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A primary care randomised controlled trial of a tailored interactive website for the self-management of respiratory infections (Internet Dr.)

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3 **management of respiratory infections (Internet Dr.)**
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Abstract

Objective To assess an internet-delivered intervention providing advice to manage respiratory infections (RTIs).

Design Open pragmatic parallel group randomised controlled trial.

Setting Primary care in United Kingdom.

Participants. Adults (aged ≥ 18) registered with GPs, recruited by postal invitation.

Intervention. Patients were randomised with computer-generated random numbers to access to the intervention website (intervention) or not (control). The intervention tailored advice about the diagnosis, natural history, symptom management (particularly paracetamol/ibuprofen use) and when to seek further help.

Outcomes Primary: NHS contacts for those reporting RTIs from monthly on-line questionnaires for 20 weeks. Secondary: hospitalisations; symptom duration/severity.

Results. 3044 participants were recruited. 271 in the intervention group and 274 in the control group reported one or more RTIs, among whom there a modest increase in NHS Direct contacts in the intervention group (intervention 37/1574 (2.4%) versus control 20/1661 (1.2%); multivariate Risk Ratio (RR) 2.25 (95% CI 1.00 to 5.07, $p=0.048$)). Conversely reduced contact with doctors occurred (239/1574 (15.2%) vs 304/1664 (18.3%); risk ratio 0.71, 0.52 to 0.98, $p=0.037$). Reduction in contacts occurred despite slightly longer illness duration (11.3 days versus 10.7 days respectively; multivariate estimate 0.60 days longer (-0.15 to 1.36, $p=0.118$) and more days of illness rated moderately bad or worse illness (0.52 days; 0.06 to 0.97, $p=0.026$). The estimate of slower symptom resolution in the intervention group was attenuated when controlling for whether individuals had used webpages which advocated ibuprofen use (length of illness 0.22 days, -0.51 to 0.95, $p=0.551$; moderately bad or worse symptoms 0.36 days, -0.08 to 0.80, $p=0.105$). There was no evidence of increased hospitalisations (risk ratio 0.25; 0.05 to 1.12; $p=0.069$).

Conclusions. An internet-delivered intervention for the self-management of RTIs modifies help-seeking behaviour and does not result in more hospital admissions due to delayed help seeking. Advising the use of ibuprofen may not be helpful.

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Article Summary: Strengths and Limitations

- This is to our knowledge the only substantial trial to date to address the effectiveness of support for the management of respiratory infections using the internet
- The rate of uptake following invitation was low, but is what would be expected for a free standing internet-delivered intervention, and 70% follow-up was achieved which is high for a free-standing internet intervention - and there was little evidence of attrition bias.
- The primary outcome has to be changed to monthly questionnaires since the intervention development had to take account of the context of the provision of NHS direct, and the monthly self-report data was the only source of data about NHS direct contacts (in addition to documenting episodes that clinicians did not include in the records), but recall of contacts made during an infection experienced in the previous month are likely to suffer minimal recall bias.
- Participants were less deprived than non-participants but controlling for deprivation made little difference to the estimates and there was no significant interaction of the intervention with deprivation.
- The number of participants who experienced one or more RTIs was lower than expected which will have reduced the power to detect differences.

Background

Most people suffer a respiratory tract infection (RTI) every year, many suffering more than once, and with 20-30% of the population consulting primary care at least once each year, which represents a significant call on health care resources^{1,2}. However, in most cases RTIs do not present a serious threat to the patient's health, and with access to the right information many illness could be self-managed at home. This is particularly important as unfortunately when a doctor is consulted antibiotics are normally given¹. Provision of such information prior to consultations could potentially result in patients having improved symptom control, lower attendance at GP surgeries, and reduced antibiotic prescription – which could be one important tool in the fight against antibiotic resistance³. A systematic review has documented several trials that have used information to modify consultations for respiratory tract infections among children⁴. However, there were only three older trials (the last published in 1991) that addressed the issue of providing specific information prior to consultation for respiratory tract infections⁴. Studies in adults also demonstrate that providing information booklets may help modify consultation behaviour⁵⁻⁷, but a wide range of symptoms and conditions were assessed in the latter studies so the precise role in interventions for modifying consultations for RTIs is less clear.

Booklets are no longer likely to be distributed as a source of advice regarding the self-management of respiratory infection given the widespread and growing access to the internet as a source of information prior to consulting - with more than 80% of families currently having access to the internet (rising by 5% each year). Web-based interventions can enable patients to access reliable self-care information from their home, make an informed decision on how best to manage their symptoms, and decide whether they need to visit their doctor. Recently a trial has reported that advice to use ibuprofen resulted in both poor symptom control (more prolonged illness) and increased complication – presumably by interfering with the inflammatory and immune response⁸. A potential problem about providing self-management advice is that patients might be encouraged to self-manage serious infections inappropriately (i.e. when they really need to see the doctor), and so develop complications unnecessarily. This is a major concern for both doctors and patients⁹⁻¹¹ – highlighting the importance of good safety-netting advice (i.e. advice about when to consult further) and the need to document the impact of interventions on hospital admissions. However it is also plausible that good self-management advice about appropriate early assessment of more severe illness could reduce hospital admissions

We have developed a theoretically informed internet-delivered intervention to manage respiratory tract infections among adults ('The Internet Doctor') that we have shown in a small exploratory trial results in higher levels of satisfaction, enablement, and understanding of illness¹². We report a larger trial of this website to address whether consultation behaviour can be modified, and to document potential harms (including hospital admissions) over a one year period.

Methods

We used very similar procedures to our previous leaflet trial.⁶ A random selection of adults in the computerised practice registers from 35 practices in southern England were identified by the practice staff, and letter sent to patients inviting them to participate. Patients willing to participate were asked to log on to the website to confirm consent. Patients were also be given contact details to enable them to email or talk to the research team before agreeing to participate or if they had problems logging in. Only one participant per household could participate.

Changes to the protocol.

We originally specified a 12 month period for measuring the primary outcome, but in developing the intervention we needed to incorporate not just advice to see the GP but also advice to use NHS direct, and therefore to document NHS direct contacts. We had not anticipated this in advance, and so required self-report of the monthly data as our primary outcome. To provide monthly follow-ups for a year would then have had two effects – engagement of participants would have been much more difficult and much more resource intensive than originally anticipated. The most meaningful and feasible assessment of the primary outcome was therefore the monthly reports of consulting their GP for those individuals who reported a respiratory infection (the intervention was not designed to help those who did not suffer an infection).

Inclusion criteria. Adult patients (aged 18+) from GPs computerised lists. **Exclusion criteria.** Patients with severe mental problems (e.g. major uncontrolled depression/schizophrenia; dementia; severe mental impairment - unable to complete outcomes) or terminally ill.

Randomisation . Once logged in, patients were randomised automatically by the website using computer generated random numbers to one of the following groups:

- 1) **Access to an interactive website** providing tailored advice; this was reinforced by email prompts and reminders to use the website; patients were given information about the natural history, self care advice, and advice about the use of over the counter medication. Outcome measures were documented online by participants following email prompts each month.
- 2) **Normal care** (as the control group, outcome measures were collected online but access to the tailored advice website was at the end of the trial)

Randomisation was not stratified with no blocking, and participants were blind to randomisation group at the point of consent (but clearly could not be blinded once they knew their randomisation group)

Study groups

Intervention group. Participants had access to the internet-delivered intervention for 20 weeks. On logging onto the website users could select tailored advice on a) whether and why they need/do not need to consult the GP, and b) how to self-care for RTIs. Patients selecting consultation advice completed questions about their symptoms and medical history, and were then presented with tailored advice recommending either self-

1 management (for mild symptoms), for more severe symptoms (e.g. haemoptysis, prolonged fever) phoning
2 the 'NHS Direct' helpline which provided nurse led advice about the need to seek further medical help, or
3 alternatively seeking medical attention immediately (for symptoms potentially posing serious risks e.g.
4 reduced conscious level, chest pain). Patients were given the opportunity to challenge this advice by
5 selecting further in-depth information about the symptoms of common complications or serious illness
6 compatible with their symptoms, and by clicking on frequently asked questions (e.g. regarding the need for
7 antibiotics and typical time-course of symptoms). The self-care section provided options to select advice on
8 self-management without medication (including rest, fluid intake) or with medication. For those who wanted
9 to take medication, over-the-counter remedies were recommended as an effective and preferable alternative
10 to seeking antibiotics from the GP, and in particular optimising the use of paracetamol and encouraging the
11 use of ibuprofen. The website was theory-based, addressing all components of the common-sense model of
12 self-regulation of illness¹³ (i.e. perceived symptoms, cause, timeline, physical and emotional consequences
13 and possibility for control/cure), and used the principles of social cognitive theory¹⁴ to address expected
14 outcomes of consultation and self-care, and build self-confidence for self-care. Extensive qualitative
15 piloting¹⁵ established that the website was accessible to people with very limited education and no previous
16 computer use, and quantitative piloting in several hundred people indicated that it increased confidence
17 when self-managing a RTI and had the potential to reduce consultations¹².

18 **Control group (normal care).** As in the intervention group, the control group had access to the GP/practice
19 in the normal way for respiratory illnesses and ILI. The control group was offered access to the website at
20 the end of the study.

21 **Primary outcome**

22 *GP consultations.* We hypothesised that the intervention would reduce the number of contacts with general
23 practitioners for individuals who suffered a respiratory tract infection. Patients were prompted by email to
24 log onto the website monthly every four weeks until 20 weeks (i.e. weeks 4,8,16,20) to complete
25 questionnaires about illnesses during the last month - since the duration of symptoms can be remembered
26 reliably over a period of a few weeks^{16,17}.

27 We also performed an assessment of the consultations that were recorded in primary care by a blinded
28 assessment of the primary care notes. Although this does not capture all contacts with health professionals
29 (and also does not capture contacts with NHS Direct) it has been shown to be reliable¹⁸.

