Using nasal sprays to prevent respiratory tract infections: a qualitative study of online consumer reviews and primary care patient interviews

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ABSTRACT

Objectives Nasal sprays could be a promising approach to preventing respiratory tract infections (RTIs). This study explored lay people’s perceptions and experiences of using nasal sprays to prevent RTIs to identify barriers and facilitators to their adoption and continued use.

Design Qualitative research. Study 1 thematically analysed online consumer reviews of an RTI prevention nasal spray. Study 2 interviewed patients about their reactions to and experiences of a digital intervention that promotes and supports nasal spray use for RTI prevention (reactively: at ‘first signs’ of infection and preventatively: following possible/probable exposure to infection). Interview transcripts were analysed using thematic analysis.

Setting Primary care, UK.

Participants 407 online customer reviews. 13 purposively recruited primary care patients who had experienced recurrent infections and/or had risk factors for severe infections.

Results Both studies identified various factors that might influence nasal spray use including: high motivation to avoid RTIs, particularly during the COVID-19 pandemic; fatalistic views about RTIs; beliefs about alternative prevention methods; the importance of personal recommendation; perceived complexity and familiarity of nasal sprays; personal experiences of spray success or failure; tolerable and off-putting side effects; concerns about medicines; and the nose as unpleasant and unhygienic.

Conclusions People who suffer disruptive, frequent or severe RTIs or who are vulnerable to RTIs are interested in using a nasal spray for prevention. They also have doubts and concerns and may encounter problems. Some of these may be reduced or eliminated by providing nasal spray users with information and advice that addresses these concerns or helps people overcome difficulties.

INTRODUCTION

Respiratory tract infections (RTIs) such as the common cold, influenza, bronchitis, tonsillitis and sinusitis are commonly experienced by most adults. Although they tend to be self-limiting, these illnesses are disruptive and unpleasant,1–5 cause substantial workplace sickness absence6 and contribute significantly to pressures on primary care.7,8 Consultations for RTIs also result in unnecessary antibiotics prescriptions, thus contributing to antibiotic resistance.9,10

Typical RTI prevention approaches reduce the likelihood of becoming infected (eg, social distancing,11 face coverings11 and handwashing11,12) or improve individuals’ immune responses (eg, vaccination13–15 nutrition,16,17 physical activity18,19). Prevention approaches can also intervene at early stages of infection by targeting the nose and the mouth as entry points for viruses.20 These approaches include using mouthwashes and rinses and nasal sprays, douches and irrigation. Products

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This is the first research about how people think and feel about using a nasal spray to prevent respiratory tract infections so adopting an exploratory, inductive, qualitative approach allowed insight into key issues.

⇒ The paper benefits from its coverage of multiple populations, data collection approaches and contexts.

⇒ The pandemic context, short study period and season meant study 2 participants had little exposure to viruses and limited opportunities to try out their sprays.

⇒ The study 2 sample lacked ethnic diversity, tended to have low levels of deprivation and consisted of more females than men.

⇒ This paper demonstrates the benefit of conducting in-depth qualitative research with target users during intervention planning, development and refinement.
may be used regularly and/or in responsible to possible/probable exposure. The mechanism of action appears to be mechanical; either forming a barrier or having a washing out action. These products may also alter the environment of the nose and/or throat, reducing the viral load and the chance the virus will survive/thrive.\(^2\) The COVID-19 pandemic has prompted a resurgence of interest in these approaches.\(^2\) Many formulations and products are under investigation, with some promising findings. For example, a systematic review concluded that iota-carrageenan nasal sprays have a good safety profile and powerful antiviral activity against the common cold.\(^3\) A series of recent reviews and commentaries conclude that these approaches should be subject to further evaluation and/or rapid roll-out in the COVID-19 pandemic. Various randomised controlled trials are ongoing. The RECUR (Reducing common infections in usual practice for recurrent respiratory tract infections) trial (ICTRN17936080) evaluates preventative use of nasal sprays to reduce the frequency, duration and severity of non-pandemic RTIs in recurrent and at-risk primary care patients while the ICE-COVID trial\(^4\) evaluates throat and nasal sprays for COVID-19 prevention in healthcare professionals (HCPs).

Along with evidence about efficacy, it is also essential to accrue evidence about the acceptability of these approaches for the people who may eventually be encouraged to adopt them. Kramer and colleagues\(^5\) describe nasal rinsing as ‘easily implementable’ as a COVID-19 public health measure. However, lay people/patients may not find these approaches easy or acceptable.\(^6\)

No published research has investigated views or experiences of using these approaches for preventing RTIs. However, research exists on similar approaches when used for symptom relief. People with chronic rhinosinusitis describe difficulties using steroid nasal sprays including forgetting to use them, and lack of confidence with technique.\(^7\) It may be considered awkward, prohibitively time consuming\(^8\) and uncomfortable, and, consequently, patients may use these methods irregularly, stopping once relief is gained.\(^9\) Together, these studies indicate that RTI prevention strategies requiring nasal application of a substance may be off-putting for some patients and regular, long-term persistence may be problematic. Identifying concerns and difficulties (along with more positive beliefs and experiences) would allow patient education to be tailored to include persuasive messages and appropriate support to help people overcome barriers.

This paper extends the literature by investigating people’s perceptions and experiences of using a nasal spray for preventing RTIs. We report findings from two qualitative studies. The first is an analysis of online consumer reviews of an RTI prevention nasal spray. The second study analyses interviews with patients heavily burdened by and/or at higher risk from RTIs about their perceptions and experiences of using a nasal spray for RTI prevention. Our aim for both studies was to explore how people think and feel about using nasal sprays to prevent RTIs and to identify barriers and facilitators to the adoption and continued use of sprays. If sprays prove effective in trials, it is important to have a behavioural evidence base to guide interventions that support optimal use. The findings will be valuable to researchers and clinicians seeking to develop or implement RTI prevention approaches, especially those involving nasal sprays or similar prophylactic products such as nasal and mouth rinses and washes.

METHODS

**Intervention development context**

The studies reported in this paper were undertaken as part of the development of a digital behavioural intervention to encourage and support people to use a nasal spray to prevent RTIs (National Institute for Health Research programme grant RP-PG-0218-20005; ‘RECUR’). A randomised controlled trial is currently evaluating the efficacy of the nasal spray intervention; within the trial the brand name of the spray is masked. Therefore, this paper simply refers to it as ‘the nasal spray’. As a regulated medical device, the safety of the spray has been established. It is available to purchase in the UK and currently retails under £10. The manufacturer instructions advise use at the first signs of a cold. In the intervention under evaluation, participants are also advised to use the spray at first signs of any suspected RTI and also in situations where exposure to RTIs is likely (eg, crowded places, close proximity to infected people).

The intervention development work used the person-based approach,\(^10\) which prioritises in-depth qualitative data collection to explore the views and experiences of potential intervention users, in order to understand the context in which users engage with interventions and behaviour change. Figure 1 shows how the studies reported here were used alongside primary qualitative research,\(^11\) a scoping review, behaviour change theory (protection motivation theory,\(^12\) social cognitive theory,\(^13\) necessity concerns framework,\(^14\) sense model\(^15\) and stakeholder and patient and public involvement (PPI) to develop and optimise the intervention. The two studies reported here influenced the development of ‘guiding principles’\(^16\) (online supplemental material 1) and the articulation of programme theory through a logic model for the intervention\(^17\) (online supplemental material 2), then enabled iterative changes to the intervention (online supplemental material 3).

**Study 1: online consumer reviews of the nasal spray**

**Data collection**

Four hundred and seven customer reviews of the nasal spray were taken from four large commercial websites (comprising 263, 93, 30 and 21 spray reviews each). The websites were selected based on having a large number of spray reviews. All reviews were included (positive, negative) except those which focused on supplier-based issues (eg, damaged product). We also removed reviews that

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were duplicated across websites. The search for reviews was conducted in August 2019.

Analysis
We used an inductive thematic analysis approach. Although the review data were ‘thin’ and brief (typically several sentences for each review), we selected this approach to remain open and explorative and to generate broad themes that summarised important topics. Coding was undertaken by SW and FM who separately coded half of the reviews each in NVivo V.12 and then worked together to review, combine, discuss and refine coding. They then developed preliminary descriptive themes to capture key issues within the data. These were subsequently inspected, reorganised and relabelled by LD and SW.

