Google Scholar were searched from 01 January 2000 to 01 May 2020 using search terms relating to nasal saline sprays and drops, respiratory health and the airborne aggressors: air pollutants, pollen and viruses (Supplementary Table 1). These aggressors were evaluated knowing that: air pollutants are the top environmental global threat to human health, pollen is the main aeroallergen causing respiratory allergy and respiratory viral pathogens are the cause of most upper respiratory infections[7-9]. Airborne bacteria were excluded as when infection is suspected it typically requires referral and follow-up, and treatment with prescription medicines may be indicated. The literature search was restricted to articles reporting findings in humans and written in the English language. The flow chart of the literature review is shown in Figure 1 and the search strategy for PubMed is shown in Supplementary Table 1. Additional articles are cited in this review to articulate the most recent

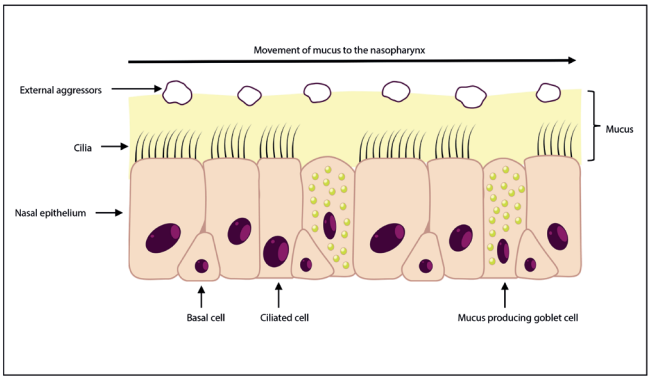

Figure 2. The nasal mucosa and mucociliary clearance. Specialised cells lining the nasal cavity are covered by up to 200 hair-like microprojections, termed cilia. Motile microtubules in cilia enable them to move rhythmically in one direction within the mucus that bathes the inside of the nose[12, 13]. The synchronised movement of cilia propels mucus, along with captured particles such as air pollutants and pollen, to the back of the nasopharynx, where they can be swallowed or coughed up[12, 13]. Mucociliary clearance of insoluble particles concludes after 24 hours of deposition in the healthy nose[15]. Mucociliary transport time ranges from 1–10 mm per hour in different regions of the nose, and is dependent on the number of ciliated cells, length of cilia, ciliary beat frequency and mucus viscosity[11, 12]. Mucociliary clearance is a vital process. Airborne aggressors may impair cilia activity and can lead to symptoms such as a congested or runny nose and potentially wider effects on the airways or distal organs[3, 8, 13, 16, 17].

understanding around the physiology and function of the nose, the impact of airborne aggressors and to provide an overview of nasal saline irrigation solutions and delivery devices.

Results and discussion

Anatomy, function and protective role of the nose

The respiratory tract is exposed daily to various airborne aggressors with the constant threat of airway inflammation and infection[10]. The respiratory system uses several defence mechanisms against inhaled pathogens and particulates, including cough clearance, anatomical barriers, aerodynamic changes and immune mechanisms[2, 3]. Critically, the first line of defence is the nose. By cleaning the air we breathe, the nose provides a natural barrier to prevent potentially harmful airborne aggressors from entering the body and causing harm[2]. Mechanical separation of the largest airborne particles (>3 µm) occurs in the vestibule and nasal valve area. Smaller particles (0.5–3 µm) are deposited on the nasal mucosa and filtered by mucociliary transport[11-13], described in Figure 2. Highly water-soluble components are 'scrubbed' from inhaled air by the nasal mucous layer[3, 11, 14].

Keeping the nose clear, clean and moisturised is vital for it to carry out its functions to protect health, as shown in Table 1[2].

Table 1. Critical functions of the nose.

Physiology and physical attributes of the nose and its function
Warming, humidifying and cleansing/filtering the air to prepare it for delivery to the lungs
Trapping large particles with the nose hairs and small particles via mucous membranes
Regulating the direction and velocity of the air stream via shelf-like bony structures in the nose (the turbinates) – this maximises exposure of inhaled air to the vasculature and nerves, as well as the mucous blanket to facilitate clearance of noxious stimuli
Slowing the air stream also allows mixing of the air with NO produced in the nasal sinuses; NO is a vasodilator and bronchodilator that increases oxygen transport throughout the body
Increasing oxygen uptake; nose breathing imposes ~50% more resistance to the air stream than mouth breathing, resulting in 10–20% more oxygen uptake and maintaining the elasticity of the lungs
Retaining some moisture from exhaled air, preventing nasal dryness

NO, nitric oxide.

This protective role can be compromised by exposure to airborne aggressors, leading to inflammation of the nasal membrane and nasal congestion that can impair mucociliary function[13, 18, 19]. Trapped particles, pollens and pathogens spend longer in the nose, which further increases the risk of inflammation, damage and symptoms of nasal congestion, rhinorrhoea and sneezing[2, 19]. These symptoms can negatively impact quality of life (QoL), causing reduced productivity, sleep deprivation, low mood, irritability and fatigue[20-24]. Nasal airway inflammation can activate the systemic immune response making the lower airway more prone to severe inflammation[2]. Other systemic health effects have been linked to exposure to airborne aggressors and are illustrated in Figure 3.

Certain populations, including young children, people with existing conditions such as asthma, COPD or heart disease, older people and pregnant women, are more at risk than others from the effects of airborne aggressors[4, 30-32].

Maintenance of nasal health

Individuals should be advised to minimise their exposure to airborne aggressors, where possible. Clear guidance is available on personal strategies that can help providers, patients and the public minimise daily exposure to air pollution to benefit respiratory health[33]. Guidance exists to help minimise exposure to allergens such as pollen[34, 35] and the WHO has further updated its advice on minimising exposure to respiratory viruses in the context of the COVID-19 pandemic[36].