30 **Secondary outcomes**

31 For each episode the index person also documented: whether they contacted NHS Direct for phone-based
32 advice; the nature of the infection; the duration of symptoms rated moderately bad (which we have shown
33 in previous research is a useful outcome and sensitive to change for individuals¹⁶ and can be remembered
34 reliably over a period of a few weeks^{16 17}); the number of days where work/normal activities were
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1 impaired¹⁷, and smoking status.

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3 Patients were also asked to complete measures of their symptoms and concern about them at the time of
4 illness, levels of health anxiety, consulting preferences, and attitudes to the intervention; a full analysis of
5 these potential mediators and moderators of outcomes will be presented in a process analysis in a future
6 paper.
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10 **Socio-demographic and comorbidity data.** We collected age, gender, and educational level from the
11 participant online and prior comorbidities and consultations from the notes review.

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13 **Sample size calculation.** We estimated that a trial among a minimum of 2266 patients would allow us to
14 detect a 25% reduction in attendance with RTIs (20% vs 15% requires 906 per group with completed
15 outcomes or 2266 allowing for 20% loss to follow-up; for $\alpha = 0.05$ and $\beta = 0.2$), and a 0.2
16 standardised effect size for continuous outcomes.
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21 **Analysis.** We performed an intention to treat analysis, and the syntax was written blind to group. No
22 interim analysis was performed. The proportions attending with RTI in the intervention and normal care
23 groups were evaluated using logistic regression to calculate odds ratios (which were converted to risk
24 ratios using the formula of Zhang¹⁹), with confidence intervals. Outcomes measured on a continuous scale
25 (duration and severity of symptoms) were analysed using multiple linear regression. All continuous
26 outcome variables were checked for the assumption of normality of residuals. The models controlled for
27 variables likely to predict consultation: gender, age, highest educational qualification, smoking status,
28 whether there were children under 16 living in the household, any comorbid condition, the number of
29 times the patient reported consulting a doctor about an RTI in the 12 months prior to the study, and Index
30 of multiple deprivation (IMD uses post codes to estimate deprivation across a number of domains;
31 <https://www.gov.uk/government/statistics/english-indices-of-deprivation-2010>). Given previous findings
32 of increased symptom burden when health professionals give advice to use ibuprofen⁸, and the findings of
33 increase symptom burden in intervention group of the current study, a post-hoc secondary analysis
34 explored the impact of controlling for whether pages advocating the use of ibuprofen had been viewed.
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Results.

43769 patients were invited, of whom 3044 participants consented (from 17/1/12 to 20/10/13) and 3355 gave reasons for declining (commonly not enough time, or insufficient access to the internet, or uncomfortable using computers, but also a variety of other reasons; see Figure 1).

Table 1 demonstrates that the groups were well balanced for a range of variables (and Table 1a shows this for those who reported at least one respiratory infection during follow-up). Although groups in the study were well balanced for deprivation, those who agreed to take part were less deprived than non-participants (IMD score 16.1 (SD 11.1) hence results controlled for IMD score.

Table 2 documents a modest increase in contacts for NHS Direct among those who had an RTI in the intervention group (37/1574 (2.4%) versus 20/1661 (1.2%), multivariate Risk Ratio (RR) 2.25 (1.00 to 5.07, $p=0.048$), but reduced contact with doctors (239/1574 (15.2%) vs 304/1664 (18.3%), Risk ratio 0.71, 95% CI 0.52 to 0.98, $p=0.037$).

Possible harms. The reduction in contacts with doctors occurred despite slightly longer illness duration (11.3 days versus 10.7 days; multivariate estimate 0.60 days longer (-0.15 to 1.36, $p=0.118$) and more days experienced of moderately bad or worse illness 4.59 versus 4.00 days (multivariate estimate 0.52 days; 0.06 to 0.97, $p=0.026$). The latter estimates of increased symptom burden were reduced when controlling for whether individuals used ibuprofen pages on the website (length of illness 0.22, -0.51 to 0.95, $p=0.551$; moderately bad or worse symptoms 0.36, -0.08 to 0.80, $p=0.105$). There was no evidence that self-management advice resulted in delayed consultations for serious illnesses (e.g. lobar pneumonia; meningitis; septicaemia) and hence increased hospitalisations: in fact there were reduced hospitalisations (Table 4).

Analysis of the follow-up data from the notes review for the whole sample is shown in Appendix 1; as expected, since most such individuals did not have a respiratory infection, there is no clear evidence of a reduction in consultations. The characteristic of those followed up and not followed up were also similar (Appendix 1, table 7).

Discussion

This is to our knowledge the only substantial trial to date to address the effectiveness of support for the management of respiratory infections using the internet. Although relatively limited follow-up was possible (20 weeks) there was reduced contact with GPs and possibly a longer term reduction in hospital admissions. There was a slight increase in contact with NHS Direct, consistent with the advice given by the intervention for management of more severe symptoms that did not warrant immediate medical attention.

Limitations. 70% follow-up was achieved which is high for a free-standing internet intervention, and there was little evidence of attrition bias. The primary outcome was initially anticipated to be at 12 months, but a shorter time period was necessary due to the need to engage participants and achieve good follow-up rates with the monthly questionnaires. Monthly questionnaires were also needed since the intervention during development had to take account of the context of the provision of NHS direct, and the monthly self-report data was the only source of data about NHS direct contacts (in addition to documenting episodes that clinicians did not include in the records). The monthly data has the limitations of self-report, and could be biased if GP consultations were discouraged by the InternetDr, but in fact InternetDr not gave advice about when to see the doctor promptly. If self-reports of RTIs were biased we would also have expected different numbers of RTIs to be reported in the intervention group which did not occur. Bias in self report would also not explain the opposite directions of consultation with NHS Direct and with GPs, and which also makes type I error unlikely. The estimate derived from primary care notes review for consultations (risk ratio 0.87, lower bound of the 95% confidence interval 0.51) was also consistent with the estimate from the monthly data (risk ratio 0.71). The rate of uptake following invitation was low, but is what would be expected for a free standing internet-delivered intervention, particularly as this is for mostly minor and common conditions that most will feel, rightly or wrongly, reasonably confident to manage. However, the patients who did participate were those that the intervention is likely to help i.e. participants who are sufficiently concerned about their symptoms to be motivated to use a self-management website. There is also a circularity in engaging participants – physicians are much more likely to refer to a free standing intervention once it has been shown to be effective, so the first priority is to demonstrate effectiveness. Participants were less deprived than non-participants but controlling for deprivation made little difference to the estimates and there was no significant interaction of the intervention with deprivation. The number of participants who experienced one or more RTIs was lower than expected which will have reduced the power to detect differences. Patients' self-reported contacts with the NHS, but recall of contacts made during an infection experienced in the previous month are likely to suffer minimal recall bias. Self-report is the only method of capturing contacts with NHS Direct and furthermore the estimates of consultations and admissions purely based on primary care notes suggested changes in the same direction and of a similar magnitude to the monthly self-reports.

Main findings.

The estimated reduction in consultations with GPs with the website was similar to the effectiveness of the pamphlet we developed for predominantly respiratory illness⁶. This suggests the internet-delivered intervention is potentially more effective than a pamphlet, given the widespread availability currently of NHS Direct online resources and other internet-delivered advice regarding infections. The estimated 25% reduction in GP consultations, even if only over a period of a few months, would provide very considerable relief in terms of pressure on services during the winter months. Perhaps more surprising is that there was a reduction in hospital admissions, albeit non-significant, suggesting the intervention is unlikely to result in delayed presentation of serious illness – and if anything could help in relieving pressure on hospital services. One explanation for reduced admission might be that those with severe symptoms were discouraged from seeing the doctor, but since InternetDr encouraged individuals to seek medical help promptly with severe symptoms this seems unlikely. Although the study was not powered to assess a reduction in antibiotic use, nevertheless the estimates of a 6-12% reduction in antibiotic prescriptions over 6-12 months is consistent with the observation that most individuals who attend the GP get antibiotics¹, so reducing attendance would be expected to potentially provide an important component in the population level fight against antibiotic resistance, given the evidence that primary care prescriptions are a key component in driving antibiotic resistance³.

Harms. In terms of major harms the upper bound of the confidence interval suggests we can be reasonably sure that no increase in hospital admissions occurred. The most surprising finding was that in the intervention group both symptom duration and the duration of more severe symptoms was increased – the latter significantly. This could be either a chance finding or possibly that we made participants more aware of symptoms. However, another possibility is that by strongly encouraging the use of not only paracetamol but also ibuprofen, the intervention may have significantly increased ibuprofen use, and recent trial evidence suggests that advising the use of ibuprofen is unlikely to help overall symptoms and is associated with the progression of symptoms (i.e. prolonging illness)⁸ - presumably due to inhibiting the inflammatory element of an effective immune response. When the analysis in the current study controlled for the use of pages that advocated ibuprofen, the finding of increase symptom duration in the intervention group was markedly attenuated. A possible explanation for this attenuation could be that use of ibuprofen pages is a marker of an individual having more severe or florid symptoms, and hence the symptoms might last longer (i.e. reverse causality: the use of ibuprofen pages was because of severe illness, not causing it). However, this explanation is rather unlikely as more florid upper respiratory symptoms and signs are associated with shorter illness duration²⁰, and reverse causality cannot explain why more severe prolonged symptoms were reported in the intervention group since the number of infections reported were almost identical in both groups. Thus the most reasonable inference is that advice to use ibuprofen was probably harmful and revised versions of the website should therefore not encourage ibuprofen use. Whatever the reasons for the finding of more severe symptoms, the presence of more severe symptoms would be expected to lead to increased consultations, which makes the reduction

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2 in the need for GP contacts more striking - supporting the earlier findings in the development of the
3 intervention that the website increases enablement and confidence in managing symptoms^{12;21}.
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6 **Conclusion.** An internet-delivered intervention for managing RTIs helps participants appropriately
7 manage their symptoms and contacts with NHS staff, and may help reduce hospital admissions, but advice
8 to use ibuprofen may be unhelpful.
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Contributors: All authors contributed significantly to the development of the protocol. All authors contributed to overseeing the management of the study, agreeing the analysis plan, and to the write-up of the paper. PL had the initial idea, led the grant application, and the initial drafting of the paper and is guarantor. LY led the development of the intervention with PA and LMCD. PL, MM, and BS performed the analysis. TT and SB performed day to day management of the study supervised by PL. All authors had full access to all of the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis. Samantha Hall, PPI representative, kindly commented on the protocol and outcomes, and contributed to steering meetings.