Study 2: interviews about using a nasal spray to prevent RTIs

Recruitment
We sought participants who experience frequent or recurrent infections and/or who are at risk of more severe RTIs. Three UK general practitioner practices identified possible participants by searching their patient lists and posting invitations and information sheets to patients who consulted for ≥1 RTI within the last year and were prescribed antibiotics. They also wrote to patients who had asthma, chronic obstructive pulmonary disease or chronic sinusitis who were at higher risk of RTIs. Patients interested in participating returned reply slips, on which they self-reported their recent RTI history. We then purposively sampled from these responses to prioritise interviewing those with higher RTI frequency and comorbid health conditions. We also sought variation as regards age and gender. We interviewed 13 participants in total.

Data collection
Interviews took place from April to August 2020, coinciding with the beginning of COVID-19 pandemic. Consequently, interviews were conducted by telephone. Participants provided written consent prior to taking part. Before the interview, participants answered brief questions about demographics and the number and type of RTIs they experienced.

Phase A: think aloud interviews (n=10)
Participants were emailed a link to our prototype web-based intervention promoting nasal spray use for RTI prevention (figure 2 provides an overview of this intervention). They worked through the website while simultaneously sharing their reactions aloud. The researcher prompted them to verbalise their thoughts and feelings as they encountered different pages, sections, messages, images and features.

Phase B: postintervention interviews (n=7)
Participants were emailed a link to the digital intervention (now optimised based on phase A feedback). A nasal spray was posted to them along with a short booklet summarising spray instructions. They were asked to use
the website and the spray independently over a period of 2–3 weeks. They then participated in an in-depth interview about their experiences. All participants also answered open-ended questions about their personal experiences of RTIs; findings from this part of the interview are published elsewhere.°

Online supplemental material 4 contains the interview schedules. SW and LD conducted the interviews; both are female postdoctoral researchers with health psychology and qualitative interviewing expertise. Interviews lasted between 46 and 104 min and were audio recorded and transcribed verbatim with identifying details removed. Participants received a £10 voucher to thank them for their time.

Analysis
We used an inductive thematic analysis approach. Transcripts from phases A and B were analysed together. The analysts familiarised themselves with the audio recordings and transcripts. Line-by-line coding of the data was conducted in NVivo V.12 whereby codes were identified and labelled to capture references to perceptions or experiences of nasal sprays for preventing RTIs. The codes were then reviewed, compared, discussed and progressively clustered and merged in order to create themes. This was an iterative process which progressed to refining and organising final themes that captured important patterns and features in the data. SW and LD led the analysis, and all other authors were involved in interpreting, discussing and finalising themes. The research team have health psychology and medical backgrounds and the lead analysts are experienced qualitative researchers.

Patient and public involvement
A panel of PPI contributors with experience of recurrent RTIs and/or health conditions that mean they are vulnerable to frequent or severe infections have inputted into the study planning and conduct, some from the grant application stage. Contributions included editing and improving our participant information sheets, consent forms and interview schedules and participating in pilot interviews helping to interpret findings and drafting this paper and lay summary of the research findings sent to participants. Two members of the PPI panel are co-authors on this paper (DS and SR-H).

This research has been reported in line with the Consolidated Criteria for Reporting Qualitative Research checklist (online supplemental material 5).

FINDINGS
Study 1: online consumer reviews of the nasal spray
Eight themes about nasal spray experiences were developed from the customer review data. These are described below and supporting quotations are provided in table 1. The wording of illustrative quotations has been edited slightly to prevent the original reviews and reviewers being identifiable (eg, through entering the quotation into a search engine). SW reworded the quotations, keeping meaning as close to the original as possible. LD checked and further edited reworded quotes to ensure it retained the meaning and could not be traced back to the original review.
Motivation to avoid infections
Reviewers described strong motivations to avoid becoming ill with cold-like illnesses. For some this was to avoid disruption to responsibilities and routines. Others were focused on avoiding unpleasant or severe symptoms or health complications for themselves or others that they might infect (eg, vulnerable family members).

Inevitability of infections
Some reviewers were fatalistic about catching colds and similar infections and believed that symptoms would inevitably develop and progress despite using the spray.

Alternative approaches to infection prevention
Some reviewers described alternative, competing or perceived superior approaches to avoiding RTIs. This included measures such as good hand hygiene, healthy eating and vitamin supplements. Some expressed a perceived confidence in the body’s own ability to fight off infections.

Recommendations from others
Reviewers sometimes described being influenced to buy and try the spray because of success stories and recommendations from others such as friends, family or HCPs.

Protection from risky situations
Some reviewers described adapting the way that the spray was used, beyond first signs and symptoms of an infection (ie, recommended use as advised on product instructions). They adopted it as a preventative measure for when they perceived a high threat of infection, for example, when travelling or in busy public places.

Ease of spray use
Reviewers often described sprays as quick and convenient to use and easily incorporated into daily life. However,
some drew attention to the importance for correct technique and timely usage for efficacy. Some found that this is not always easily achievable.

**Experiencing side effects**

Reviewers commonly reported side effects including an unpleasant taste or feel in throat or nose, sinus pain, headache or watery eyes. Side effects differed in severity across reviewers. When describing side effects, reviewers often referred to weighing up the experience of side effects against the impact of having a cold-like infection, reaching a range of conclusions about which was most desirable.

**Expectations and experiences of success and failure**

Some reviewers expressed confidence in the efficacy of the spray and referred to its ability to completely prevent colds and influenza from developing or at least reduce the severity of symptoms and shorten their duration. Some reported lack of success or inconsistent results whereby sometimes infections happened despite use (although sometimes these were perceived as possibly milder than they would have otherwise been). Some reviewers emphasised the difficulties in judging whether the spray worked or not, given that it was uncertain how symptoms would have developed over time without spray use. However, doubts and uncertainties did not necessarily deter future use.

**Study 2: interviews about using a nasal spray to prevent RTIs**

**Participants**

Table 2 describes the study 2 participant characteristics.

**Themes**

Eight themes were developed (table 3). These are described below.

**Excitement and optimism about a novel prevention method**

Overall, participants described positive and optimistic views about using the spray, seeing it as novel and of interest and personal relevance. For a few participants,
<table>
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<th>Theme</th>
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| Excitement and optimism about a novel prevention method | “Then, when this came along it was like lightbulbs going off. I’m thinking, oh my God, this is going to be a way that I can safeguard myself and continue to be active within his life. I’m really excited about the uses of it.” (Participant 10)  
“I would quite happily give it a go.” (Participant 11)  
“A hundred per cent I’d be up for giving it a go.” (Participant 5)  
“I will give it a go I can tell you that now.” (Participant 6) |
| Identifying first signs of infection  | “I tend to just feel more rundown, tired, a bit headachy.” (Participant 7)  
“A lot of the times when I’m sneezing it’s just because of my hay fever. It was quite difficult to tell.” (Participant 9)  
“If I know it’s coming, by the time I’m doing something about it, I guess because my immune system’s got no great strength, it’s almost like too little, too late.” (Participant 10) |
| Considering use in risky situations | “I can say, ‘Well, I’ve got to go out. There’s a chance I may be in contact with other people, so I’ll use the spray.’ It’s like another layer of protection.” (Participant 12)  
“COVID-19 makes it more appealing, actually. I was quite intrigued about whether it would work for COVID.” (Participant 11)  
“I don’t know, on a bus, supermarket, at the cinema, at the theatre… Like when you get home from the theatre you could start using it then, even if you haven’t had any signs of anything. That was something that I thought was really useful to have. I could see that scenario.” (Participant 10) |
| Consequences of feeling protected   | “…that could only be helpful. I’m genuinely interested from those points of view, because I could get protection in the small part of my life where I’m allowing myself to be at risk, plus I think if I felt safer, I might therefore go out more and feel less frightened about the world.” (Participant 10)  
“It just meant that I could get on with things. Did I feel invincible? No, but I felt like I didn’t have to worry too much, whereas I think if I was coming down with a cold I would have worried about work and being ill and not being able to complete work. I felt more relaxed, maybe, more confident.” (Participant 11)  
“But then would it encourage more people to actually go out and be slightly more reckless with sprays and masks and protection, washing their hands, touching their face because they’re going, ‘Oh, I’m using the spray, it’s okay.’ That’s the other side of it.” (Participant 12) |
| Concerns about medicines             | “Part of it is because I don’t like using medications, and I particularly don’t like nasal sprays. I think over the last year or so I’ve used far too many and I’m a bit fed up of putting things in my nose. I think there’s something off-putting about that.” (Participant 11)  
“I mean, to be fair, if it worked and it stopped me taking my medication, I’d much rather use a spray than medicine.” (Participant 8)  
“At the same time, I was like, oh well if you don’t have to ask a doctor and it’s not an actual medication is it actually going to work?” (Participant 9) |
| Unpleasantness and hygiene           | “It’s not particularly pleasant, is it, watching people sticking things up their noses and their noses run and stuff.” (Participant 11)  
“You spray it up and then it all runs down. That sounds disgusting.” (Participant 4)  
“I was also worried that if I used it, it would pour everywhere. It didn’t really.” (Participant 9)  
“I wouldn’t [re]use anything that went into an orifice like an inhaler, or something I stuck up my nose, I wouldn’t keep it and use it for another time.” (Participant 10) |
| Familiarity and confidence           | “I’m not very good at stuff like that. …I don’t think I’ve ever really tried one [a nasal spray]. I’m just kind of wary of it.” (Participant 9)  
“It’s common sense really. I’ve been using a [different type of] spray for years.” (Participant 4)  
“It’s so straightforward using a nasal spray… I wouldn’t bother with the video… Particularly at my age range, you’ve probably used nasal sprays several if not many times over your lifetime so you just would just use it.” (Participant 1)  
“I think [I was] probably arrogant, I probably thought, ‘Oh, for goodness sake, I don’t need to be shown how to use a nasal spray!’ Although, clearly I did because once I used it as recommended, I didn’t get a headache.” (Participant 13) |
| Reactions to possible or actual side effects | “I think it’s good that it’s listing the side effects, but they’re not severe side effects. Obviously, if they’re only very, very small, like causing a headache, you can take some paracetamol for that. If it stops you getting an infection or prolonging the infection, then a headache, just stopping that is very minor.” (Participant 5)  
“I’d rather have that then a full-blown infection. That is on the plus side, even if it can cause a headache.” (Participant 8)  
“I thought I’d try it again, and I did aim it more towards the ear, and although I did get a slight headache, it was much better and it went away very quickly.” (Participant 13) |