It may not always be feasible to avoid exposure to airborne aggressors[37, 38]. Providing information on the role of the nose in protecting health, and education on how to care for the nose, may reduce the negative effects of airborne aggressors. Saline nasal solutions are available over the counter and can be used alone or as an adjunct to other therapies such as intranasal steroids and oral antihistamines to reduce the effect of airborne aggressors in the nose and to improve nasal health[39, 40].

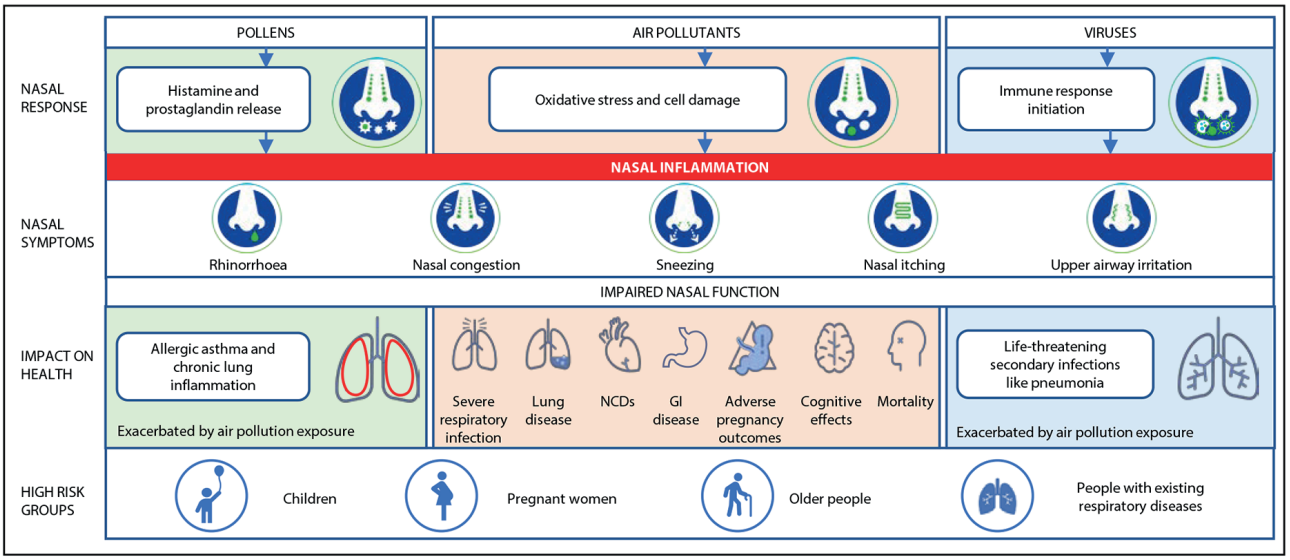

Figure 3. The nose plays a critical role in our body's response to airborne aggressors. Nasal airway inflammation can reduce mucociliary clearance[3, 8, 13, 17] and activate the systemic immune response making the lower airway more prone to severe inflammation[2]. Pollens are some of the most common precipitants of an allergic response mounted by the nasal epithelium[25, 26]. Air pollutants can also induce inflammation in the nasal epithelium, activate various immunocompetent cells, and may aggravate pollen- or viral-induced damage of the nasal epithelium[27, 28]. When they bypass the nose and reach the lower airways of sensitised people, they can induce allergic asthma, which can be life-threatening[4]. Systemic health effects may include cardiovascular disease, stroke and gastrointestinal inflammatory diseases[6, 29]. Viral pathogens reaching the lungs can cause secondary infections such as pneumonia, bronchitis and bronchiolitis; these conditions can be severe or fatal[8].

The exact mechanism of action of saline nasal irrigation is unknown; the general consensus is that benefits are primarily due to mechanical intervention[41-46]:

- Flushing out thick mucus, crusts, debris and airborne aggressors
- Washing away inflammatory mediators, thus favouring resolution of nasal symptoms
- Improving mucociliary clearance (MCC).

Saline nasal sprays and drops

Saline can be administered to the nose in a small volume (less than 5 mL per nostril) via spray devices that deliver a fine mist or jet of saline into the nose[40], low volume nebulisers (micronised nasal douches) or via nasal drops that are often preferred for use with young children. Evidence suggests that nasal sprays effectively reach the nasal cavity[47]; this is important when targeting the nasal mucosa, whereas high-pressure and high-volume saline can penetrate sinus cavities[47]. High-volume devices have been associated with a greater incidence of discomfort, burning, and eustachian tube dysfunction as compared with low-volume devices[48]. Nasal saline sprays offer convenience, acceptability and ease of use, all of which are likely to increase compliance[48, 49]. Among practising family physicians in the US who actively recommended saline nasal irrigation to their patients, nasal spray was the method of choice (recommended by 78%)[50].

There is some evidence in adults and children that tonicity of the saline solution alters its efficacy, with hypertonic saline (HS) solutions (>0.9% NaCl) associated with greater symptom improvement and MCC than isotonic saline (IS) solutions (0.9% NaCl)[38, 51, 52]. In addition to a mechanical action in the nose, hypertonicity may reduce mucosal oedema due to osmotic pressure-induced water transport through the mucosal epithelial membrane, thereby reducing nasal congestion and improving MCC[52].

Clinical effectiveness of saline nasal sprays and drops

Based on the literature search findings, 29 articles were analysed to determine the clinical effectiveness of saline nasal sprays and drops. These articles comprised: 19 articles identified from the PubMed searches, four articles identified from the Cochrane systematic reviews (three of which were published prior to the year 2000) and six guidance documents identified from the other searches (Figure 1). The publications varied considerably with regard to study design, number of subjects, study duration and the parameters assessed. Despite the heterogeneity, a congruent trend in the findings could be established.

National guidelines and clinical summaries recommend the use of saline nasal sprays or drops for nasal conditions as well as for daily nasal hygiene, (some advise starting from birth), to support optimal nasal function. These are summarised in Table 2.