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Table 1 Baseline characteristics*

	Control	Intervention
Female	779/1432 (54.4%)	816/1490 (54.8%)
Age	57.14 (13.1)	56.78 (13.5)
Ever smoked	699/1425 (49.1%)	688/1483 (46.4%)
IMD score	12.6 (7.9)	12.9 (8.1)
Comorbid condition	511/1418 (36.0%)	549/1481 (37.1%)
Number of times consulted a doctor about RTI in the previous year	0.50 (1.2)	0.54 (1.2)
Household composition:		
• Alone	178/1432 (12.4%)	191/1489 (12.8%)
• Spouse/partner	963/1432 (67.3%)	1015/1489 (68.2%)
• Other adult(s)	147/1432 (10.3%)	145/1489 (9.7%)
• Children under 16	144/1432 (10.1%)	138/1489 (9.3%)
Highest qualifications		
• No formal educational qualifications	108/1432 (7.5%)	121/1490 (8.1%)
• Cses/ o'levels/ gcses (or similar)	265/1432 (18.5%)	279/1490 (18.7%)
• A'levels (or similar)	151/1432 (10.5%)	157/1490 (10.5%)
• Diploma/other vocation qualification	317/1432 (22.1%)	322/1490 (21.6%)
• Degree	218/1432 (15.2%)	244/1490 (16.4%)
• Postgraduate or professional qualification	373/1432 (26.1%)	367/1490 (24.6%)

*Data are means (SD) or numbers (%).

Table 1a Baseline characteristics of participants who reported at least one RTI*

	Control	Intervention
Female	506/920 (55.0%)	491/852 (57.6%)
Age	56.28 (12.95)	56.76 (12.93)
Ever smoked	448/918 (48.8%)	393/850 (46.2%)
Comorbid condition	329/912 (36.1%)	324/850 (38.1%)
Number of times consulted a doctor about RTI in the previous year	0.54 (1.17)	0.54 (1.19)
Household composition:		
• Alone	110/920 (12.0%)	98/851 (11.5%)
• Spouse/partner	612/920 (66.5%)	589/851 (69.2%)
• Other adult(s)	96/920 (10.4%)	87/851 (10.2%)
• Children under 16	102/920 (11.1%)	77/851 (9.1%)
Highest qualifications		
• No formal educational qualifications	66/920 (7.2%)	62/852 (7.3%)
• Cses/ o'levels/ gcse (or similar)	166/920 (18.0%)	143/852 (16.8%)
• A'levels (or similar)	102/920 (11.1%)	88/852 (10.3%)
• Diploma/other vocation qualification	203/920 (22.1%)	196/852 (23.0%)
• Degree	139/920 (15.1%)	148/852 (17.4%)
• Postgraduate or professional qualification	244/920 (26.5%)	215/852 (25.2%)

*Data are means (SD) or numbers (%).

Table 2. Monthly reports of health service use and duration of illness (weeks 4,8,12,16 and 20) for participants who reported at least one respiratory infection during the 20 weeks

	Control	Intervention	Univariate risk ratio (95% CI; p-value)	Multivariate risk ratio (95% CI; p-value)*
Reported episodes of respiratory tract infection	1665/5697 (29.23%)	1578/5291 (29.82%)	1.03 (0.93, 1.12; p=0.566)	1.04 (0.94, 1.14; p=0.461)
Of those who reported a respiratory tract infection:				
Saw a doctor about illness (as a proportion of the number of episodes)	304/1664 (18.27%)	239/1574 (15.18%)	0.75 (0.56, 1.01; p=0.061)	0.71 (0.52, 0.98; p=0.037)
Contacted NHS Direct about illness	20/1661 (1.20%)	37/1574 (2.35%)	2.34 (1.07, 5.10; p=0.034)	2.25 (1.00, 5.07; p=0.048)
			Difference (95% CI; p-value)	
Length of illness (days)	10.68 (9.45)	11.30(9.89)	0.58 (-0.15, 1.30; p=0.119)	0.60 (-0.15, 1.36; p=0.118)
Days moderately bad or worse	4.00 (5.48)	4.59 (6.88)	0.47 (0.03, 0.92; p=0.035)	0.52 (0.06, 0.97; p=0.026)

Table 3 Health service use recorded in primary care records in the 20 weeks following the date of consent for participants who reported at least one episode of RTI

	Control	Intervention	Univariate risk ratio (95% CI; p-value)	Multivariate risk ratio (95% CI; p-value)
Any consultations	98/912 (10.8%)	88/851 (10.3%)	0.96 (0.73, 1.26; p=0.782)	0.89 (0.65, 1.23; p=0.514)
Any antibiotic prescriptions	66/880 (7.5%)	64/827 (7.7%)	1.03 (0.74, 1.43; p=0.853)	0.94 (0.64, 1.38; p=0.759)
Any hospitalisations	7/823 (0.9%)	1/765 (0.1%)	0.15 (0.02, 1.24; p=0.079)	0.13 (0.02, 1.11; p=0.062)
Any referrals	10/824 (1.2%)	8/771 (1.0%)	0.86 (0.34, 2.14; p=0.740)	0.77 (0.26, 2.24; p=0.625)

*Multivariate model controls for gender, age, highest educational qualification, smoking status, whether there are children under 16 living in the household, any comorbid condition, IMD score, and the number of times the patient reported consulting a doctor about an RTI in the 12 months prior to the study

Table 4 Health service use recorded in primary care records in the 12 months following the date of consent for patients who experience at least one episode of RTI in the first 20 weeks.

	Control	Intervention	Univariate risk ratio (95% CI; p=value)	Multivariate risk ratio (95% CI; p=value)
Any consultations	176/912 (19.3%)	164/851 (19.3%)	0.99 (0.82, 1.16; p=0.989)	0.93 (0.73, 1.16; p=0.509)
Number of consultations**				
Any antibiotic prescriptions	115/851 (13.5%)	107/794 (13.5%)	0.99 (0.78, 1.30; p=0.982)	1.00 (0.74, 1.33; p=0.997)
Any hospitalisations	8/748 (1.1%)	1/689 (0.2%)	0.14 (0.02, 1.08; p=0.059)	0.13 (0.02, 1.05; p=0.056)
Any referrals	14/750 (1.9%)	12/699 (1.7%)	0.92 (0.43, 1.96; p=0.830)	0.87 (0.35, 2.16; p=0.799)

*Multivariate model controls for gender, age, highest educational qualification, smoking status, whether there are children under 16 living in the household, any comorbid condition, IMD score, and the number of times the patient reported consulting a doctor about an RTI in the 12 months prior to the study

**reported as the mean (s.d.). The median is 0 and the IQR is (0,0). The range is 0-8.

Appendix 1

Table 5. Health service use in the 20 weeks following the date of consent based on review of primary care notes

	Control	Intervention	Univariate risk ratio (95% CI; p=value)	Multivariate risk ratio (95% CI; p=value)
Any reconsultations	126/1418 (8.89%)	118/1483 (7.96%)	0.90 (0.71, 1.14; p=0.368)	0.95 (0.79, 1.15; p=0.612)
Number of reconsultations**	0.18 (0.75)	0.16 (0.66)	0.88 (0.64, 1.21; p=0.434)	0.97 (0.69, 1.35; p=0.854)
Any antibiotic prescriptions	86/1378 (6.24%)	83/1448 (5.73%)	0.92 (0.68, 1.23; p=0.569)	0.88 (0.63, 1.24; p=0.473)
Any hospitalisations	8/1301 (0.61%)	2/1368 (0.15%)	0.25 (0.05, 1.12; p=0.069)	0.24 (0.05, 1.13; p=0.072)
Any referrals	10/1302 (0.77%)	10/1375 (0.73%)	0.95 (0.39, 2.26; p=0.903)	0.98 (0.37, 2.59; p=0.965)

*Multivariate model controls for gender, age, highest educational qualification, smoking status, whether there are children under 16 living in the household, any comorbid condition, IMD score and the number of times the patient reported consulting a doctor about an RTI in the 12 months prior to the study

**reported as the mean (s.d.). The median is 0 and the IQR is (0,0). The range is 0-8.

Table 6. Health service use in the 12 months following the date of consent based on review of primary care notes

	Control	Intervention	Univariate risk ratio (95% CI; p=value)	Multivariate risk ratio (95% CI; p=value)
Any reconsultations	242/1418 (17.07%)	249/1483 (16.79%)	0.98 (0.83, 1.15; p=0.843)	0.85 (0.65, 1.12; p=0.259)
Number of reconsultations**	0.30 (0.88)	0.28 (0.77)	0.92 (0.75, 1.14; p=0.456)	0.97 (0.79, 1.21; p=0.806)
Any antibiotic prescriptions	156/1332 (11.71%)	155/1389 (11.16%)	0.95 (0.77, 1.17; p=0.651)	0.97 (0.76, 1.23; p=0.811)
Any hospitalisations	11/1189 (0.92%)	4/1239 (0.32%)	0.35 (0.11, 1.09; p=0.071)	0.35 (0.11, 1.10; p=0.073)
Any referrals	16/1192 (1.34%)	15/1249 (1.20%)	0.89 (0.44, 1.80; p=0.755)	1.11 (0.48, 2.52; p=0.808)

*Multivariate model controls for gender, age, highest educational qualification, smoking status, whether there are children under 16 living in the household, any comorbid condition, IMD score and the number of times the patient reported consulting a doctor about an RTI in the 12 months prior to the study