There was a very pronounced excitement, with the spray seen as a way of transforming their quality of life. Others were more muted in their enthusiasm but still interested and willing to try the spray. Even participants who were not fully convinced that the spray would work still considered it worth a try.

Participants found the explanations in the Immune Defence digital intervention about how the spray works to be understandable and plausible, in particular how the spray created an inhospitable environment for viruses. These ideas were particularly relevant and persuasive based on understandings about viruses and infection that participants were rapidly developing during the COVID-19 pandemic.

Identifying first signs of infection
Most participants were aware of their early RTI signs and felt able to recognise and react promptly to them by using a spray. However, sometimes participants found it difficult to tell whether a symptom signalled an oncoming infection. The crossover between hay fever and RTI symptoms was a particular area of uncertainty.

A minority of participants also described how they never experienced common early signs of infection and...
only became aware of oncoming illness through a severe symptom typical of a later stage of an infection (eg, cough). Some therefore anticipated struggling to intervene in time.

Considering use in risky situations
Participants were particularly interested in using the spray in risky situations to prevent infections. Some participants considered that this mode of use may help protect against COVID-19, although some remained cautious.

Some participants easily identified risky situations, where they would be happy to use the spray preventatively such as supermarkets, hospital appointments, concerts, airplanes and public transport. However, other participants debated or expressed uncertainty about what level of exposure would count as ‘risky’. For some, most situations were currently considered risky (ie, during the COVID-19 pandemic). Others felt that if other mitigations were in place (such as social distancing or face masks) the spray was redundant for RTI prevention.

Consequences of feeling protected
A few participants anticipated that the protection against RTIs afforded by the spray would change how they felt, thought and behaved including feeling safer, less fearful, more relaxed and more comfortable mixing with people with RTIs. A minority expressed concern that using the spray could lead to negative consequences for infection prevention behaviours. They speculated that other people (not themselves) might adopt less cautious behaviour overall. This concern appeared to be heightened by the COVID-19 context and included worries that, if other people were using the spray, they might be less likely to engage in other preventative behaviours such as masks and social distancing.

Concerns about medicines
Participants appeared to perceive RTI prevention nasal sprays as a form of medicine (the spray is officially a ‘medical device’). Conceptualisation of the spray in this way seemed to persist for most participants to some degree despite encountering and understanding our intervention message that the spray is not a medicine and our comparison of regular spray use to regular hand sanitising. In line with perceiving the spray as a form of medicine, participants raised questions and concerns that are typical of medicines. For example, they were interested in ingredients and wanted to check for allergies, interactions or contraindications with their routine medications. Participants also expressed apprehensions regarding overuse which they felt could lead to side effects, addiction or the spray becoming ineffective.

Participants often discussed trying to avoid using medicines. While this could raise concerns about using the spray, a few considered the spray a means of avoiding needing medication for RTI symptoms or disease exacerbations (eg, antibiotics, steroids).

Although thinking of the spray as a medicine elicited concerns relating to medicines, thinking of the spray as something without medicine ‘status’ also appeared problematic; a minority of participants expressed slight doubt about how effective the spray could be if it was not a medicine, and not already regularly prescribed or recommended by the National Health Service.

Unpleasantness and hygiene
A few participants described how actions relating to noses and nasal mucous were unpleasant and socially unacceptable. A few (specifically those unfamiliar with using any type of nasal spray) found that the concept of a nasal spray inactivating and cleaning out viruses raised concerns about a messy and wet procedure. However, those who tried out the spray did not find this occurred. Given their awareness that viruses might be present in the nose, some participants were also concerned about how to use the spray hygienically. For example, they wondered whether germs left on the nozzle could infect them if they used the spray again later.

Familiarity and confidence
There was considerable variability in how much detailed information people felt they needed about exactly how to use the spray. This seemed to relate to lack of confidence and was prominent in participants who had not used any type of nasal spray before. One participant found using a spray daunting, was anxious about getting it right and found detailed instructions reassuring. Conversely, participants who had previously used another type of nasal spray appeared comfortable trying a spray and had fewer questions and concerns, seeing it as obvious and commonsense. However, this confidence could be unhelpful; one confident participant bypassed the instructions, tried the spray using the incorrect technique and experienced strong side effects. They described having thoughts about never using the spray again before realising the value of the technique instructions. Generally, people welcomed access to detailed guidance about spray technique and especially appreciated that the tips were aimed at helping them to reduce chance of side effects.

Reactions to possible or actual side effects
Participants considered knowing about the potential side effects of the spray important, paid keen attention to this information, but overall did not consider them off-putting. Participants stated that they would be willing to try the spray and would review their position and stop using the spray if bad side effects were experienced.

DISCUSSION
This paper is the first published research to explore how people think and feel about using nasal sprays, an emerging area of RTI prevention. Various important perceptions and experiences were identified which are discussed below in terms of their relevance for
encouraging people to adopt and persist with this type of RTI prevention approach, if trial evidence supports their effectiveness.

Existing theory and research

Our findings align well with expectancy value theories of health behaviour such as health belief model\(^40\) and the necessity concerns framework.\(^34\) These theories emphasise implicit cost-benefit analysis; a person adopts and perseveres with preventative health behaviours generally or adherence to a medicine specifically based on perceived efficacy, necessity and tolerability. We found strong beliefs about necessity in both studies. Study 1 participants wanted to avoid the physical and social impacts of RTIs and study 2 participants (with recurrent RTIs or vulnerabilities to severe RTIs) welcomed our information and advice and considered sprays a novel and potentially effective prevention method. Considerable interest in strategies to prevent RTIs has been recently documented in vulnerable and/or recurrent patients\(^39\) but research with younger and/or healthy participants in non-pandemic times reveals weaker or mixed beliefs about the necessity of avoiding infections.\(^1\)\(^2\)\(^41\)\(^45\) Both studies reported here also highlighted a range of beliefs and concerns that could plausibly reduce engagement with using nasal sprays. Concerns around discomfort and regime complexity also arose in studies about nasal irrigation and sprays for sinusitis relief.\(^4\)\(^29\) According to expectancy value theories, reducing concerns and costs (alongside increasing necessity beliefs) will improve initiation and continuation of the behaviour.