Table 2. Guidelines and healthcare organisations that recommend use of saline nasal irrigation.

Reference	Guideline	Population	Treatment	Recommendations
CHU Sainte-Justine. Nasal hygiene, 2018[53]	Healthcare guidance in Canada	From birth onwards	IS (syringe, <2 years old) Up to 10 mL* Minimum frequency: Summer: Once daily Winter: 2–3 times per day Cold/congestion: 3–6 times per day IS (spray, >2 years old) 5 sprays per nostril Minimum frequency: Summer: Once daily Winter: 2 times per day Cold/congestion: 3–4 times per day	Daily nasal cleaning with saline solutions is recommended from birth to eliminate secretions and small particles, thus reducing congestion. A nasal spray can help acceptability in older children.
France Health Insurance. Nose wash in children, 2019[54]	Healthcare guidance in France	From birth onwards	IS (vials, <6 months old) IS (spray, >6 months old)	Daily nasal cleaning with saline solutions is recommended from birth to reduce congestion.
National Institute for Health and Care Excellence. Treatment summary: Rhinitis, 2019[55]	National Institute for Health and Care Excellence	Children with rhinitis	IS (sprays and drops)	Use of nasal saline drops or spray is recommended to help liquefy mucous secretions in children with rhinitis, especially in infants before feeding.
Scadding et al., 2017[56]	British Society for Allergy & Clinical Immunology	Children with AR	IS (sprays and wash)	IS nasal irrigation in children with AR is well tolerated, inexpensive, easy to use with no evidence of adverse effect to health with regular use.
Green et al., 2012[57]	Allergic rhinitis in South Africa	Children with AR	Not stated	Use of saline nasal preparations is strongly recommended in infants.
National Institute for Health and Care Excellence. Clinical Knowledge Summary: Common Cold, 2016[58]	National Institute for Health and Care Excellence	Adults and children with common cold	IS (sprays and drops)	Nasal saline drops may help relieve nasal congestion in some people. Sterile sodium chloride 0.9% nasal drops are available on prescription or over the counter. One or two drops applied to the nostrils of infants can help feeding.

*Premature: 1–3 mL per nostril, <6 months: 3–5 mL per nostril, >6 months: 5–10 mL per nostril. AR, allergic rhinitis; IS, isotonic saline.

Allergic rhinitis (AR)

Several small randomised controlled trials (RCTs) in adults and children with AR or rhinoconjunctivitis have demonstrated that use of HS nasal sprays 2–4 times per day improved nasal symptoms and QoL vs no treatment or baseline[51, 59, 60], reduced antihistamine use[59, 60] and improved the efficacy of other topical therapies[61, 62]. According to the meta-analysis by Hermelingmeier et al., the application of nasal saline via a small-volume spray was found to yield more distinct improvements in symptoms of AR than the use of nasal irrigation with larger volumes (200–400 mL)[46].

In adults and children with AR, clearing excessive nasal secretions and decreasing pre-existing oedema may improve the efficacy of topical therapies. When combined with antihistamine use, HS spray used 4 times per day significantly improved QoL and symptom scores in adults with AR vs histamine alone[61]. Addition of twice-daily HS nasal spray to intranasal corticosteroid (INS) therapy provided a significant improvement in nasal symptoms in children compared with INS or saline alone[62].The key studies are summarised in Table 3.

Other benefits of nasal saline include its potential to reduce the use of nasal decongestants, which is important since they are appropriate for use on a short-term basis only. In a cross-sectional study of 895 adults self-medicating persistent rhinitis (AR or rhinosinusitis), the risk of intranasal decongestant overuse was reduced with use of saline nasal solution (odds ratio: 0.61; $p<0.01$), although the method of saline nasal delivery was not specified[65].

Table 3. Saline nasal irrigation and allergic rhinitis in children and adults.

Reference	Study design	Population, sample size*	Study groups	Treatment protocol	Primary clinical endpoint(s)	Key findings	Adverse effects
Head et al., 2018[40]	Cochrane systematic review	Adults and children (aged 2–15 years), 14 RCTs (747 participants) up to November 2017	Five studies used nasal sprays vs: 1. No SNI 2. Other pharmacological treatments	SNI delivered by any means (including nasal sprays) and with any volume, tonicity and alkalinity	1. Patient-reported disease severity	**SNI, including with sprays, may reduce disease severity** in both adults and children with AR compared with no SNI.	No reported AEs in the saline groups
Wang et al., 2020[63]	Systematic review and meta-analysis up to December 2018	RCTs with adults and children (aged 3–16 years); 12 articles (819 patients)	1. SNI vs no SNI 2. SNI vs INS spray 3. SNI + INS spray or oral AH vs INS spray or oral AH 4. IS vs HS	Various delivery methods (including nasal sprays), with any frequency and duration	1. Symptom scores	**SNI, including with sprays, improved local symptoms of AR in children and adults** vs no SNI ($p<0.1$). HS may be more effective than IS in relieving local symptoms in children.	No reported AEs in adults or children using nasal sprays
Gutierrez-Cardona et al., 2017[49]	Systematic review from January 1946 to June 2015	40 studies with children (aged 4–12 years) (819 patients)	Various	Various delivery methods (including nasal sprays), with any frequency and duration	1. Acceptability and tolerance of SNI 2. Symptom control 3. QoL scores	Overall, SNI **appeared to have a positive impact on QoL**, being accepted and tolerated in the majority of children (78–100%). **Fine nasal spray was the most accepted method of delivery**.	IS and HS were well tolerated. Saline nasal sprays reported to be better accepted than other NSIs
Hermelingmeier et al., 2012[46]	Systematic review and meta-analysis from 1994 to 2010	10 RCTs (n>400) in adults and children (aged 5–15 years)	1. HS or IS SNI 2. No treatment 3. Other treatment	Various delivery methods (including nasal sprays), with any frequency and duration	1. Improvement in symptoms (sneezing, itching, obstruction, and secretion) 2. QoL 3. MCT	**Regular use of HS improved symptoms of AR in adults and children** and reduced antihistamine use in children vs baseline. When combined with antihistamine use, HS spray improved QoL and symptoms in subjects with AR. Small-volume nasal saline sprays yielded more distinct improvements in symptoms of AR than larger volumes (200–400 mL).	No evidence that regular, daily SNI adversely affects the patient's health or causes unexpected AEs
Di Berardino et al., 2017[59]	RCT (two-arm, non-blinded, single-centre, parallel-group) with two periods of 6 days each	40 adults with seasonal AR (pollen)	1. HS SNI 2. No treatment Rescue antihistamines, as needed	HS nasal aerosol spray, one puff (0.13 mL) in both nostrils 3 times per day, for 6 days in low-pollen season and 6 days in peak season	1. Nasal symptoms (rhinorrhoea, nasal blockage, nasal itching and sneezing) 2. Antihistamine use 3. MCC	**HS nasal spray significantly decreased nasal symptoms** ($p=0.01$) **and antihistamine use** ($p=0.035$) vs no treatment. MCC was significantly worse in the no treatment group vs baseline ($p=0.011$) but not in the treatment group, suggesting HS SNI favoured elution of the allergen.	AEs not reported
Cordray et al., 2005[51]	RCT (three-arm, single-blinded, parallel-group, with 7-day duration of treatment and follow-up)	15 adults with seasonal AR (pollen)	Nasal spray 1. HS (Dead Sea) 2. Aqueous triamcinolone 3. IS as a control	HS spray, two sprays per nostril, 3 times per day; aqueous triamcinolone 110 µg into each nostril once daily; IS spray, two sprays per nostril, 3 times per day	1. Rhinoconjunctivitis QoL score	**HS nasal spray clinically and significantly improved symptoms** from baseline ($p<0.0001$); QoL improved by 23%. No significant improvement with IS.	Two patients withdrew due to AEs (treatment group not stated)