**reported as the mean (s.d.). The median is 0 and the IQR is (0,0). The range is 0-8.

Table 7. Characteristics of participants followed up and not followed up

	Did not complete 20 week follow up questions	Did complete 20 week follow up questions
Control group	353/871 (40.5%)	1079/2052 (52.6%)
Intervention group	518/871 (59.5%)	973/2052 (47.4%)
Female	489/871 (56.1%)	1,106/2,051 (53.9%)
Age	52.9 (14.9)	58.7 (12.1)
Ever smoked	428/862 (49.7%)	959/2,046 (46.9%)
IMD score	13.8 (9.0)	12.3 (7.4)
Comorbid condition	290/ 861 (33.7%)	770/2,038 (37.8%)
Number of times consulted a doctor about RTI in the previous year	0.71 (1.4)	0.4 (1.1)
Household composition:		
• Alone	113/871 (13.0%)	256/2050 (12.5%)
• Spouse/partner	550/871 (63.2%)	1428/2050 (70.0%)
• Other adult(s)	101/871 (11.6%)	191/2050 (9.3%)
• Children under 16	107/871 (12.3%)	175/2050 (8.5%)
Highest qualifications		
• No formal educational qualifications	76/871 (8.7%)	153/2051 (7.5%)
• Cses/ o'levels/ gses (or similar)	180/871 (20.7%)	364/2051 (17.8%)
• A'levels (or similar)	93/871 (10.7%)	215/2051 (10.5%)
• Diploma/other vocation qualification	191/871 (21.9%)	448/2051 (21.8%)
• Degree	142/871 (16.3%)	320/2051 (15.6%)
• Postgraduate or professional qualification	189/871 (21.7%)	551/2051 (26.9%)

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TRIAL CHECKLIST based on CONSORT statement:

	Reported?	If Y: Page no
1a. TITLE Identify the study as RCT	<u>Y</u>	<u>1</u>
1b. Abstract: Use structured format	<u>Y</u>	<u>2</u>
Introduction 2a. Back ground and rationale	<u>Y</u>	<u>4</u>
2b. Specific trial objectives	<u>Y</u>	<u>4</u>
Protocol: 3a. Trial design	<u>Y</u>	<u>5</u>
3b Changes to methods after trial commencement	<u>Y</u>	<u>6,7</u>
4a Study population eligibility criteria	<u>Y</u>	<u>5</u>
4b Settings and location where data was collected	<u>Y</u>	<u>5</u>
5. Intervention and timing	<u>Y</u>	<u>5</u>
5. Objectives	<u>Y</u>	<u>4</u>
6a Outcome measures: pre-specified 1y/2y outcomes	<u>Y</u>	<u>6</u>
6a Outcome measures: any changes	<u>Y</u>	<u>6</u>
7a Sample size	<u>Y</u>	<u>7</u>
7b Interim analysis/stopping rules	<u>Y</u>	<u>7</u>
Randomisation: 8a methods used	<u>Y</u>	<u>5</u>
8b type of randomization	<u>Y</u>	<u>5</u>
9 mechanism used to implement (e.g. sequential pots)	<u>Y</u>	<u>5</u>
10 who generated allocation sequence, who assigned	<u>Y</u>	<u>5</u>
Blinding 11a Who blinded after assignment	<u>Y</u>	<u>5,7</u>
11b Description of the similarity of interventions	<u>Y</u>	<u>6</u>
Stats methods 12a Methods used to compare groups	<u>Y</u>	<u>7</u>
12b Other analyses (subgroups, adjusted)	<u>Y</u>	<u>7</u>
Results 13a Provide trial flow diagram (assigned,treated,analysed)	<u>Y</u>	<u>Fig 1</u>
13b Losses, exclusions, reasons	<u>Y</u>	<u>8and Fig 1</u>
Recruitment 14a Periods and follow-up	<u>Y</u>	<u>8, Fig1</u>
14b Why trial ended or stopped	<u>Y</u>	<u>8</u>

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4	15. Baseline data for outcomes	<u>Y</u>	<u>table 1</u>
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6	16. State numbers analysed and intention to treat	<u>Y</u>	<u>7, table 2</u>
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8	Outcomes: 17a) Estimated effect sizes and precision	<u>Y</u>	<u>tables 2-4</u>
9			
10	17b For Binary absolute and relative effect sizes	<u>Y</u>	<u>tables 2-4</u>
11			
12	18. Ancillary analyses subgroup/adjusted/pre-specified)	<u>Y</u>	<u>7</u>
13			
14	19. Harms/adverse events	<u>Y</u>	<u>8</u>
15			
16	20. Trial limitations	<u>Y</u>	<u>9</u>
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18	21 Generaliseability	<u>Y</u>	<u>9</u>
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20	22 Interpretation	<u>Y</u>	<u>9-10</u>
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22	Other: 23 Registration	<u>Y</u>	<u>2</u>
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24	24 Site of full trial protocol	<u> </u>	<u>This can be provided</u>
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BMJ Open

A primary care randomised controlled trial of a tailored interactive website for the self-management of respiratory infections (Internet Dr.)

Journal:	<i>BMJ Open</i>
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Secondary Subject Heading:	Infectious diseases, Respiratory medicine, General practice / Family practice
Keywords:	Respiratory infections < THORACIC MEDICINE, Public health < INFECTIOUS DISEASES, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

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Manuscripts

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2 **Title: A primary care randomised controlled trial of a tailored interactive website for the self-**
3 **management of respiratory infections (Internet Dr.)**
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6 **Paul Little*; Beth Stuart; Panayiota Andreou; Lisa McDermott; Judith Joseph; Mark Mullee; Mike**
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Abstract

Objective To assess an internet-delivered intervention providing advice to manage respiratory infections (RTIs).

Design Open pragmatic parallel group randomised controlled trial.

Setting Primary care in United Kingdom.

Participants. Adults (aged ≥ 18) registered with GPs, recruited by postal invitation.

Intervention. Patients were randomised with computer-generated random numbers to access to the intervention website (intervention) or not (control). The intervention tailored advice about the diagnosis, natural history, symptom management (particularly paracetamol/ibuprofen use) and when to seek further help.

Outcomes Primary: NHS contacts for those reporting RTIs from monthly on-line questionnaires for 20 weeks. Secondary: hospitalisations; symptom duration/severity.

Results. 3044 participants were recruited. 271 in the intervention group and 274 in the control group reported one or more RTIs, among whom there a modest increase in NHS Direct contacts in the intervention group (intervention 37/1574 (2.4%) versus control 20/1661 (1.2%); multivariate Risk Ratio (RR) 2.25 (95% CI 1.00 to 5.07, $p=0.048$)). Conversely reduced contact with doctors occurred (239/1574 (15.2%) vs 304/1664 (18.3%); risk ratio 0.71, 0.52 to 0.98, $p=0.037$). Reduction in contacts occurred despite slightly longer illness duration (11.3 days versus 10.7 days respectively; multivariate estimate 0.60 days longer (-0.15 to 1.36, $p=0.118$) and more days of illness rated moderately bad or worse illness (0.52 days; 0.06 to 0.97, $p=0.026$). The estimate of slower symptom resolution in the intervention group was attenuated when controlling for whether individuals had used webpages which advocated ibuprofen use (length of illness 0.22 days, -0.51 to 0.95, $p=0.551$; moderately bad or worse symptoms 0.36 days, -0.08 to 0.80, $p=0.105$). There was no evidence of increased hospitalisations (risk ratio 0.25; 0.05 to 1.12; $p=0.069$).

Conclusions. An internet-delivered intervention for the self-management of RTIs modifies help-seeking behaviour and does not result in more hospital admissions due to delayed help seeking. Advising the use of ibuprofen may not be helpful.

ISRCTN 91518452

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Article Summary: Strengths and Limitations

- This is to our knowledge the only substantial trial to date to address the effectiveness of support for the management of respiratory infections using the internet
- The rate of uptake following invitation was low, but is what would be expected for a free standing internet-delivered intervention, and 70% follow-up was achieved which is high for a free-standing internet intervention - and there was little evidence of attrition bias.
- The primary outcome has to be changed to monthly questionnaires since the intervention development had to take account of the context of the provision of NHS direct, and the monthly self-report data was the only source of data about NHS direct contacts (in addition to documenting episodes that clinicians did not include in the records), but recall of contacts made during an infection experienced in the previous month are likely to suffer minimal recall bias.
- Participants were less deprived than non-participants but controlling for deprivation made little difference to the estimates and there was no significant interaction of the intervention with deprivation.
- The number of participants who experienced one or more RTIs was lower than expected which will have reduced the power to detect differences.

Background

Most people suffer a respiratory tract infection (RTI) every year, many suffering more than once, and with 20-30% of the population consulting primary care at least once each year, which represents a significant call on health care resources^{1,2}. However, in most cases RTIs do not present a serious threat to the patient's health, and with access to the right information many illness could be self-managed at home. This is particularly important as unfortunately when a doctor is consulted antibiotics are normally given¹. Provision of such information prior to consultations could potentially result in patients having improved symptom control, lower attendance at GP surgeries, and reduced antibiotic prescription – which could be one important tool in the fight against antibiotic resistance³. A systematic review has documented several trials that have used information to modify consultations for respiratory tract infections among children⁴. However, there were only three older trials (the last published in 1991) that addressed the issue of providing specific information prior to consultation for respiratory tract infections⁴. Studies in adults also demonstrate that providing information booklets may help modify consultation behaviour⁵⁻⁷, but a wide range of symptoms and conditions were assessed in the latter studies so the precise role in interventions for modifying consultations for RTIs is less clear.

Booklets are no longer likely to be distributed as a source of advice regarding the self-management of respiratory infection given the widespread and growing access to the internet as a source of information prior to consulting - with more than 80% of families currently having access to the internet (rising by 5% each year). Web-based interventions can enable patients to access reliable self-care information from their home, make an informed decision on how best to manage their symptoms, and decide whether they need to visit their doctor. Recently a trial has reported that advice to use ibuprofen resulted in both poor symptom control (more prolonged illness) and increased complication – presumably by interfering with the inflammatory and immune response⁸. A potential problem about providing self-management advice is that patients might be encouraged to self-manage serious infections inappropriately (i.e. when they really need to see the doctor), and so develop complications unnecessarily. This is a major concern for both doctors and patients⁹⁻¹¹ – highlighting the importance of good safety-netting advice (i.e. advice about when to consult further) and the need to document the impact of interventions on hospital admissions. However it is also plausible that good self-management advice about appropriate early assessment of more severe illness could reduce hospital admissions

We have developed a theoretically informed internet-delivered intervention to manage respiratory tract infections among adults ('The Internet Doctor') that we have shown in a small exploratory trial results in higher levels of satisfaction, enablement, and understanding of illness¹². We report a larger trial of this website to address whether consultation behaviour can be modified, and to document potential harms (including hospital admissions) over a one year period.