A theoretical review\(^46\) argues that medication adherence should be conceptualised as a type of causal learning and reasoning. People learn about how medications effect outcomes through a dynamic interplay of top-down (pre-existing beliefs and expectations about treatments) and bottom-up processes (personal experiences with symptom change and side effects, particularly early in the course of treatment). This learning influences their ongoing adherence. Causal learning theory\(^46\) predicts that learning a link between an intervention and positive outcomes (and therefore strong adherence) in the context of a nasal spray for RTI prevention could be challenging for several reasons. First, people have limited data on which to reach conclusions from (e.g., several infections per year, rather than daily symptoms). Second, other variables confound interpretations of spray efficacy (e.g., other RTI prevention behaviours). Third, sprays may not prevent infections 100% of the time, especially when use is suboptimal (timing, technique, dosage). Our findings about optimism about the spray are positive; people are likely to begin using sprays with expectancies that will facilitate interpreting a link between the spray and positive outcomes. However, some participants described doubt about effectiveness and some highlighted the difficulty of drawing strong conclusions from one’s own experience. This, alongside the identified focus on side effects and concerns about using medicines, suggests that causal learning of a treatment benefit may be difficult and this may undermine adherence.

Finally, perceived ease or difficulty of using the spray and confidence for using it were also prominent within our findings. Social cognitive theory highlights self-efficacy as a key predictor of behaviour.\(^47\) Intervention complexity and lack of confidence, alongside poor adherence, have also been emphasised in research on nasal irrigation for sinus symptom relief.\(^4\)\(^29\)

Intervention development

We undertook the two studies reported here while developing the Immune Defence nasal spray intervention. Study findings informed the planning of initial intervention content (study 1) and optimisation of that content (study 2). For instance, our intervention content addressed concerns about overusing medicines, side effects and hygiene as well as avoided disgust reactions. We provided persuasive information to challenge0 fatalism about catching RTIs, helped people to build positive expectations of the spray and to continue to hold these even if it does not appear to work every time. We promoted the benefits of feeling protected, while explaining the importance of continuing other RTI prevention behaviours. We emphasised the simplicity of spray use (and ensured a straightforward experience via clear, easy instructions) and we presented information to suit both experienced nasal spray users and less confident beginners. Online supplemental material 6 provides further details about how study findings influenced intervention content.

Strengths, limitations and future research

A key strength of this paper was its combination of findings from different samples and data collection methods allowing insights into a variety of people and experiences. Some of our data reflect experiences of people who were already motivated to buy the spray and who had some experience of using it, but we also gathered data from people for whom RTI prevention is clinically relevant but who did not currently use nasal sprays. We also collected data from pre-COVID-19 and early pandemic contexts.

Study 1 was a large sample but collected and analysed thin, brief data with little contextual information and no knowledge of reviewer demographic and clinical characteristics. Furthermore, the reviews cannot be verified as genuine as they were on commercial websites. However, the details of problems, concerns and doubts that were largely supported (and extended) in study 2 give confidence that we have captured genuine data.

Study 2 examined the reactions to the Immune Defence intervention content allowing insight into what is interesting, confusing, concerning, off-putting about the nasal spray as described by a specific rationale and set of instructions. While some of the detail is therefore particularly pertinent to the Immune Defence nasal spray intervention, the overall themes may be generalisable to other nasal sprays and similar products, prevention behaviours, instructions and advice. Phase b of study 2 was designed


9
to explore how people experience beginning to use the spray for the first time. A significant limitation, however, is that only seven participants took part in this phase. They also tried the spray over just 3 weeks, in a partial COVID-19 national lockdown and during the summer months. They therefore experienced little exposure to viruses and consequently had limited opportunity to use the spray in the intended ways. Tracking more participants over longer periods will provide a clearer picture of usage and adherence and will be particularly useful for shedding light on factors that may only become apparent over time (eg, experiencing or not experiencing benefits). Qualitative and quantitative data collection on spray adherence, experiences and beliefs is currently in progress as part of the Immune Defence process evaluation.

While our findings suggest nasal sprays for RTI prevention are of interest to clinically higher risk subgroups and considered particularly valuable in the pandemic context, whether lower risk groups (eg, healthy adults) have similar perceptions has not been established. Furthermore, some of the recent and current trials of nasal sprays and similar approaches relate specifically to HCPs at risk during provision of medical care. Findings about lay people’s motivations, facilitators and barriers may not transfer well to HCPs; their expertise and the occupational setting may mean different factors are important. Additional research may therefore be needed with these groups.

CONCLUSION
People who suffer frequent or severe infections or who are clinically vulnerable to RTIs are interested in using a nasal spray to prevent RTIs and see this as useful or even a ‘game changer’. They also have some doubts and concerns and may expect to encounter (or actually encounter) certain difficulties. Many of the information needs, misunderstandings, concerns and difficulties exposed through the current research may be remedied by ensuring interventions are designed to help people overcome these issues.

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Contributors LY, AWAG and PL conceived the study idea and initial study design with later input from BA, LD, SW, KG, FM, JD-D, KB, SR-H and DS. SW led the data collection with assistance from LD, SW, LD and FM led the data analysis with input from all authors at different stages. LD and SW drafted the manuscript. All authors contributed to critically editing and approving the final manuscript. AWAG is the guarantor for this work.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not required.

Ethics approval This study involves human participants and ethics and research governance approvals were granted by the University of Southampton for study 1 (ERG01522934). Ethics approvals were granted by the NHS and the University of Southampton review boards for study 2 (REC/HR19/SC/0354; ERG0148223). Participants gave informed consent to participate in the study before taking part.

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Data availability statement No data are available.

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**Supplementary material 1: RECUR (“Immune Defence”) Guiding principles – Nasal sprays**

<table>
<thead>
<tr>
<th>User context</th>
<th>Key design objective</th>
<th>Intervention design features</th>
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<tbody>
<tr>
<td>Our users have a range of nasal spray experience. Some have used sprays before, such as for hayfever, but perhaps not using the techniques we recommend for this spray. Some have never used a nasal spray before. The idea of using sprays preventatively is a novel idea for most target users.</td>
<td>To support new and experienced nasal spray users to build skills to develop a correct spray technique.</td>
<td>• Provide an instructional video on a 'live model' demonstrating correct spray technique and modelling behaviour to build skills for new users. • Provide an instructional booklet to be kept with the spray for ease of use and a reminder of how to use the spray correctly. • Highlight specific advice which will be helpful for new and experienced sprays users (e.g. do not inhale deeply when the spray is in your nose). • Advise everyone to watch the video including experienced sprays users, highlighting that this spray is administered in a different way.</td>
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<tr>
<td>Our target group perceive the spray as exciting and they are hopeful it will work. However, they may not always experience benefits when they begin using it and this could lead to disappointment and (depending on other factors, including side effects) discontinuation or suboptimal adherence. Some users also have previous experience of trying other prevention strategies with little success, leading to a fatalistic perspective of RTIs.</td>
<td>To support people to set and maintain positive expectations of spray efficacy, even when RTIs still occur.</td>
<td>• Explain the mechanism of how the spray works so that people understand that the aim of the spray is to reduce viral load not prevent viruses entering the body at all. • Emphasise how sprays reduce the duration and severity of an RTI, as well as preventing them in the first place, to avoid feelings of disappointment if people do get an RTI after using the spray. • Address the potential lack of efficacy beliefs by providing advice for future use (e.g. using the spray quickly at first signs of infection, using the correct technique) and motivating the user to keep trying the spray, even if they got an infection.</td>
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</tbody>
</table>
| Concerns about nasal spray side effects are fairly common and may lead to discontinuation of use. | To reduce people's concerns about possible negative effects of spray use. | • Provide reassuring information to address concerns about potential side effects, specifically regarding the mildness and tolerability of the spray.  
• Change perceptions of side effects – framing them positively as 'normal' by describing what to expect. Explaining side effect symptoms as a sign that the spray is working effectively (e.g. getting to the areas it needs to in order to work).  
• Compare side effects to worse outcomes if nasal spray was not used e.g. getting an infection.  
• Provide advice and skills training on how to optimise your nasal spray technique to avoid side effects.  
• Advise on how to cope with side effects if they did happen e.g. how to deal with a nosebleed. |
| --- | --- | --- |
| People may see nasal sprays as medicines because of their mode of administration and previous experiences with sprays that are medicines (e.g. hayfever, sinus). Many people have concerns about over-use of medicines. | To help develop an alternative way of thinking about the spray, to reassure people about safety and to persuade people that nasal sprays are safe. | • Explain that nasal sprays work in a similar way to handwashing/hand gel. This provides a familiar example of something that is not a medicine but helps prevent infections. Both prevention methods are common behaviours, simple and acceptable, and they neutralise/remove germs/viruses before they can infect you and make you ill.  
• Address the concern that the spray is a medicine by clarifying that it is not a medicine and that it is safe and non-addictive. |
The intervention will be delivered during the COVID-19 pandemic where the threat levels and national recommendations are constantly changing.