Reference	Study design	Population, sample size*	Study groups	Treatment protocol	Primary clinical endpoint(s)	Key findings	Adverse effects
Rogkakou et al., 2005[61]	RCT (two-arm, non-blinded, parallel-group, with 4-week duration of treatment and follow-up)	14 adults with AR (pollen)	1. 10 mg cetirizine with HS nasal spray 2. 10 mg cetirizine	10 mg of cetirizine daily with and without HS nasal spray 4 times per day	1. Daytime and night-time symptom score 2. QoL index 3. Acoustic rhinomanometry	**Addition of HS nasal spray to antihistamine therapy provided a significant additional benefit** for daytime and night-time symptoms at Week 4 ($p \leq 0.05$) and QoL of the patients ($p \leq 0.02$).	No AEs reported
Garavello et al., 2005[60]	RCT (two-arm, non-blinded, parallel-group, with 7-week duration of treatment and follow-up)	40 children (aged 9.1 ± 2.5 years) with seasonal rhinoconjunctivitis (pollen)	1. 3% HS 2. No treatment	3% HS, three sprays per nostril (50 µL per spray) 3 times per day	1. Nasal and ocular symptom score	**Clinically and statistically significant reduction in symptoms with HS nasal spray** after the 7th week in comparison with study start. On average 5% less antihistamine was used during the period of regular nasal irrigation.	No AEs reported in the treatment group
Chen et al., 2014[62]	RCT (three-arm, non-blinded, parallel-group, with 12-week duration of treatment and follow-up)	61 children with AR (moderate to severe); mean age 6 years (range 2–15 years)	1. FP nasal spray 2. HS (seawater) nasal spray 3. FP nasal spray + HS (seawater) nasal spray	200 µg FP daily for 4 weeks, then 100 µg daily for 4 weeks then 50 µg daily for 4 weeks; 4–6 sprays of HS, twice a day for 12 weeks; FP + HS spray, both as above for 12 weeks	1. Disease severity, as measured by patient-reported nasal symptom score assessed on a 4-point scale (nasal itching, rhinorrhoea, nasal obstruction and sneezing)	**Significant improvements in total symptom scores in patients given FP + saline** at Weeks 4, 8, and 12 compared with patients given FP or saline ($p<0.05$).	No AEs reported
Marcuccio et al., 2019[64]	Observational, retrospective study	49 children (aged 3–6 years) with rhinitis	0.9% IS followed by 1% HS Pre- vs post-treatment	0.9% IS, two sprays per nostril, twice a day for 20 days followed by 1% HS, twice a day for 10 days Treatment was repeated for a period of 6 months	1. Mean paediatric sleep questionnaire score	**Mean paediatric sleep questionnaire score decreased post-SNI vs before treatment** ($p<0.05$). SNI in children with rhinitis improved nasal symptoms and signs of rhinitis, and quality of sleep of children and their caregivers.	AEs not reported
Madison et al., 2016[37]	Literature review from 2008 to October 2015	Two studies in children with AR (aged 2–15 years) (101 subjects)	Only the study by Chen[62] included HS (seawater) nasal spray in the treatment arm	Saline nasal spray	Clinical symptoms score	**Daily nasal irrigation with a saline spray was an effective adjuvant treatment for AR** in combination with a reduced dose of INS.	Use of INS with nasal saline spray was well tolerated in a paediatric population

*Number of subjects included in analysis, where known.

AE, adverse effect; AH, antihistamine; AR, allergic rhinitis; FP, fluticasone propionate; HS, hypertonic saline; INS, intranasal corticosteroid; IS, isotonic saline; MCC, mucociliary clearance; MCT, mucociliary clearance time; QoL, quality of life; RCT, randomised controlled trial; RR, risk ratio; SNI, saline nasal irrigation.

Table 4. Saline nasal irrigation and upper respiratory tract infection.