Methods

We used very similar procedures to our previous leaflet trial.⁶ A random selection of adults in the computerised practice registers from 35 practices in southern England were identified by the practice staff, and letter sent to patients inviting them to participate. Patients willing to participate were asked to log on to the website to confirm consent. Patients were also be given contact details to enable them to email or talk to the research team before agreeing to participate or if they had problems logging in. Only one participant per household could participate.

Changes to the protocol.

We originally specified a 12 month period for measuring the primary outcome, but in developing the intervention we needed to incorporate not just advice to see the GP but also advice to use NHS direct, and therefore to document NHS direct contacts. We had not anticipated this in advance, and so required self-report of the monthly data as our primary outcome. To provide monthly follow-ups for a year would then have had two effects – engagement of participants would have been much more difficult and much more resource intensive than originally anticipated. The most meaningful and feasible assessment of the primary outcome was therefore the monthly reports of consulting their GP for those individuals who reported a respiratory infection (the intervention was not designed to help those who did not suffer an infection).

Inclusion criteria. Adult patients (aged 18+) from GPs computerised lists. **Exclusion criteria.** Patients with severe mental problems (e.g. major uncontrolled depression/schizophrenia; dementia; severe mental impairment - unable to complete outcomes) or terminally ill.

Randomisation . Once logged in, patients were randomised automatically by the website using computer generated random numbers to one of the following groups:

- 1) **Access to an interactive website** providing tailored advice; this was reinforced by email prompts and reminders to use the website; patients were given information about the natural history, self care advice, and advice about the use of over the counter medication. Outcome measures were documented online by participants following email prompts each month.
- 2) **Normal care** (as the control group, outcome measures were collected online but access to the tailored advice website was at the end of the trial)

Randomisation was not stratified with no blocking, and participants were blind to randomisation group at the point of consent (but clearly could not be blinded once they knew their randomisation group)

Study groups

Intervention group. Participants had access to the internet-delivered intervention for 20 weeks. On logging onto the website users could select tailored advice on a) whether and why they need/do not need to consult the GP, and b) how to self-care for RTIs. Patients selecting consultation advice completed questions about their symptoms and medical history, and were then presented with tailored advice recommending either self-

1 management (for mild symptoms), for more severe symptoms (e.g. haemoptysis, prolonged fever) phoning
2 the 'NHS Direct' helpline which provided nurse led advice about the need to seek further medical help, or
3 alternatively seeking medical attention immediately (for symptoms potentially posing serious risks e.g.
4 reduced conscious level, chest pain). Patients were given the opportunity to challenge this advice by
5 selecting further in-depth information about the symptoms of common complications or serious illness
6 compatible with their symptoms, and by clicking on frequently asked questions (e.g. regarding the need for
7 antibiotics and typical time-course of symptoms). The self-care section provided options to select advice on
8 self-management without medication (including rest, fluid intake) or with medication. For those who wanted
9 to take medication, over-the-counter remedies were recommended as an effective and preferable alternative
10 to seeking antibiotics from the GP, and in particular optimising the use of paracetamol and encouraging the
11 use of ibuprofen. The website was theory-based, addressing all components of the common-sense model of
12 self-regulation of illness¹³ (i.e. perceived symptoms, cause, timeline, physical and emotional consequences
13 and possibility for control/cure), and used the principles of social cognitive theory¹⁴ to address expected
14 outcomes of consultation and self-care, and build self-confidence for self-care. Extensive qualitative
15 piloting¹⁵ established that the website was accessible to people with very limited education and no previous
16 computer use, and quantitative piloting in several hundred people indicated that it increased confidence
17 when self-managing a RTI and had the potential to reduce consultations¹².

18 **Control group (normal care).** As in the intervention group, the control group had access to the GP/practice
19 in the normal way for respiratory illnesses and ILI. The control group was offered access to the website at
20 the end of the study to minimise resentful demoralisation¹⁶.

21 **Primary outcome**

22 *GP consultations.* We hypothesised that the intervention would reduce the number of contacts with general
23 practitioners for individuals who suffered a respiratory tract infection. Patients were prompted by email to
24 log onto the website monthly every four weeks until 20 weeks (i.e. weeks 4,8,16,20) to complete
25 questionnaires about illnesses during the last month - since the duration of symptoms can be remembered
26 reliably over a period of a few weeks^{17,18}.

27 We also performed an assessment of the consultations that were recorded in primary care by a blinded
28 assessment of the primary care records. Although this does not capture all contacts with health professionals
29 (and also does not capture contacts with NHS Direct) it has been shown to be reliable¹⁹.

30 **Secondary outcomes**

31 The use of antibiotics was documented as prescription of antibiotics from patient records.

32 For each episode the index person also documented: whether they contacted NHS Direct for phone-based
33 advice; the nature of the infection; the duration of symptoms rated moderately bad (which we have shown
34 in previous research is a useful outcome and sensitive to change for individuals¹⁸ and can be remembered
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1 reliably over a period of a few weeks^{17 18}); the number of days where work/normal activities were
2 impaired¹⁸, and smoking status.
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4 Patients were also asked to complete measures of their symptoms and concern about them at the time of
5 illness, levels of health anxiety, consulting preferences, and attitudes to the intervention; a full analysis of
6 these potential mediators and moderators of outcomes will be presented in a process analysis in a future
7 paper.
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9 **Socio-demographic and comorbidity data.** We collected age, gender, and educational level from the
10 participant online and prior comorbidities and consultations from the notes review.
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12 **Sample size calculation.** We estimated that a trial among a minimum of 2266 patients would allow us to
13 detect a 25% reduction in attendance with RTIs (20% vs 15% requires 906 per group with completed
14 outcomes or 2266 allowing for 20% loss to follow-up; for $\alpha = 0.05$ and $\beta = 0.2$), and a 0.2
15 standardised effect size for continuous outcomes.
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21 **Analysis.** We performed an intention to treat analysis, and the syntax was written blind to group. No
22 interim analysis was performed. The proportions attending with RTI in the intervention and normal care
23 groups were evaluated using logistic regression to calculate odds ratios (which were converted to risk
24 ratios using the formula of Zhang²⁰), with confidence intervals. Outcomes measured on a continuous scale
25 (duration and severity of symptoms) were analysed using multiple linear regression. All continuous
26 outcome variables were checked for the assumption of normality of residuals. The models controlled for
27 variables likely to predict consultation: gender, age, highest educational qualification, smoking status,
28 whether there were children under 16 living in the household, any comorbid condition, the number of
29 times the patient reported consulting a doctor about an RTI in the 12 months prior to the study, and Index
30 of multiple deprivation (IMD uses post codes to estimate deprivation across a number of domains;
31 <https://www.gov.uk/government/statistics/english-indices-of-deprivation-2010>). Given previous findings
32 of increased symptom burden when health professionals give advice to use ibuprofen⁸, and the findings of
33 increase symptom burden in intervention group of the current study, a post-hoc secondary analysis
34 explored the impact of controlling for whether pages advocating the use of ibuprofen had been viewed.
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Results.

43769 patients were invited, of whom 3044 participants consented (from 17/1/12 to 20/10/13) and 3355 gave reasons for declining (commonly not enough time, or insufficient access to the internet, or uncomfortable using computers, but also a variety of other reasons; see Figure 1). Table 1 demonstrates that the groups were well balanced for a range of variables (and table 1a shows this for those who reported at least one respiratory infection during follow-up). Although groups in the study were well balanced for deprivation, those who agreed to take part were less deprived than non-participants (IMD score 16.1 (SD 11.1) hence results controlled for IMD score.

Table 1 Baseline characteristics*

	Control	Intervention
Female	779/1432 (54.4%)	816/1490 (54.8%)
Age	57.14 (13.1)	56.78 (13.5)
Ever smoked	699/1425 (49.1%)	688/1483 (46.4%)
IMD score	12.6 (7.9)	12.9 (8.1)
Comorbid condition	511/1418 (36.0%)	549/1481 (37.1%)
Number of times consulted a doctor about RTI in the previous year	0.50 (1.2)	0.54 (1.2)
Household composition:		
• Alone	178/1432 (12.4%)	191/1489 (12.8%)
• Spouse/partner	963/1432 (67.3%)	1015/1489 (68.2%)
• Other adult(s)	147/1432 (10.3%)	145/1489 (9.7%)
• Children under 16	144/1432 (10.1%)	138/1489 (9.3%)
Highest qualifications		
• No formal educational qualifications	108/1432 (7.5%)	121/1490 (8.1%)
• Cses/ o'levels/ gses (or similar)	265/1432 (18.5%)	279/1490 (18.7%)
• A'levels (or similar)	151/1432 (10.5%)	157/1490 (10.5%)
• Diploma/other vocation qualification	317/1432 (22.1%)	322/1490 (21.6%)
• Degree	218/1432 (15.2%)	244/1490 (16.4%)
• Postgraduate or professional qualification	373/1432 (26.1%)	367/1490 (24.6%)

*Data are means (SD) or numbers (%).

Table 1a Baseline characteristics of participants who reported at least one RTI*

	Control	Intervention
Female	506/920 (55.0%)	491/852 (57.6%)
Age	56.28 (12.95)	56.76 (12.93)
Ever smoked	448/918 (48.8%)	393/850 (46.2%)
Comorbid condition	329/912 (36.1%)	324/850 (38.1%)
Number of times consulted a doctor about RTI in the previous year	0.54 (1.17)	0.54 (1.19)
Household composition:		
• Alone	110/920 (12.0%)	98/851 (11.5%)
• Spouse/partner	612/920 (66.5%)	589/851 (69.2%)
• Other adult(s)	96/920 (10.4%)	87/851 (10.2%)
• Children under 16	102/920 (11.1%)	77/851 (9.1%)
Highest qualifications		
• No formal educational qualifications	66/920 (7.2%)	62/852 (7.3%)
• Cses/ o'levels/ gcses (or similar)	166/920 (18.0%)	143/852 (16.8%)
• A'levels (or similar)	102/920 (11.1%)	88/852 (10.3%)
• Diploma/other vocation qualification	203/920 (22.1%)	196/852 (23.0%)
• Degree	139/920 (15.1%)	148/852 (17.4%)
• Postgraduate or professional qualification	244/920 (26.5%)	215/852 (25.2%)

*Data are means (SD) or numbers (%).