Emerging evidence suggests that nasal sprays may be useful in providing additional protection against viruses like COVID-19, which act similarly to common RTIs but have severe consequences, particularly for vulnerable groups.

Our target group clearly spot the similarities between COVID and seasonal/normal RTIs. Those using the intervention in a pandemic context may be concerned with either or both COVID/normal RTIs.

Some of our target group have incorrect beliefs that the spray can replace government COVID recommendations or that the spray is not needed because of other behaviours mitigating the usefulness (e.g. mask wearing, social distancing).

<table>
<thead>
<tr>
<th>To ensure the intervention is suitable for delivery during rapidly changing COVID-19 pandemic context.</th>
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<tbody>
<tr>
<td>• Be able to quickly update intervention content when needed to reflect latest guidelines and research evidence.</td>
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<tr>
<td>• Explain how effective the spray might be for COVID-19.</td>
</tr>
<tr>
<td>• Correct misconceptions about nasal sprays and COVID-19 by explaining that the spray is another layer of protection to be used with other behaviours to ensure the best protection possible again infections.</td>
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BMJ Open, et al. Williamson S
Supplementary material 2: Logic model

**PROBLEM**

Recurrent respiratory tract infections (RTIs)
- Common cause of sickness absence
- Recurrent RTIs have a significant impact on quality of life
- Threat of antibiotic resistance
- Need to find alternative self-management strategies

**INTERVENTION COMPONENTS**

- Providing persuasive information that nasal sprays will help prevent RTIs e.g. explanation of how nasal sprays prevent RTIs
- Providing information and training on when and how to use nasal sprays e.g. demonstration of correct nasal spray technique
- Providing reassuring information to address concerns about nasal sprays e.g. reassurance about side effects

**INTERVENTION PROCESSES**

- Promoting positive outcome expectancies
- Improved skills/self-efficacy
- Reducing nasal spray concerns

**KEY PROTECTIVE BEHAVIOUR**

- Effective use of nasal sprays
- Limit viral replication

**IMMUNE FUNCTION**

- Reduction in days of illness with RTIs

**OUTCOME**
## Supplementary material 3: Table of Changes extract

This is a simplified extract from a “table of changes” used to optimise the Immune Defence nasal spray intervention. It has been edited for clarity for readers outside of research team.

<table>
<thead>
<tr>
<th>Website Section/content referred to</th>
<th>Original website content wording</th>
<th>Participant comments: positive, or likely to promote engagement/adherence</th>
<th>Participant comments: negative, or likely to impair engagement/adherence</th>
<th>Action/Changes</th>
<th>Final website content wording</th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;When do I use the spray?&quot;</td>
<td>There are 3 ways to use the spray.</td>
<td><strong>INTERVIEWER:</strong> So what would you say you are kind of first signs of infection? <strong>PARTICIPANT 1:</strong> Mine are usually sneezing and a tickle. <strong>INTERVIEWER</strong> Yes, so you'd be able to identify yourself in those symptoms? <strong>PARTICIPANT 1:</strong> Oh yes, yes.</td>
<td><strong>PARTICIPANT 7:</strong> I think that makes sense, and you haven't said, 'These are necessarily the signs that you would get when you feel an infection coming on.' You say, 'That's what often people say they are,' so... <strong>INTERVIEWER:</strong> So are your first signs recognisable in there, or not? <strong>PARTICIPANT 7:</strong> No. I don't know. I think I tend to just feel more rundown, tired, a bit headachy. I don't know. I wouldn't say I get a runny nose at all. No, I wouldn't say they are, to be honest!</td>
<td>We added a catch-all statement about a wide range of early signs of RTIs, acknowledging idiosyncrasies and building confidence in spotting own first signs.</td>
<td>There are 3 ways to use the spray.</td>
</tr>
<tr>
<td>Description of first signs of an infection that should trigger use of the spray.</td>
<td>1. When you first feel an infection coming on. It works best if you use it as soon as you notice any symptoms. Often people say their first signs are:  - Sneezing;  - A runny nose;  - A tickle in the nose; or  - A tickle in the back of the throat;</td>
<td><strong>PARTICIPANT 3:</strong> So I suppose when I first feel an infection coming on is when the sore throat starts. <strong>INTERVIEWER:</strong> So that would be your first sign of an infection happening? <strong>PARTICIPANT 3:</strong> That would be the warning sign, definitely.</td>
<td><strong>PARTICIPANT 4:</strong> [participant reads website] &quot;Often people say the first signs are sneezing&quot;, yes, agree with that; &quot;runny nose&quot;, yes; &quot;tickle in the back of the throat&quot;; or &quot;tickle in the nose&quot;? <strong>PARTICIPANT 4:</strong> Yes. The other thing is a headache or feeling hot and cold - feeling hot is another sign for me anyway. <strong>PARTICIPANT 3:</strong> It's great. It's absolutely everything that I and my family feel and experience.</td>
<td><strong>PARTICIPANT 1:</strong> I can't think of any other additional things that would indicate that I had a nasal infection coming on. I would perhaps personally, sometimes I get a thick throat, like the equivalent of catarrh building up... but whether that comes under a tickle, I don't know, but that's what I personally would get as an indication, like just a thickening of the mucus. <strong>INTERVIEWER:</strong> Would you say those first signs of infection are similar to what you experience, or is it different? <strong>PARTICIPANT 10:</strong> Yes.</td>
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I think the first signs, they are but the first signs are often an aching, aren't they and sore? I get sore skin and aching lip, just a general ache as a first sign quite often of these bugs. So sometimes they are, but I suppose that might be the difference between colds and flu, I don't know. Sore throat I'd say, rather than a tickle in the back of the throat, but you say often...I'm not sure about these symptoms. Maybe sometimes, but not always. I think for me I often feel achy and have this very funny sensitive skin which seems a bit sore all the time, that would be the first sign, but maybe as I say, that's the difference between flu and cold, I don't know. If that's what people say then that's what most people say then that's a thing, isn't it?