Reference	Study design	Population, sample size*	Study groups	Treatment protocol	Primary clinical endpoint(s)	Key findings	Adverse effects
King et al., 2015[39]	Cochrane systematic review	Adults and children (3 weeks to 12 years), five RCTs (749 participants) up to August 2014	Topical nasal saline treatment (liquid, drops or spray) vs: 1. Routine care 2. Other nose sprays	SNI delivered by any means and with any volume, tonicity and alkalinity	1. Symptom relief 2. Time to resolution of symptomatic illness	**NSI (liquid, drops or spray) may improve symptoms of acute URTIs.**	No serious AEs; minor nasal discomfort was reported by a minority of subjects
Tano & Tano, 2004[72]	RCT (crossover study, 10 weeks of treatment, 2 weeks of washout and 10 weeks of observation)	60 adult males with URTI symptoms	1. IS nasal spray 2. No treatment	IS saline spray (twice daily, three puffs per nostril)	1. Symptoms via patient diary	**Daily use of IS spray reduced the number of days with nasal secretion and/or blocked nose** (mean 6.4 days) vs the observation period (mean 11 days; p=0.027); 40% symptom reduction with spray use. Subjects had a mean of 0.7 episodes of URTI during the spray period vs 1.0 episode during observation only (p=0.05).	Two subjects withdrew due to nasal dryness during the nasal spray period. No serious AEs reported
Adam et al., 1998[70]	RCT (three-arm, over 1 year)	119 adults with URTI	1. HS nasal spray (pickling salt and baking soda) 2. IS nasal spray 3. No treatment	HS or IS nasal spray 3 times per day, two squirts per nostril until symptom resolution	1. Nasal symptom score (nasal congestion, rhinorrhoea and headache)	**Neither saline preparation had an effect on duration or severity of nasal symptoms compared with no treatment control.** However, the length of treatment duration was not recorded.	In the HS nasal spray group, 32% of subjects noted burning vs 13% in the IS group (p=0.05)
Passali et al., 2005[71]	RCT (two-arm non-blinded, parallel-group, with 15-day duration of treatment)	200 adults with acute viral rhinosinusitis (common cold)	1. IS micronised spray 2. IS lavage	IS micronised spray, 4 times per day for 15 days; IS lavage (via a 20 mL syringe)	1. Inspiratory and expiratory rhinomanometric resistance 2. Acoustic rhinometry 3. MCT 4. Nasal symptoms score	**IS micronised nasal spray, but not nasal lavage, improved inspiratory and expiratory rhinomanometric resistance (p<0.01) and nasal volumes (acoustic rhinometry) (p<0.001) vs baseline.** IS nasal spray normalised MCT to a physiological level (p<0.001) and reduced symptom scores (p<0.001) vs baseline.	AEs not reported
Šlapak et al., 2008[66]	RCT (multicentre, open-label, 3-week treatment phase followed by 9-week prevention phase)	390 children (aged 6–10 years) with URTI (common cold or flu)	Standard treatment + IS via different delivery methods: 1. Medium jet flow 2. Fine spray 3. Eye and nose wash with a fine spray 4. Standard treatment only (control)	IS via a fine spray or medium jet, 6 times per day during acute illness phase and 3 times per day during the preventative phase; volumes were larger than typical aerosolised sprays	1. Nasal symptom score 2. Nasal breathing score 3. Health status score (physician assessed) 4. Other medication use	**During acute illness, children using IS (spray and jet) showed faster resolution of nasal secretion and obstruction, improvement in health status score for common cold, and reduction in nasal decongestant and mucolytic medication use (all p<0.05)**. By Week 8, IS (spray and jet) vs control was associated with reduced nasal secretions and nasal obstruction (p<0.05); less use of other medications (p<0.05); fewer illness days (31% vs 75%), school absences (15% vs 35%), and complications (8% vs 32%) (all p<0.05).	No serious AEs reported; discomfort was associated with the higher flow rate of the jet rather than the saline solution or spray

Reference	Study design	Population, sample size*	Study groups	Treatment protocol	Primary clinical endpoint(s)	Key findings	Adverse effects
Koksal et al., 2016[68]	RCT (double-blind study)	Children with URTI (aged <2 years)	1. HS (2.3%) nasal drops 2. IS (0.9%) nasal drops 3. No intervention	Daily instillation of HS or IS drops; use of nasal aspirator or nasal pumps was allowed in all groups	1. Nasal symptom scores	**Both HS and IS nasal drops improved nasal congestion and rhinorrhoea** ($p>0.05$); no significant difference between HS and IS groups. Sleep quality and feeding were improved in both treatment vs no treatment groups ($p<0.001$).	No difference in nasal bleeding between no treatment and treatment groups ($p>0.05$)
Bollag et al., 1984[69]	RCT (2-day duration)	46 children (aged 3 weeks to 2 years) with acute URTI	1. IS drops (0.9%) 2. Phenylephrine drops (0.25%) 3. No treatment	IS drops, four drops per nostril every 2 hours as needed; phenylephrine drops, four drops 4 times a day ≤ 3 days	1. Nasal symptom score 2. Respiratory symptom severity 3. Activity signs	**Subjects in all three groups improved with no difference between the IS group and the no treatment group for any endpoint.** Data were incomplete, reporting only mean scores for each group at baseline and follow-up 2 days later, with baseline scores varying considerably.	6/15 subjects did not tolerate treatment with saline nasal drops; 7/16 did not tolerate treatment with phenylephrine drops
Montanari et al., 2010[67]	Observational, non-interventional, prospective, comparative, cohort study for 5 months over the common cold season	435 children (aged 2 months to 2 years) with symptoms of common cold	1. Nasal aspirator and IS drops 2. IS drops	Aspirator then IS drops, then a subsequent aspiration, ≥3 times per day and before feeding; IS drops, ≥3 times per day and before feeding	1. Clinical assessment	**Both treatments significantly improved rhinorrhoea, oral breathing, and other upper respiratory symptoms** after 10 days of treatment vs baseline (p value not reported). Use of nasal aspirator and IS drops decreased the number of EOM episodes vs IS drops alone ($p<0.05$).	Crying and nasal bleeding were reported in both groups, were mild, resolved rapidly and considered not related to treatment. Two serious AEs were reported and considered not related to treatment
Rabago et al., 2009[50]	Survey	330 practising family physicians in the USA	NA	Electronic questionnaire	NA	**90% of practising family physicians in the USA actively recommended SNI** to their patients for upper respiratory conditions; nasal spray was the most frequently recommended method (78%).	AEs not reported

*Number of subjects included in analysis, where known.