Table 2 documents a modest increase in contacts for NHS Direct among those who had an RTI in the intervention group (37/1574 (2.4%) versus 20/1661 (1.2%), multivariate Risk Ratio (RR) 2.25 (1.00 to 5.07, $p=0.048$), but reduced contact with doctors (239/1574 (15.2%) vs 304/1664 (18.3%), Risk ratio 0.71, 95% CI 0.52 to 0.98, $p=0.037$).

Table 2. Monthly reports of health service use and duration of illness (weeks 4,8,12,16 and 20) for participants who reported at least one respiratory infection during the 20 weeks

	Control	Intervention	Univariate risk ratio (95% CI; p-value)	Multivariate risk ratio (95% CI; p-value)*
Reported episodes of respiratory tract infection	1665/5697 (29.23%)	1578/5291 (29.82%)	1.03 (0.93, 1.12; p=0.566)	1.04 (0.94, 1.14; p=0.461)
Of those who reported a respiratory tract infection:				
Saw a doctor about illness (as a proportion of the number of episodes)	304/1664 (18.27%)	239/1574 (15.18%)	0.75 (0.56, 1.01; p=0.061)	0.71 (0.52, 0.98; p=0.037)
Contacted NHS Direct about illness	20/1661 (1.20%)	37/1574 (2.35%)	2.34 (1.07, 5.10; p=0.034)	2.25 (1.00, 5.07; p=0.048)
			Difference (95% CI; p-value)	
Length of illness (days)	10.68 (9.45)	11.30(9.89)	0.58 (-0.15, 1.30; p=0.119)	0.60 (-0.15, 1.36; p=0.118)
Days moderately bad or worse	4.00 (5.48)	4.59 (6.88)	0.47 (0.03, 0.92; p=0.035)	0.52 (0.06, 0.97; p=0.026)

Possible harms. The reduction in contacts with doctors occurred despite slightly longer illness duration (11.3 days versus 10.7 days; multivariate estimate 0.60 days longer (-0.15 to 1.36, p=0.118) and more days experienced of moderately bad or worse illness 4.59 versus 4.00 days (multivariate estimate 0.52 days; 0.06 to 0.97, p=0.026). The latter estimates of increased symptom burden were reduced when controlling for whether individuals used ibuprofen pages on the website (length of illness 0.22, -0.51 to 0.95, p=0.551; moderately bad or worse symptoms 0.36, -0.08 to 0.80, p=0.105). There was no evidence that self-management advice resulted in delayed consultations for serious illnesses (e.g. lobar pneumonia; meningitis; septicaemia) and hence increased hospitalisations: in fact there were reduced hospitalisations, albeit not statistically significant, both in the shorter term (20 weeks) and longer term (1 year) (tables 3-6).

Table 3 Health service use recorded in primary care records in the 20 weeks following the date of consent for participants who reported at least one episode of RTI

	Control	Intervention	Univariate risk ratio (95% CI; p=value)	Multivariate risk ratio (95% CI; p=value)
Any consultations	98/912 (10.8%)	88/851 (10.3%)	0.96 (0.73, 1.26; p=0.782)	0.89 (0.65, 1.23; p=0.514)
Any antibiotic prescriptions	66/880 (7.5%)	64/827 (7.7%)	1.03 (0.74, 1.43; p=0.853)	0.94 (0.64, 1.38; p=0.759)
Any hospitalisations	7/823 (0.9%)	1/765 (0.1%)	0.15 (0.02, 1.24; p=0.079)	0.13 (0.02, 1.11; p=0.062)
Any referrals	10/824 (1.2%)	8/771 (1.0%)	0.86 (0.34, 2.14; p=0.740)	0.77 (0.26, 2.24; p=0.625)

*Multivariate model controls for gender, age, highest educational qualification, smoking status, whether there are children under 16 living in the household, any comorbid condition, IMD score, and the number of times the patient reported consulting a doctor about an RTI in the 12 months prior to the study

Table 4 Health service use recorded in primary care records in the 12 months following the date of consent for patients who experience at least one episode of RTI in the first 20 weeks.

	Control	Intervention	Univariate risk ratio (95% CI; p=value)	Multivariate risk ratio (95% CI; p=value)
Any reconsultations	176/912 (19.3%)	164/851 (19.3%)	0.99 (0.82, 1.16; p=0.989)	0.93 (0.73, 1.16; p=0.509)
Number of reconsultations**				
Any antibiotic prescriptions	115/851 (13.5%)	107/794 (13.5%)	0.99 (0.78, 1.30; p=0.982)	1.00 (0.74, 1.33; p=0.997)
Any hospitalisations	8/748 (1.1%)	1/689 (0.2%)	0.14 (0.02, 1.08; p=0.059)	0.13 (0.02, 1.05; p=0.056)
Any referrals	14/750 (1.9%)	12/699 (1.7%)	0.92 (0.43, 1.96; p=0.830)	0.87 (0.35, 2.16; p=0.799)

*Multivariate model controls for gender, age, highest educational qualification, smoking status, whether there are children under 16 living in the household, any comorbid condition, IMD score, and the number of times the patient reported consulting a doctor about an RTI in the 12 months prior to the study

**reported as the mean (s.d.). The median is 0 and the IQR is (0,0). The range is 0-8.

Table 5. Health service use in the 20 weeks following the date of consent based on review of primary care notes

	Control	Intervention	Univariate risk ratio (95% CI; p=value)	Multivariate risk ratio (95% CI; p=value)
Any reconsultations	126/1418 (8.89%)	118/1483 (7.96%)	0.90 (0.71, 1.14; p=0.368)	0.95 (0.79, 1.15; p=0.612)
Number of reconsultations**	0.18 (0.75)	0.16 (0.66)	0.88 (0.64, 1.21; p=0.434)	0.97 (0.69, 1.35; p=0.854)
Any antibiotic prescriptions	86/1378 (6.24%)	83/1448 (5.73%)	0.92 (0.68, 1.23; p=0.569)	0.88 (0.63, 1.24; p=0.473)
Any hospitalisations	8/1301 (0.61%)	2/1368 (0.15%)	0.25 (0.05, 1.12; p=0.069)	0.24 (0.05, 1.13; p=0.072)
Any referrals	10/1302 (0.77%)	10/1375 (0.73%)	0.95 (0.39, 2.26; p=0.903)	0.98 (0.37, 2.59; p=0.965)

*Multivariate model controls for gender, age, highest educational qualification, smoking status, whether there are children under 16 living in the household, any comorbid condition, IMD score and the number of times the patient reported consulting a doctor about an RTI in the 12 months prior to the study

**reported as the mean (s.d.). The median is 0 and the IQR is (0,0). The range is 0-8.

Table 6. Health service use in the 12 months following the date of consent based on review of primary care notes

	Control	Intervention	Univariate risk ratio (95% CI; p=value)	Multivariate risk ratio (95% CI; p=value)
Any consultations	242/1418 (17.07%)	249/1483 (16.79%)	0.98 (0.83, 1.15; p=0.843)	0.85 (0.65, 1.12; p=0.259)
Number of consultations**	0.30 (0.88)	0.28 (0.77)	0.92 (0.75, 1.14; p=0.456)	0.97 (0.79, 1.21; p=0.806)
Any antibiotic prescriptions	156/1332 (11.71%)	155/1389 (11.16%)	0.95 (0.77, 1.17; p=0.651)	0.97 (0.76, 1.23; p=0.811)
Any hospitalisations	11/1189 (0.92%)	4/1239 (0.32%)	0.35 (0.11, 1.09; p=0.071)	0.35 (0.11, 1.10; p=0.073)
Any referrals	16/1192 (1.34%)	15/1249 (1.20%)	0.89 (0.44, 1.80; p=0.755)	1.11 (0.48, 2.52; p=0.808)

*Multivariate model controls for gender, age, highest educational qualification, smoking status, whether there are children under 16 living in the household, any comorbid condition, IMD score and the number of times the patient reported consulting a doctor about an RTI in the 12 months prior to the study

**reported as the mean (s.d.). The median is 0 and the IQR is (0,0). The range is 0-8.

Analysis of the follow-up data from the notes review for the whole sample is shown in tables 5 and 6; as expected, since most such individuals did not have a respiratory infection, there is no clear evidence of a reduction in consultations. The characteristic of those followed up and not followed up were also similar (table 7).

Table 7. Characteristics of participants followed up and not followed up

	Did not complete 20 week follow up questions	Did complete 20 week follow up questions
Control group	353/871 (40.5%)	1079/2052 (52.6%)
Intervention group	518/871 (59.5%)	973/2052 (47.4%)
Female	489/871 (56.1%)	1,106/2,051 (53.9%)
Age	52.9 (14.9)	58.7 (12.1)
Ever smoked	428/862 (49.7%)	959/2,046 (46.9%)
IMD score	13.8 (9.0)	12.3 (7.4)
Comorbid condition	290/ 861 (33.7%)	770/2,038 (37.8%)
Number of times consulted a doctor about RTI in the previous year	0.71 (1.4)	0.4 (1.1)
Household composition:		
• Alone	113/871 (13.0%)	256/2050 (12.5%)
• Spouse/partner	550/871 (63.2%)	1428/2050 (70.0%)
• Other adult(s)	101/871 (11.6%)	191/2050 (9.3%)
• Children under 16	107/871 (12.3%)	175/2050 (8.5%)
Highest qualifications		
• No formal educational qualifications	76/871 (8.7%)	153/2051 (7.5%)
• Cses/ o'levels/ gceses (or similar)	180/871 (20.7%)	364/2051 (17.8%)
• A'levels (or similar)	93/871 (10.7%)	215/2051 (10.5%)
• Diploma/other vocation qualification	191/871 (21.9%)	448/2051 (21.8%)
• Degree	142/871 (16.3%)	320/2051 (15.6%)
• Postgraduate or professional qualification	189/871 (21.7%)	551/2051 (26.9%)

Discussion

This is to our knowledge the only substantial trial to date to address the effectiveness of support for the management of respiratory infections using the internet. Although relatively limited follow-up was possible (20 weeks) there was reduced contact with GPs and possibly a longer term reduction in hospital admissions. There was a slight increase in contact with NHS Direct, consistent with the advice given by the intervention for management of more severe symptoms that did not warrant immediate medical attention.