<table>
<thead>
<tr>
<th>How does the spray work?</th>
<th>It's a bit like using soap when you wash your hands, only better.</th>
<th>PARTICIPANT 4 [Reading website] How does it work? “It's a bit like using soap and wash your hands only better!” Oh, I like that.</th>
</tr>
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<tbody>
<tr>
<td>Comparison of using the nasal spray to washing.</td>
<td>The spray traps viruses and washes them out of the nose; and make the nose and throat a very unfriendly place for viruses.</td>
<td>INTERVIEWER: What sounds particularly appealing about giving it a go? PARTICIPANT 5: It says that, well, the whole bit of how does it work? “The spray traps the viruses and washes them out of your nose. Makes your nose and throat a very unfriendly place for the viruses. This means it's much harder for them to survive”. I'd be willing to give that a go!</td>
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<td>In various places the content refers to a washing/washing out metaphor and a comparison to washing hands with soap and</td>
<td>This means it's much harder for them to survive</td>
<td>PARTICIPANT 4: The spray traps the viruses and washes them out of the nose. Ooh, how does it wash it out of the nose? You spray it up and then it all runs down. That sounds disgusting. Do you spray it and then blow out? INTERVIEWER: You've got a question there about how to use it essentially, is that right?</td>
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<td>PARTICIPANT 4: It says here just well, I know you know what it says but, 'Spray traps the viruses and washes them out of the nose.' All right. Let's read the next sentence. “Makes the nose and throat a very unfriendly place for viruses. This means it's much harder for them to survive”. We retained the hand cleaning metaphor but change to a comparison with hand gel rather than soap and water to provide a closer match to the spray action and avoid the procedure sounding difficulty or unpleasant. Hand gel use is currently (early)</td>
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<td>It's a bit like a hand gel, but specially designed for your nose. The spray helps to clean the virus from your nose.</td>
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<td></td>
<td>The spray also makes the nose and throat a very unfriendly place for viruses. This means it's much harder for them to survive so they</td>
</tr>
<tr>
<td>Water to remove germs before they can do harm.</td>
<td>So they can't take hold and make you ill.</td>
<td>INTERVIEWER: Does the explanation about how it works make sense to you, about the soap and hands? PARTICIPANT 3: Yes, indeed. Yes, I'll say!</td>
</tr>
<tr>
<td>Video – instructions how to use the spray</td>
<td>Part of the video demonstrates high risk situations in which you should use the nasal spray. It depicts a person being sneezed on by</td>
<td>INTERVIEWER: I heard you had a little bit of a giggle at one point. PARTICIPANT 3: [Laughs] Yes, that was just the second person sneezed all over the girl who was doing the demonstration.</td>
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<tr>
<td>Video – instructions how to use the spray</td>
<td>PARTICIPANT 5: Yes, no, I think it's good. It's very informative and it's good that it gives people, like it shows people how to correctly use the spray because sometimes, the instructions on the boxes and in the packets and things, they aren't always as clear. INTERVIEWER: Do you think you'd find that useful yourself if you were trying out the spray for the first time? PARTICIPANT 5: Yes, definitely.</td>
<td>INTERVIEWER: we do have a link there to a video. You don't need to click on that. I just wanted to ask you, with the information that's here would you need to click on that link to see the video, or do you think that you'd be okay with the instructions there? PARTICIPANT 7: I wouldn't because obviously I've used sprays before. Somebody that hasn't used, and is a bit wary of it, would probably click on it. INTERVIEWER: Would you be inclined to watch the video yourself if you wanted instructions, or would you be more…? PARTICIPANT 1: No, to be honest, it's so straightforward using a nasal spray… I wouldn't bother with the video… Particularly at my age range, you've probably used nasal sprays several if not many times over your lifetime so you just would just use it. INTERVIEWER: What did you think about that video? PARTICIPANT 4: Yes, it's common sense really. I've been using [another] spray for years... I do keep my head straight. I do do my one or two good puffs. I don't breathe out and spray it everywhere. It's common sense. PARTICIPANT 2 When I first got [the spray], I used it once, even though I didn't have any need to use it and</td>
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<td></td>
<td></td>
<td>Click <a href="#">here</a> to see a short video to help you master the spray technique. This video is worth watching even if you have used nasal sprays before. The technique for this spray might be a bit different. Using the spray correctly give you the best chance of fighting infections!</td>
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</table>
within seconds it had given me a headache, exactly as it did the very first time I used it about a year or so ago on the recommendation that was given to me. I felt, right, I'm not going to use it anymore. The only way I can describe the headache is it's like a freezer headache. It's exactly the same, if you take a bite of an iced lolly or something. That sort of, right between the eyes. I read about how it says that if that happens, you should aim it more towards your ear, rather than straight up...[later in interview]...[INTERVIEWER]: Why did you decide not to watch the video? PARTICIPANT 2: I think I was probably rushing off to do something, or I got distracted or, no, I didn't. I think probably arrogant, I probably thought, 'Oh, for goodness sake, I don't need to be shown how to use a nasal spray.' Although, clearly I did because once I used it as recommended, I didn't get a headache.

Readers interested in using the Person-Based Approach to intervention development and who wish to use a Table of Changes to assist the process may find resources on this website helpful: https://www.lifeguideonline.org/pba
Supplementary material 4:
Study 2 - Interview Schedules for Phase A and Phase B

Phase A: Think-aloud interviews

Prompts about key pages of intervention content [e.g. menus/ first page etc.]

- What are your first impressions of this page?
- What are you thinking now?
- What made you choose that option?
- What do you think about [this activity, this information, this strategy/tool/idea]?
- Can you tell me a bit more about why you think that?
- [in response to an expression of like/dislike] What is it you like/don’t like about that?
- That’s really interesting…..
- [picking up on vocalisations/tone of voice etc] I noticed that you paused/groaned/laughed/sighed etc. at……… Can you tell me what you thought about that?

After working through the key pages of intervention content:

- Overall, what do you think about the web pages?
- Can you tell me anything you thought was particularly good about the web pages?
- Can you tell me anything about the web pages that you were less keen on?
- Which parts did you find most relevant to you? Which parts were the least relevant to you?
- Having looked at the web pages, can you tell me how you feel about trying to use a nasal spray to try to reduce these sorts of infections
- How much of what you’ve seen today do you think is relevant to coronavirus?*
- How at risk do you feel about getting these infections at the moment?
- What do you feel about the recommendation to use the spray when at high risk and how this applies to coronavirus?*
- What device did you use to look at the website today?
  - If you were using the website over a longer period of time, how would you access the website?
  - Would you use mobile phone at all?
**Phase B: Post-intervention interviews**

- Can you start by telling me overall how you got on with trying the spray?

**Questions if they have tried the spray:**
- Can you tell me all about how you found using the nasal spray?
- Can you tell me about anything you liked or found easy?
- Can you tell me about anything you disliked or found difficult?
  - Can you let me know if there was anything you found helped with that?
  - Can you tell me about anything that worried you about using the spray?
- Can you tell me about when you used the nasal spray?
  - When did you think to use it?
  - Can you tell me about whether any situations came up where you could have used the spray (e.g. first symptoms, feeling a risk of catching an infection)? Can you tell about how you decided whether to use the spray?
- Can you tell me about what you thought were the advantages of using the nasal spray?
- Can you tell me about what you thought were the disadvantages of using the nasal spray?
- Can you tell me what it’s been like for you trying these activities/changes whilst in (partial) lockdown because of coronavirus/COVID-19**?
  - Explore the context – have they been self-isolating? Shielding?
  - What have your infections been like during this time? (More/less?)
  - What aspects of lockdown have made it easier to try these activities/manage your infections?
  - What aspects of lockdown have made it harder to try these activities/manage your infections?
  - Can you tell me about any information or advice that was difficult for you to follow during lockdown?

**Questions if they have not managed to try the spray:**
- Can you tell about what you thought about the idea of using a spray to try to prevent infections?
- Can you tell me about anything about the spray that you liked or found easy?
- Can you tell about anything about the spray that seemed off-putting or difficult for you?
- Can you tell me about anything that worried you about using the spray?
- Can you tell me anything you feel would help you in the future with trying the spray?
- Can you tell me about whether any situations came up where you could have used the spray (e.g. first symptoms, feeling a risk of catching an infection)?
- Can you tell about how you decided whether to use the spray?
- Can you tell me about what you thought were the advantages of using the nasal spray?
Can you tell me about what you thought were the disadvantages of using the nasal spray?
Can you tell me what it’s been like for you trying these activities/changes whilst in (partial) lockdown because of coronavirus/COVID-19?*
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  - Can you tell me about any information or advice that was difficult for you to follow during lockdown?

Website questions:
- What did you think of website that gave you information and advice about using the nasal spray?
- Can you tell me about anything that you liked about the website?
- Can you tell me about anything that you disliked?
- Can you tell me about anything that you would change in the website?
- Can you tell me about anything that you thought was particularly relevant to you?
- Can you tell me about anything that you thought was not particularly relevant to you?
- Can you tell me about any information or advice that didn’t make sense?
- How do you think that could be changed?
- Could you tell me about anything that you thought didn’t work properly?
- Can you tell me about whether you went onto the website more than once? (explore why they returned/whether they found what they needed).
- Since looking at the website, how do you feel about infections now?

Spray Instructions:
- On the website, it mentions 3 situations where you should use the spray. What did you think about these instructions?
- On the website, it mentions how often to use the spray in each of these 3 situations. What did you think about these instructions? (prompting around the instructions).
- On the website, there is a video about how to use the spray. What did you think about this?
- Can you tell me what you thought about the paper booklet about the spray? (repeat questions above as necessary- liked, disliked etc).

Open-ended Questions about personal experiences of RTIs:
1. Can you tell me all about your experience of these sorts of infections [repeat list of RTIs if necessary: colds, flu, coughs, chest infections, bronchitis, ear infections, sinusitis, sore throats, throat infections and tonsillitis].
o Prompts:
  ▪ Can you tell me about the types of illnesses you tend to get?
  ▪ Can you tell me about when you tend to get these illnesses?
  ▪ What's it like for you when you have them?
  ▪ How often do you get them?
  ▪ How long do they last?

2. Can you tell me about why you think you get these sorts of illnesses?
   o Prompts:
     ▪ Can you tell me about what you think the causes of these illnesses are?
     ▪ Any other reasons why you think you get them?

3. Can you tell me about things you do to try and stop getting these illnesses?
   o Prompts:
     ▪ What made you decide to use these things? Why is it important for you to x/y/z? (e.g. eat healthy, exercise, get the flu jab)
     ▪ How helpful do you find these things?
     ▪ Why do you think they work?