AEs, adverse effects; EOM, external otitis media; HS, hypertonic saline; IS, isotonic saline; MCT, mucociliary clearance time; NA, not applicable; RCT, randomised controlled trial; SNI, saline nasal irrigation; URTI, upper respiratory tract infection.

Acute upper respiratory tract infections

Saline nasal sprays and drops probably improve symptoms of acute upper respiratory tract infections (URTIs) such as the common cold and rhinosinusitis[39]. In a study of 390 children aged 6–10 years with URTI, use of IS delivered 6 times per day for 3 weeks via fine spray or medium-strength jet resulted in significantly faster resolution of nasal secretion and obstruction, as well as reduced nasal decongestant and mucolytic medication use. No serious adverse effects were reported; discomfort was associated with the higher flow rate of the jet rather than the nasal saline solution or spray[66].

Nasal drops may be easier to administer for infants than nasal sprays. Studies in children under 2 years old with symptoms of URTI have shown that daily use of HS or IS nasal drops, with and without nasal aspirator use, can significantly improve nasal symptoms vs baseline or no treatment[67, 68] leading to improvements in feeding and sleeping[68]. Combined use of IS nasal drops with aspiration of mucus may help avoid further complications such as ear infections[67], which are common in young children, occurring after approximately 20% of common colds[58]. One small RCT in infants with URTI aged 3 weeks to 2 years found no difference in respiratory symptoms following 2 days of treatment with normal saline drops, phenylephrine drops or no treatment; a similar number of infants did not tolerate saline or phenylephrine drops[69].

There are very few studies with well-defined inclusion criteria that have examined saline nasal sprays and symptom relief for adults with URTIs; those published report conflicting results[70, 71]. However, prophylactic use of IS saline nasal sprays for URTIs may be beneficial. A well-designed study of 60 adult males with URTI symptoms found that twice-daily use of an IS nasal spray for 10 weeks resulted in significantly fewer episodes of URTIs and fewer days with nasal symptoms compared with an observation (no intervention) phase[72]. In a study of children with URTI, use of IS during a preventative phase (after 8 weeks of daily use of IS spray or jet) supported prophylactic use with significantly fewer illness days (31% vs 75%), school absences (15% vs 35%), and complications (8% vs 32%) ($p<0.05$ for all) than the control group. There was higher parent satisfaction with IS use vs standard care[66]. The studies are summarised in Table 4.

Further well-designed, sufficiently powered RCTs are warranted in both adults and children to establish the place of saline nasal sprays as a standard intervention in acute URTI treatment and prevention.

Daily nasal hygiene in healthy individuals

The health benefits of daily nasal hygiene are well recognised in infants and children[73-76] and regular, daily use of nasal saline

Clinical perspective 1. Dr Glenis Scadding, MD
Honorary Consultant Physician in Allergy and Rhinology at the Royal National Throat, Nose and Ear Hospital, and Honorary Senior Lecturer at University College London, UK.

Washing the nose gently with saline helps to remove unwanted substances, preventing allergic reactions and improving mucociliary function. The simplest way to do this is by using a sterile saline nasal spray: One or two puffs in each nostril, aimed at the inside of the lateral nasal wall. Such treatment is suitable for all ages, even for pregnant women. A solution that is slightly hypertonic, or sterilised sea water, can give the best results in some people. The only people for whom I do not suggest this are those with hypertension as they should not be taking in extra sodium. However, if necessary, they could use the spray and then spit it out when it reaches the back of the throat, rather than swallowing it. For a child over 4 years of age, being taught how to administer the spray and then being allowed to do it themselves is more likely to result in acceptance.

My practice is to advise patients with seasonal allergic rhinitis to use saline sprays regularly – on waking, after exposure to allergens and pollutants, and on retiring. Coupled with avoidance of known allergens, this may be sufficient to give good symptom control. If this is not achieved, then pharmacotherapy such as an intranasal corticosteroid can be added, at least 10 minutes after the saline. When rhinitis is perennial, a once- or twice-daily application can be employed to reduce symptoms and to clean the nose prior to intranasal corticosteroid use. There is also evidence that daily nasal saline use reduces the likelihood of symptomatic colds. Therefore, for patients who suffer with frequent or debilitating colds, I suggest use of nasal saline after using public transport or being in contact with several other people.

Clinical perspective 2 Dr Gary Wong, MD
Professor, Department of Pediatrics and School of Public Health, Chinese University of Hong Kong, Hong Kong.

One should minimise exposure to various noxious stimuli, and this is particularly important for people with underlying nasal allergies. Nasal airway inflammation can also activate the systemic immune response making the lower airway more prone to severe inflammation (one airway response).

If we can wash the irritants away regularly with saline nasal spray, this will reduce the chance of the cells from the immune system reacting to these irritants and, thus, reduce nasal inflammation. Saline nose drops/sprays are widely used in children of all age groups, from infants to adolescents, during episodes of URTI, exacerbations of allergic rhinitis, or irritation from exposure to air pollutants.