Limitations. 70% follow-up was achieved which is high for a free-standing internet intervention, and there was little evidence of attrition bias. There was no differential attrition bias which suggest that resentful demoralisation was minimised by offering the delayed intervention^{21,22}. The primary outcome was initially anticipated to be at 12 months, but a shorter time period was necessary due to the need to engage participants and achieve good follow-up rates with the monthly questionnaires. Monthly questionnaires were also needed since the intervention during development had to take account of the context of the provision of NHS direct, and the monthly self-report data was the only source of data about NHS direct contacts (in addition to documenting episodes that clinicians did not include in the records). The monthly data has the limitations of self-report, and could be biased if GP consultations were discouraged by the InternetDr, but in fact InternetDr not gave advice about when to see the doctor promptly. If self-reports of RTIs were biased we would also have expected different numbers of RTIs to be reported in the intervention group which did not occur. Bias in self report would also not explain the opposite directions of consultation with NHS Direct and with GPs, and which also makes type I error unlikely. The estimate derived from primary care notes review for consultations (risk ratio 0.87, lower bound of the 95% confidence interval 0.51) was also consistent with the estimate from the monthly data (risk ratio 0.71). The rate of uptake following invitation was low, but is what would be expected for a free standing internet-delivered intervention, particularly as this is for mostly minor and common conditions that most will feel, rightly or wrongly, reasonably confident to manage. However, the patients who did participate were those that the intervention is likely to help i.e. participants who are sufficiently concerned about their symptoms to be motivated to use a self-management website. There is also a circularity in engaging participants – physicians are much more likely to refer to a free standing intervention once it has been shown to be effective, so the first priority is to demonstrate effectiveness. Participants were less deprived than non-participants but controlling for deprivation made little difference to the estimates and there was no significant interaction of the intervention with deprivation. The number of participants who experienced one or more RTIs was lower than expected which will have reduced the power to detect differences. Patients' self-reported contacts with the NHS, but recall of contacts made during an infection experienced in the previous month are likely to suffer minimal recall bias. Self-report is the only method of capturing contacts with NHS Direct and furthermore the estimates of consultations and admissions purely based on primary care notes suggested changes in the same direction and of a similar magnitude to the monthly self-reports.

Main findings.

The estimated reduction in consultations with GPs with the website was similar to the effectiveness of the pamphlet we developed for predominantly respiratory illness⁶. This suggests the internet-delivered intervention is potentially more effective than a pamphlet, given the widespread availability currently of NHS Direct online resources and other internet-delivered advice regarding infections. The estimated 25% reduction in GP consultations, even if only over a period of a few months, would provide very considerable relief in terms of pressure on services during the winter months. Perhaps more surprising is that there was a reduction in hospital admissions, albeit non-significant, suggesting the intervention is unlikely to result in delayed presentation of serious illness – and if anything could help in relieving pressure on hospital services. One explanation for reduced admission might be that those with severe symptoms were discouraged from seeing the doctor, but since InternetDr encouraged individuals to seek medical help promptly with severe symptoms this seems unlikely. Although the study was not powered to assess a reduction in antibiotic use, nevertheless the estimates of a 6-12% reduction in antibiotic prescriptions over 6-12 months is consistent with the observation that most individuals who attend the GP get antibiotics¹, so reducing attendance would be expected to potentially provide an important component in the population level fight against antibiotic resistance, given the evidence that primary care prescriptions are a key component in driving antibiotic resistance³.

Harms. In terms of major harms the upper bound of the confidence interval suggests we can be reasonably sure that no increase in hospital admissions occurred. The most surprising finding was that in the intervention group both symptom duration and the duration of more severe symptoms was increased – the latter significantly. This could be either a chance finding or possibly that we made participants more aware of symptoms. However, another possibility is that by strongly encouraging the use of not only paracetamol but also ibuprofen, the intervention may have significantly increased ibuprofen use, and recent trial evidence suggests that advising the use of ibuprofen is unlikely to help overall symptoms and is associated with the progression of symptoms (i.e. prolonging illness)⁸ - presumably due to inhibiting the inflammatory element of an effective immune response. When the analysis in the current study controlled for the use of pages that advocated ibuprofen, the finding of increase symptom duration in the intervention group was markedly attenuated. A possible explanation for this attenuation could be that use of ibuprofen pages is a marker of an individual having more severe or florid symptoms, and hence the symptoms might last longer (i.e. reverse causality: the use of ibuprofen pages was because of severe illness, not causing it). However, this explanation is rather unlikely as more florid upper respiratory symptoms and signs are associated with shorter illness duration²³, and reverse causality cannot explain why more severe prolonged symptoms were reported in the intervention group since the number of infections reported were almost identical in both groups. Thus the most reasonable inference is that advice to use ibuprofen was probably harmful and revised versions of the website should therefore not encourage ibuprofen use. Whatever the reasons for the finding of more severe symptoms, the presence of more severe symptoms would be expected to lead to increased consultations, which makes the reduction

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2 in the need for GP contacts more striking - supporting the earlier findings in the development of the
3 intervention that the website increases enablement and confidence in managing symptoms^{12;24}.
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6 **Conclusion.** An internet-delivered intervention for managing RTIs helps participants appropriately
7 manage their symptoms and contacts with NHS staff, and may help reduce hospital admissions, but advice
8 to use ibuprofen may be unhelpful.
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For peer review only

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Figure 1. CONSORT diagram

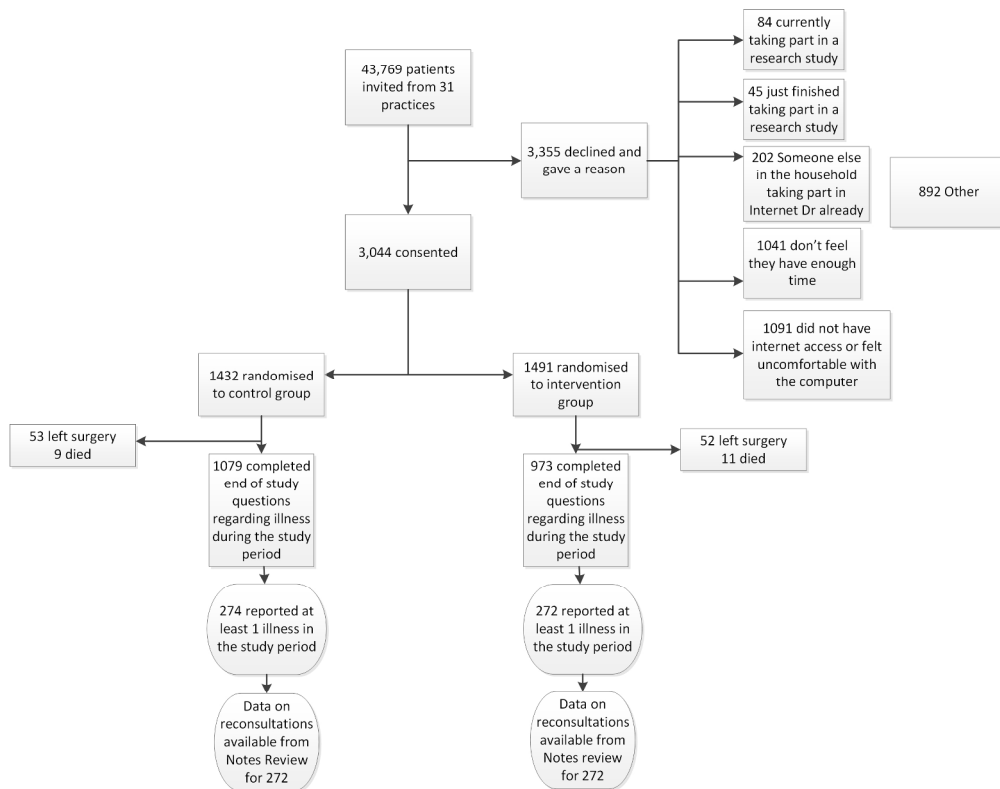


Figure 1 CONSORT Diagram
238x198mm (300 x 300 DPI)

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TRIAL CHECKLIST based on CONSORT statement:

	Reported?	If Y: Page no
1a. TITLE Identify the study as RCT	<u>Y</u>	<u>1</u>
1b. Abstract: Use structured format	<u>Y</u>	<u>2</u>
Introduction 2a. Back ground and rationale	<u>Y</u>	<u>3</u>
2b. Specific trial objectives	<u>Y</u>	<u>3</u>
Protocol: 3a. Trial design	<u>Y</u>	<u>4</u>
3b Changes to methods after trial commencement	<u>Y</u>	<u>5,6</u>
4a Study population eligibility criteria	<u>Y</u>	<u>4</u>
4b Settings and location where data was collected	<u>Y</u>	<u>4</u>
5. Intervention and timing	<u>Y</u>	<u>4</u>
5. Objectives	<u>Y</u>	<u>3</u>
6a Outcome measures: pre-specified 1y/2y outcomes	<u>Y</u>	<u>5</u>
6a Outcome measures: any changes	<u>Y</u>	<u>5</u>
7a Sample size	<u>Y</u>	<u>6</u>
7b Interim analysis/stopping rules	<u>Y</u>	<u>6</u>
Randomisation: 8a methods used	<u>Y</u>	<u>4</u>
8b type of randomization	<u>Y</u>	<u>4</u>
9 mechanism used to implement (e.g. sequential pots)	<u>Y</u>	<u>4</u>
10 who generated allocation sequence, who assigned	<u>Y</u>	<u>4</u>
Blinding 11a Who blinded after assignment	<u>Y</u>	<u>4,6</u>
11b Description of the similarity of interventions	<u>Y</u>	<u>5</u>
Stats methods 12a Methods used to compare groups	<u>Y</u>	<u>7</u>
12b Other analyses (subgroups, adjusted)	<u>Y</u>	<u>76</u>
Results 13a Provide trial flow diagram (assigned,treated,analysed)	<u>Y</u>	<u>Fig 1</u>
13b Losses, exclusions, reasons	<u>Y</u>	<u>8 and Fig 1</u>
Recruitment 14a Periods and follow-up	<u>Y</u>	<u>8, Fig1</u>
14b Why trial ended or stopped	<u>Y</u>	<u>8</u>