4. When you have these sorts of illnesses is there anything you do to try and make it go away quicker?
   o Prompts
     ▪ Any things you take, or things you do, or avoid doing?
     ▪ What made you decide to use these things? Why is it important for you to x/y/z?
     ▪ How helpful do you find these things?
     ▪ Why do you think they work?

[*coronavirus question and probing was not in the original interview schedule and was added in for later interviews*]
**Supplementary material 5: COREQ checklist**

Tong et al 2007, 32 item check list: [https://academic.oup.com/inghc/article/19/6/349/1791966](https://academic.oup.com/inghc/article/19/6/349/1791966)

<table>
<thead>
<tr>
<th>Domain 1: Research team and reflexivity</th>
<th>Item</th>
<th>Guide questions/description</th>
<th>Manuscript section where information can be found</th>
</tr>
</thead>
<tbody>
<tr>
<td>Personal Characteristics</td>
<td>1</td>
<td>Interviewer/facilitator</td>
<td>Method- data collection – Phase B: Post-intervention interviews (page 8)</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Credentials</td>
<td>Method- data collection – Phase B: Post-intervention interviews (page 8)</td>
</tr>
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<td></td>
<td>3</td>
<td>Occupation</td>
<td>Method- data collection – Phase B: Post-intervention interviews (page 8)</td>
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<td>4</td>
<td>Gender</td>
<td>Method- data collection – Phase B: Post-intervention interviews (page 8)</td>
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<td>5</td>
<td>Experience and training</td>
<td>Method- data collection – Phase B: Post-intervention interviews (page 8)</td>
</tr>
<tr>
<td>Relationship with participants</td>
<td>6</td>
<td>Relationship established</td>
<td>Method- recruitment – Study 2 (page 7)</td>
</tr>
<tr>
<td>Participant knowledge of the interviewer</td>
<td>7</td>
<td>What did the participants know about the researcher? e.g. personal goals, reasons for doing the research</td>
<td>Method- recruitment – Study 2 (page 7)</td>
</tr>
<tr>
<td>Interviewer characteristics</td>
<td>8</td>
<td>What characteristics were reported about the interviewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic</td>
<td>Method- data collection (page 8) Funding statement (page 25)</td>
</tr>
</tbody>
</table>

**Domain 2: study design**

<table>
<thead>
<tr>
<th>Item</th>
<th>Guide questions/description</th>
<th>Manuscript section where information can be found</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>Methodological orientation and Theory</td>
<td>What methodological orientation was stated to underpin the study? e.g. <em>grounded theory, discourse analysis, ethnography, phenomenology, content analysis</em></td>
</tr>
<tr>
<td>10</td>
<td>Sampling</td>
<td>How were participants selected? e.g. <em>purposive, convenience, consecutive, snowball</em></td>
</tr>
<tr>
<td>11</td>
<td>Method of approach</td>
<td>How were participants approached? e.g. <em>face-to-face, telephone, mail, email</em></td>
</tr>
<tr>
<td>12</td>
<td>Sample size</td>
<td>How many participants were in the study?</td>
</tr>
<tr>
<td>13</td>
<td>Non-participation</td>
<td>How many people refused to participate or dropped out? Reasons?</td>
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</tr>
<tr>
<td>14. Setting of data collection</td>
<td>Where was the data collected? e.g. home, clinic, workplace</td>
<td>Method- data collection (page 7, page 8)</td>
</tr>
<tr>
<td>15. Presence of non-participants</td>
<td>Was anyone else present besides the participants and researchers?</td>
<td>Not reported in main manuscript for conciseness. Participants were asked to be in a quiet room with no interruptions but we do not know for sure if it was always possible as most interviews were via telephone. Field notes and interview recordings from one face-to-face interview suggest a spouse was present and commenting occasionally.</td>
</tr>
<tr>
<td>16. Description of sample</td>
<td>What are the important characteristics of the sample? e.g. demographic data, date</td>
<td>Findings – Table 2 (page 14)</td>
</tr>
<tr>
<td>Data collection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>17. Interview guide</td>
<td>Were questions, prompts, guides provided by the authors? Was it pilot tested?</td>
<td>Method- PPI section (page 9), data collection – post-intervention interviews (page 8); Supplementary Material 4</td>
</tr>
<tr>
<td>18. Repeat interviews</td>
<td>Were repeat interviews carried out? If yes, how many?</td>
<td>Method- data collection – post-intervention interviews (page 8), Table 2 (page 14).</td>
</tr>
<tr>
<td>19. Audio/visual recording</td>
<td>Did the research use audio or visual recording to collect the data?</td>
<td>Method- data collection – post-intervention interviews (page 8)</td>
</tr>
<tr>
<td>20. Field notes</td>
<td>Were field notes made during and/or after the interview or focus group?</td>
<td>Method- data collection – post-intervention interviews (page 8)</td>
</tr>
<tr>
<td>21. Duration</td>
<td>What was the duration of the interviews or focus group?</td>
<td>Method- data collection – post-intervention interviews (page 8)</td>
</tr>
<tr>
<td>22. Data saturation</td>
<td>Was data saturation discussed?</td>
<td>Not reported in main manuscript for conciseness. The authors are very cautious about claims of data saturation. Data saturation for the current analysis was not aimed for but may have been achieved or approached. Recruitment ceased when iterative intervention development was concluded i.e. the research team were satisfied that the interventions were as engaging</td>
</tr>
</tbody>
</table>

Not reported in main manuscript for conciseness. Our recruitment method does not allow us to know why participants did not respond to our invitation to participate.
as possible and a range of different viewpoints from patients with different clinical and demographic characteristics had been heard and used.

Transcripts returned

Was transcripts returned to participants for comment and/or correction?

n/a

Domain 3: analysis and findings

**Data analysis**

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>24. <strong>Number of data coders</strong></td>
<td>How many data coders coded the data?</td>
<td>Method - data collection – analysis (page 7, page 9)</td>
</tr>
<tr>
<td>25. <strong>Description of the coding tree</strong></td>
<td>Did authors provide a description of the coding tree?</td>
<td>Method - data collection – analysis (page 7, page 9) A coding tree was not used. We present a description of our process of inductive thematic analysis.</td>
</tr>
<tr>
<td>26. <strong>Derivation of themes</strong></td>
<td>Were themes identified in advance or derived from the data?</td>
<td>Method - data collection – analysis (page 7, page 9)</td>
</tr>
<tr>
<td>27. <strong>Software</strong></td>
<td>What software, if applicable, was used to manage the data?</td>
<td>Method - data collection – analysis (page 7, page 9)</td>
</tr>
<tr>
<td>28. <strong>Participant checking</strong></td>
<td>Did participants provide feedback on the findings?</td>
<td>n/a</td>
</tr>
</tbody>
</table>

**Reporting**

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>29. <strong>Quotations presented</strong></td>
<td>Were participant quotations presented to illustrate the themes / findings? Was each quotation identified? e.g. participant number</td>
<td>Findings Table 1 (page 12) and throughout the findings section.</td>
</tr>
<tr>
<td>30. <strong>Data and findings consistent</strong></td>
<td>Was there consistency between the data presented and the findings?</td>
<td>Findings (page 10)</td>
</tr>
<tr>
<td>31. <strong>Clarity of major themes</strong></td>
<td>Were major themes clearly presented in the findings?</td>
<td>Findings (page 10)</td>
</tr>
<tr>
<td>32. <strong>Clarity of minor themes</strong></td>
<td>Is there a description of diverse cases or discussion of minor themes?</td>
<td>n/a</td>
</tr>
</tbody>
</table>
### Supplementary material 6: Themes and how they were used for intervention development