Saline nose drops/sprays may be of particular benefit for infants and young children who have smaller, less developed nasal passages than adults, meaning nasal congestion is very common. Infants are obligatory nose-breathers and so blockage of nasal passages is of importance, because it tends to impair their feeding and sleep. Nasal saline sprays and drops can facilitate relief of the blockage prior to feeding or sleeping, especially during episodes of URTI, and frequency of use is best matched to their feeding and sleeping schedule (i.e. around 4–6 times per day). Note that URTIs in newborns are very uncommon and allergic rhinitis does not manifest so early in life. Therefore, a newborn (first 4–6 weeks of age) with symptoms suggestive of nasal blockage must be referred to a physician to rule out the possibility of other congenital problems causing such symptoms.

In general, nasal spray is simple to use and does not pose major difficulties for most parents and caregivers. Side effects with saline nose drops/sprays are minimal to none. Isotonic solutions may be less irritating than hypertonic solutions in children and are often used to help clear thick secretions, washing away potential allergens and irritants (e.g. air pollutants).

sprays or drops is recommended in several guidelines (Table 2).

A large survey of primary care paediatricians in Italy revealed that almost all of the respondents (99.3%) recommended use of saline nasal irrigation. It was considered both a prophylactic and a therapeutic measure by most respondents who prescribed it every day for healthy children and more frequently when they were ill. Most of the primary care paediatricians (87%) indicated an isotonic solution as the preferred solution, and the most frequently recommended administration device was a nasal spray. IS was preferred for prophylaxis and HS for therapy[75].

Studies in healthy adults have also shown significantly improved nasal function following the use of IS and HS nasal sprays[52, 77], summarised in Table 5.

Other benefits of daily nasal hygiene may include the following:

- Helps clear inhaled airborne aggressors that can cause nasal congestion, allergies and sinus problems
- Improves MCC
- Thins excess mucus in the nose, which can help relieve nasal congestion and discomfort
- Helps cleanse and hydrate nasal tissues, to prevent nasal dryness
- Improves the effectiveness of medicated nasal sprays, when nasal saline is used first

Tolerability of saline nasal sprays and drops

Adults and children (aged 2–15 years) generally have minimal side effects from use of saline nasal sprays[40], with no evidence of adverse effect to health with regular use. No serious adverse effects occurred in children aged 3 weeks to 2 years treated with IS nasal drops, although parents noted some babies had difficulty with the drops[39]. Intranasal saline is considered to be a low-risk, and often effective, intervention during pregnancy[78]. Most people, including children, find saline nasal sprays useful and easy to use[49, 79].

Transient adverse reactions, such as nasal irritation and nasal discomfort have been described[39]. A systematic review and meta-analysis of HS use in children with AR found there was a higher rate of adverse effects in those using HS (4.5%) than those using IS (2.3%); this was not statistically significant (p=0.36)[38]. Side effects were more common (10–20% of the cases) when very-high-volume devices were used[44]. Patients should be advised to keep saline nasal spray and drop devices clean and to not share them with others to avoid potential contamination[80].

Areas for further research

Few RCTs have evaluated the use of IS nasal spray in adults and children with AR; it is not known if similar improvements in symptoms and QoL, as well as reduced antihistamine use, could be obtained using IS rather than HS nasal sprays.

A pilot study in adults with acute URTI found that use of an HS nasal wash and oral gargle significantly reduced duration of illness, use of symptomatic medication, transmission to household contacts and viral shedding vs no intervention[81]. In a subgroup of patients with coronavirus infection, the intervention appeared likely to be effective in reducing symptoms and duration of the illness[82], suggesting nasal washes could play a role in preventing and controlling the transmission of respiratory infectious pathogens, including severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). A larger study, powered for clinical and virological endpoints to confirm these findings[81, 83], could be extended to include the use of HS nasal sprays to increase treatment acceptability and compliance.

A limitation of this review is the small number of RCTs available for evaluation as well as the heterogeneity of the available studies regarding the amount, frequency and duration of nasal irrigation, the type of saline solution used and the range of outcome measures reported. The evidence suggests that saline nasal sprays and drops improve nasal function and are easy to use, with no evidence of adverse effect to health with regular use. High-quality, adequately powered research into their use for daily hygiene in both adults and children is warranted, particularly in the context of rising air pollution and pollen levels, and the heightened threat of respiratory viral outbreaks.

Clinical perspective 3. Dr Sundeep Salvi, MD, PhD in the health effects of air pollution.
Pulmonologist, Pulmocare Research and Education (PURE) Foundation, India.

In the same way that people brush their teeth every day to maintain their oral hygiene, encouraging regular, daily use of a saline nasal spray seems a logical step to support optimal nasal function. This may be especially important for patients who present with nasal symptoms when air pollution or pollen levels are elevated, or during the winter months.

Regular use of nasal saline is unlikely to be associated with adverse effects, meaning the potential for benefit far outweighs any risk. Thus, it appears to be an effective, inexpensive and well-tolerated treatment for different nasal ailments, and may help to prevent problems in healthy individuals exposed to everyday airborne aggressors. Further studies will help define the optimal volume, frequency and tonicity of the solutions used, which could then be tailored to the individual patient's needs.

With global levels of air pollution rising, increasing pollen counts and the omnipresent threat of a major respiratory viral outbreak, now more than ever, patients are seeking advice on everyday practical solutions to protect their health. In our recent review article, we detail recommendations to assist healthcare providers when advising patients and the public regarding personal-level strategies to mitigate the risk imposed by air pollution to benefit respiratory health[33]. Other strategies to consider include regular, daily nasal hygiene.

Table 5. Saline nasal irrigation in healthy subjects.