<table>
<thead>
<tr>
<th>Study findings</th>
<th>Summary of theme/finding</th>
<th>“Immune Defence” nasal spray intervention component/content</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motivation to avoid infections (study 1)</td>
<td>High motivation to avoid RTI (for a range of health, work, social reasons)</td>
<td>These findings, in conjunction with our target group characteristics (recurrent RTIs/vulnerable to RTIs) meant we decided to not include significant content to convince of the necessity of avoiding infections. We kept content about the impact of RTIs and necessity of avoiding them brief and used this section predominantly to show empathy, establish a connection with users and help convince them that the intervention was relevant to them.</td>
</tr>
<tr>
<td>Excitement and optimism about a novel prevention method (study 2)</td>
<td>Explanation of spray mechanism and ways of using generated interest, hope, willingness to try.</td>
<td>Acknowledge current feeling and experiences of lack of control/inevitability but then build a convincing rationale for how the spray provides a chance to prevent/avoid RTIs. Describe a novel, interesting, plausible mechanism that people can understand as working in a different way to current/past prevention strategies they may have tried and experienced as ineffective.</td>
</tr>
<tr>
<td>Inevitability (study 1)</td>
<td>Beliefs/experiences that RTIs are inevitable and can’t be prevented or course altered once they have begun</td>
<td></td>
</tr>
<tr>
<td>Alternative approaches to infection prevention (study 1)</td>
<td>Belief that other approaches are (more) helpful for preventing RTIs</td>
<td>Do not attempt to persuade that any specific existing behaviours/habits/prevention methods are unhelpful/unnecessary, but refer to overall experience of wanting to gain more control and protection from infections. Position the spray as an extra protection measure (along with novelty message and convincing rationale about how it works).</td>
</tr>
<tr>
<td>Recommendations from others (study 1)</td>
<td>Other people’s recommendations are important</td>
<td>Provide a strong message of recommendation. This is given authority by NHS, University involvement and ‘meet the team’ of experts page and reference to scientific research.</td>
</tr>
<tr>
<td>Protection from risky situations (study 1)</td>
<td>Interest in using spray to protect oneself from RTIs in situations perceived to be high risk</td>
<td>Provide a positive message about being able to take steps to protect yourself.</td>
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<tr>
<td>------------------------------------------</td>
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</tr>
<tr>
<td>Considering use in risky situations (study 2)</td>
<td>Considerable interest in using spray to protect oneself from RTIs in situations perceived to be high risk, especially during COVID-19 pandemic. Some ability to correctly identify high risk situations but also some difficulty/uncertainty, especially in the context of the COVID-19 pandemic.</td>
<td>Help users identify high risk situations to use the spray in. Provide examples of when to use the spray (using some examples that study participants spontaneously came up with – e.g. Public transport, aeroplanes, childcare/grandchildren situations). Use follow-up intervention emails to revisit/remind about the types of situations and the ability of the spray to work in addition to existing mitigations. We had to edit intervention emails in real time to ensure situations and examples are well aligned with pandemic risk levels, lockdowns, restrictions. Description of the spray as an extra layer of protection in addition to existing mitigations (e.g. Face coverings, handwashing).</td>
</tr>
<tr>
<td>Ease or difficulty (study 1)</td>
<td>Participants vary in how easy or difficult they find using the spray. Overall, it is easy but some aspects of it require attention for best results. Depending, in part, on past experiences of nasal sprays people may be under or over-confident in using the spray. This could lead to either anxiety about using the spray or failing to follow the instructions.</td>
<td>Persuasion (text) and demonstration (video) that the spray use is easy, quick and convenient. Acknowledgment that it may take more than one use to perfect the technique (e.g. “After a few tries you will work out what feels comfortable for you”, “you’ll soon get the hang of it”). Clear instructions to ensure that it is experienced as easy and identified uncertainties and concerns are eliminated. Short instructions, supplemented by optional more detail (website: drop down sections; booklet=short infographic style instructions plus reference to website for further information) Persuasive text to stop people skipping important information by highlighting why it is useful/new (e.g. “check out this video to see how to use your nasal spray. This video is worth watching even if you have used nasal sprays before. The technique for this spray...”</td>
</tr>
<tr>
<td>Familiarity, confidence and information needs (study 2)</td>
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</table>

<table>
<thead>
<tr>
<th>Experience</th>
<th>Description</th>
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<tbody>
<tr>
<td>Experiencing side effects (study 1)</td>
<td>Side effects of the spray are common, milder ones are tolerated if benefits are expected/experienced. Strong side effects can prevent further use. Reassuring information about side effects is valued. People describe being willing to try the spray despite minor side effects. Severe side effects seem likely to influence discontinuation.</td>
</tr>
<tr>
<td>Reactions to possible/actual side effects (study 2)</td>
<td>Explanation that side effects are minor Framing of sensations in nose and throat (e.g. tingling, noticeable taste) as normal and a positive sign the spray is working/reaching the right place rather than a side effect Comparisons of mild side effects with more severe and prolonged symptoms of 'full blown infection'. Instruction and demonstration on how to avoid the more severe side effects (spray technique). Instructions on how to cope with side effects (e.g. position to adopt for nose bleeds, use of saline solution for dry/irritated nose, eating/drinking to eliminate unpleasant taste).</td>
</tr>
</tbody>
</table>
| Identifying early signs of infection (Study 2) | Participants often but not always have awareness of first signs of infection and confidence in being able to use the spray in response Give sufficient information about which first signs are relevant by listing main signs that people recognise as relevant to RTIs (feeling in throat, malaise) but also allowing for idiosyncratic first signs. Acknowledge the difficulty distinguishing some symptoms (e.g. Runny nose, sneezing - hayfever & RTI overlap). Explain and reassure that it would be advisable and safe to use on a symptom that turned out not to be an RTI symptom. Given that we know people may miss first signs, refer to failure to act quickly enough as a possible explanation for situations where
<table>
<thead>
<tr>
<th>Topic</th>
<th>Description</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expectations and experiences of success and failure (study 1)</td>
<td>Users experience combinations of success and failure with the spray which then influence the continuation of use.</td>
<td>Promote excitement, interest, positivity and expectations of success (via convincing explanation of how it works)</td>
</tr>
<tr>
<td>Excitement and Optimism about a novel prevention method (study 2)</td>
<td>Idea of spray elicits interest, hope, willingness to try. For some this is very pronounced, for others it is more muted or sceptical.</td>
<td>Provide a rationale for how spray use might lead to partial success (not avoiding infections but having shorter and less severe).</td>
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<td>Provide a rationale for why it might not always work (using too late)</td>
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<td></td>
<td>Encourage persistence if it does not appear to work, including attributing failure to using it too late and explaining that it may nonetheless have reduced infection severity and duration.</td>
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<td></td>
<td>Encourage formation of the spray as a low risk / safe / easy intervention suitable for regular use in order to help them to conclude that potential for benefit outweighs concerns, even if they do not experience clear cut evidence of success (i.e. It is like a hand gel, not a medicine, and with no serious side effects)</td>
</tr>
<tr>
<td>Excitement and optimism about a novel prevention method (study 2)</td>
<td>Idea of spray elicits interest, hope, willingness to try. For some this is very pronounced, for others it is more muted or sceptical.</td>
<td>Boost positive expectancies of the spray’s psychosocial effects including how the spray can make you feel more confident and in control and that it feels good to feel more protected [emails]</td>
</tr>
<tr>
<td>Consequences of feeling protected (study 2)</td>
<td>Feeling protected may make people feel safer, more confident and more able to participate in valued activities. It could also make people take more risks.</td>
<td>Alongside positive expectations of spray efficacy, promote continued adherence to COVID-19 regulations/guidance/mitigations; positioning the spray as an additional, not a replacement behaviour.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Do not refer to or recommend against any current infection control behaviours (e.g. Keeping distance from ill people, good respiratory hygiene, good diet, being physically fit)</td>
</tr>
<tr>
<td>Concern about medicines (Study 2)</td>
<td>People see nasal sprays as a medicine, eliciting medication-related expectations that it will be a powerful and effective product.</td>
<td>Explicitly position the spray as not a medicine, whilst maintaining expectations that it will be a powerful and effective product.</td>
</tr>
</tbody>
</table>
| Concerns such as overuse, allergies, contraindications | Compare it instead to hand gel (noting the similar mechanisms—cleaning away virus before it can cause illness).

Provide reassuring information about how often it is safe to use it and how it can be used with any prescription and over-the-counter medications.

Position spray as a means of avoiding using medications such as antibiotics, over-the-counter cold relief.

NB- we expect concerns related to medicines to persist to some degree in some participants despite our ‘not a medicine’ message. The spray might, to a layperson, feel like a medicine in terms of its mode of administration and anticipated efficacy. Our content nonetheless promotes beliefs about it being a simple, safe and effective intervention. |
| Disgust and hygiene (Study 2) | Noses and nasal sprays can be considered disgusting and/or messy and unhygienic |
| Reassurance that the spray procedure is not wet, messy or unpleasant. This required a change (between study 2a and study 2b) from our original description of the spray being not like a medicine but like washing hands with soap and water. We adopted a neater/cleaner explanation (like hand gel). The public were becoming very familiar with hand gel as an important infection control product at this point in the COVID-19 pandemic. Emphasise easiness of using the spray. Instructions on how to use hygienically. |