Reference	Study design	Population, sample size*	Study groups	Treatment protocol	Primary clinical endpoint(s)	Key findings	Adverse effects
Talbot et al., 1997[52]	Crossover study with subjects acting as their own control	21 healthy adults	1. HS (3%) nasal spray 2. IS (0.9%) nasal spray	Ten sprays with an atomiser of HS or IS (both buffered to pH 7.6) to one side of the nose; after 1 minute, another ten sprays given	1. MCC pre- and 10–20 minutes post-treatment	**MCC times decreased by 17% in normal healthy subjects after instillation of 3% buffered HS solution vs baseline** (p=0.007); no significant difference for IS vs baseline (2% decrease; p=0.71). HS produced a mean improvement in transit time vs baseline of 3.1 minutes (p=0.002) and 0.14 minutes in the IS group (p=0.69).	AEs not reported
Keojampa et al., 2004[77]	Double-blind trial with subjects acting as their own control	22 healthy adults	1. HS (3%) nasal spray 2. IS (0.9%) nasal spray	Ten sprays per nostril, once only	1. MCC pre- and 10–20 minutes post-treatment 2. Nasal patency (acoustic rhinometry 10 minutes post-treatment)	**Both saline solutions improved nasal clearance; but clearance was faster with 3% HS.** No change in nasal patency (healthy adults without nasal oedema). HS and IS spray improved MCC times (p<0.0001 and p=0.002, respectively); HS improved MCT more than IS (39.6% vs 24.1%; p=0.007).	AEs not reported
Marchisio et al., 2014[75]	Cross-sectional survey	Survey of 860 randomly selected National Health Service primary care paediatricians	Included IS nasal spray	NA	NA	**NSI was used by 99.3% of respondents, although with differing frequency. Most (87%) preferred IS solution and the most frequently recommended method was a nasal spray (67.7%).** It was considered both a prophylactic and a therapeutic measure by 60.3% of respondents, who prescribed it every day for healthy children and more frequently when they were ill.	Over 98% of respondents considered use of nasal saline irrigation in pre-school children as safe and effective

*Number of subjects included in analysis, where known.

AE, adverse event; HS, hypertonic saline; IS, isotonic saline; MCC, mucociliary clearance; MCT, mucociliary clearance time; NA, not applicable.

Conclusions

Minimising exposure to airborne aggressors such as air pollutants, pollen and respiratory viruses is important for everyone to reduce associated ill-health effects. Daily nasal hygiene may reduce the effects of noxious stimuli in the nose, helping to support respiratory health. Several small RCTs have demonstrated that the daily use of saline nasal sprays (IS or HS) significantly reduced nasal symptoms vs no treatment in adults and children with AR. There are few studies with well-defined inclusion criteria in the area of symptom relief for URTIs; however, prophylactic use of IS nasal sprays may be beneficial.

Thus, saline nasal sprays are effective in cleansing the nose, and offer convenience and ease of use, which may increase patient acceptability and compliance compared with high-volume nasal washes. The consensus in the literature is that use of HS and IS nasal sprays is well tolerated, easy to use, with no evidence that regular, daily use adversely affects the patient's health or causes unexpected side effects[46].

Saline nasal irrigation techniques are easily taught in primary care settings, including the pharmacy. Patients report effective education as key to successful initiation and maintenance of nasal cleansing[49, 50]. Healthcare providers, including the community pharmacist, can play a vital role in the successful initiation and maintenance of saline nasal spray use, helping patients to breathe well and stay healthy.

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SS, GS and GW contributed their clinical perspectives to the manuscript. The content within the 'clinical perspectives' sections represents the independent perspective and opinion of each specialist; GSK Consumer Healthcare does not promote or recommend any off-label usage of any mentioned products.

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Supplementary Material

Supplementary Table 1. PubMed search strategy details.

Search terms [Title/abstract]	Results (n)	Potentially relevant articles (n)	Relevant articles (n)
Saline nasal irrigation and respiratory health			
#1 (spray OR drop OR solution OR atomi* OR nebuli* OR irrigat* OR hygien*) AND (nose OR nasal OR intranasal) AND (saline OR sea OR salt OR sodium chloride OR hypertonic OR hypotonic OR isotonic) NOT (cystic fibrosis OR surgery) NOT (chronic[Title]) AND #2 (respiratory OR health OR airway OR lung OR rhinit* OR rhinorrhoea OR obstruction OR congest* OR discharg* OR blocked OR stuffy OR runny OR sneezing)	313	60	19
Saline nasal irrigation and allergic rhinitis			
#1 (spray OR drop OR solution OR atomi* OR nebuli* OR irrigat* OR hygien*) AND (nose OR nasal OR intranasal) AND (saline OR sea OR salt OR sodium chloride OR hypertonic OR hypotonic OR isotonic) NOT (cystic fibrosis OR surgery) NOT (chronic[Title]) AND #3 (allergic rhinitis OR allerg* OR hayfever OR hay fever OR pollen OR aeroallergen OR hypersensitivit*	123	23	10†
Saline nasal irrigation and upper respiratory tract infections			
#1 (spray OR drop OR solution OR atomi* OR nebuli* OR irrigat* OR hygien*) AND (nose OR nasal OR intranasal) AND (saline OR sea OR salt OR sodium chloride OR hypertonic OR hypotonic OR isotonic) NOT (cystic fibrosis OR surgery) NOT (chronic[Title]) AND #4 (respiratory tract infection OR respiratory infection OR viral infection OR virus OR rhinit* OR rhinosinusitis OR common cold OR rhinovirus OR influenza OR flu OR coronavirus OR COVID-19 OR SARS-COV	238	28	7†
Saline nasal irrigation and air pollutants			
#1 (spray OR drop OR solution OR atomi* OR nebuli* OR irrigat* OR hygien*) AND (nose OR nasal OR intranasal) AND (saline OR sea OR salt OR sodium chloride OR hypertonic OR hypotonic OR isotonic) NOT (cystic fibrosis OR surgery) NOT (chronic[Title]) AND #5 (air pollut* OR particulate matter OR particle pollut* OR air contamina*)	3	0	0

*The asterisk at the end of a truncated word was used to search for all terms that began with the word root. PubMed searches include US and UK spelling variants of search terms.

†These articles were included in the results for saline nasal irrigation and respiratory health.