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4	15. Baseline data for outcomes	<u>Y</u>	<u>table 1</u>
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6	16. State numbers analysed and intention to treat	<u>Y</u>	<u>8, table 2</u>
7			
8	Outcomes: 17a) Estimated effect sizes and precision	<u>Y</u>	<u>tables 2-4</u>
9			
10	17b For Binary absolute and relative effect sizes	<u>Y</u>	<u>tables 2-4</u>
11			
12	18. Ancillary analyses subgroup/adjusted/pre-specified)	<u>Y</u>	<u>7</u>
13			
14	19. Harms/adverse events	<u>Y</u>	<u>10</u>
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16	20. Trial limitations	<u>Y</u>	<u>14</u>
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18	21 Generaliseability	<u>Y</u>	<u>14</u>
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20	22 Interpretation	<u>Y</u>	<u>14-15</u>
21			
22	Other: 23 Registration	<u>Y</u>	<u>2</u>
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24	24 Site of full trial protocol	<u> </u>	<u>This can be provided</u>
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26	25. Funding	<u>Y</u>	<u>1</u>
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For peer review only

Correction

Little P, Stuart B, Andreou P, *et al.* Primary care randomised controlled trial of a tailored interactive website for the selfmanagement of respiratory infections (Internet Doctor). *BMJ Open* 2016;6:e009769. doi:10.1136/bmjopen-2015-009769

There is a labeling mistake in the analysis of this paper. Although the mistake alters the estimates very slightly it does not alter the inferences.

The misunderstanding was that the 24 week follow-up (the last data point) was thought to be 20 weeks, and the real 20 week data was then not included. The most complete use of the data is therefore to include both the 20 and 24 weeks data. If the complete 24 weeks of data is used throughout this means the following changes to the tables: In the Abstract, the Results section should read: “**Results** 3044 participants were recruited. 852 in the intervention group and 920 in the control group reported one or more RTIs, among whom there a modest increase in NHS Direct contacts in the intervention group (intervention 44/1734 (2.5%) versus control 24/1842 (1.3%); multivariate Risk Ratio (RR) 2.53 (95% CI 1.10 to 5.82, p=0.029)). Conversely reduced contact with doctors occurred (283/1734 (16.3%) vs 368/1845 (20.0%); risk ratio 0.71, 0.53 to 0.95, p=0.019). Reduction in contacts occurred despite slightly longer illness duration (11.3 days versus 10.9 days respectively; multivariate estimate 0.48 days longer (-0.16 to 1.12, p=0.141) and more days of illness rated moderately bad or worse illness (0.53 days; 0.12 to 0.94, p=0.012). The estimate of slower symptom resolution in the intervention group was attenuated when controlling for whether individuals had used webpages which advocated ibuprofen use (length of illness 0.22 days, -0.51 to 0.95, p=0.551; moderately bad or worse symptoms 0.36 days, -0.08 to 0.80, p=0.105). There was no evidence of increased hospitalisations (risk ratio 0.13; 0.02 to 1.01; p=0.051).”

Table 2 is the characteristics of those who reported at least one illness and that does not change. The main impact is on the numbers in Table 3 (monthly report) and Table 4 (notes reviews at 20 weeks in those who reported an infection). These now use 24 weeks of data. There were no changes to the inferences.

The title of table 5 is changed as it is actually based on 24 weeks rather than 20 weeks of data.

Table 6 is revised to use 24 rather than 20 weeks. No change to the inferences.

Table 7 is all notes reviews at 12 months and remains unchanged.

Table 8 is characteristics of those lost to follow up which also remains unchanged.

The relationship with ibuprofen remains unchanged. (length of illness 0.22, -0.51 to 0.95, p=0.551; moderately bad or worse symptoms 0.36, -0.08 to 0.80, p=0.105).

The corrected Tables are shown below:

Table 3 Monthly reports of health service use and duration of illness (4,8,12,16,20,24 weeks) for participants who reported at least one respiratory infection during the 24 weeks

	24 weeks of reported infections and 24 weeks of reported health service use			
	Control	Intervention	Univariate risk ratio (95% CI; p value)	Multivariate risk ratio* (95% CI; p=value)
Reported episodes of respiratory tract infection	1,853/ 6,776 (27.4%)	1,742/6,264 (27.8%)	1.02 (0.93, 1.01; p=0.641)	1.03 (0.94, 1.13; p=0.525)
Of those who reported a respiratory tract infection				
Saw a doctor about illness (as a proportion of the number of episodes)	368/1845 (20.0%)	283/1734 (16.3%)	0.74 (0.53, 0.93; p=0.025)	0.71 (0.53, 0.95; p=0.019)
Contacted NHS Direct about illness	24/1842 (1.3%)	44/1734 (2.5%)	2.39 (1.11, 5.16; p=0.025)	2.53 (1.10, 5.82; p=0.029)
Length of illness (days)	10.88 (9.67)	11.34 (9.91)	0.43 (-0.27, 1.14; p=0.226)	0.48 (-0.16, 1.12; p=0.141)
Days moderately bad or worse	4.16 (5.69)	4.66 (6.89)	0.51 (0.10, 0.92; p=0.015)	0.53 (0.12, 0.94; p=0.012)

*Multivariate model controls for gender, age, highest educational qualification, smoking status, whether there are children aged under 16 years living in the household, any comorbid condition, index of multiple deprivation score, and the number of times the patient reported consulting a doctor about an RTI in the 12 months prior to the study.

Table 4 Health service use recorded in primary care records in the 24 weeks following the date of consent for participants who reported at least one episode of respiratory tract infection (RTI)

	24 weeks of reported infections and 24 weeks of notes review data			
	Control (%)	Intervention (%)	Univariate risk ratio (95% CI; p=value)	Multivariate risk ratio* (95% CI; p=value)
Any consultations	127/912 (13.9%)	111/851 (13.0%)	0.94 (0.74, 1.18; p=0.588)	0.92 (0.70, 1.21; p=0.556)
Any antibiotic prescriptions	83/880 (9.4%)	79/827 (9.6%)	1.01 (0.75, 1.35; p=0.953)	1.02 (0.82, 1.43; p=0.911)
Any hospitalisations	8/823 (0.9%)	1/765 (0.1%)	0.13 (0.02, 1.07; p=0.058)	0.13 (0.02, 1.01; p=0.051)
Any referrals	14/824 (1.7%)	12/771 (1.6%)	0.92 (0.43, 1.96; p=0.830)	0.87 (0.35, 2.16; p=0.799)

*Multivariate model controls for gender, age, highest educational qualification, smoking status, whether there are children aged under 16 years living in the household, any comorbid condition, index of multiple deprivation score, and the number of times the patient reported consulting a doctor about an RTI in the 12 months prior to the study.

Table 5 Health service use recorded in primary care records in the 12 months following the date of consent for patients who experience at least one episode of respiratory tract infection (RTI) in the first 24 weeks

	Control	Intervention	Univariate risk ratio (95% CI; p=value)	Multivariate risk ratio (95% CI; p=value)
Any reconsultations	176/912 (19.3%)	164/851 (19.3%)	0.99 (0.82 to 1.16; p=0.989)	0.93 (0.73 to 1.16; p=0.509)
Number of reconsultations†	0.36 (1.01)	0.33 (0.85)	0.91 (0.71, 1.17; p=0.475)	0.94 (0.72, 1.21; p=0.619)
Any antibiotic prescriptions	115/851 (13.5%)	107/794 (13.5%)	0.99 (0.78 to 1.30; p=0.982)	1.00 (0.74 to 1.33; p=0.997)
Any hospitalisations	8/748 (1.1%)	1/689 (0.2%)	0.14 (0.02 to 1.08; p=0.059)	0.13 (0.02 to 1.05; p=0.056)
Any referrals	14/750 (1.9%)	12/699 (1.7%)	0.92 (0.43 to 1.96; p=0.830)	0.87 (0.35 to 2.16; p=0.799)

*Multivariate model controls for gender, age, highest educational qualification, smoking status, whether there are children aged under 16 years living in the household, any comorbid condition, index of multiple deprivation score, and the number of times the patient reported consulting a doctor about an RTI in the 12 months prior to the study.

†Reported as the mean (SD). The median is 0 and the IQR is (0, 0). The range is 0–8.

Table 6. Health service use in the 24 weeks following the date of consent based on review of primary care notes

	Control	Intervention	Univariate risk ratio (95% CI; p=value)	Multivariate risk ratio (95% CI; p=value)
Any reconsultations	165/1418 (11.6%)	149/1483 (10.1%)	0.86 (0.70, 1.06; p=0.169)	0.86 (0.67, 1.09; p=0.216)
Number of reconsultations†	0.22 (0.82)	0.18 (0.69)	0.82 (0.62, 1.08; p=0.156)	0.89 (0.67, 1.19; p=0.438)
Any antibiotic prescriptions	108/1378 (7.8%)	101/1448 (7.0%)	0.89 (0.68, 1.15; p=0.380)	0.92 (0.68, 1.24; p=0.592)
Any hospitalisations	8/1301 (0.6%)	3/1388 (0.2%)	0.35 (0.09, 1.33; p=0.125)	0.36 (0.10, 1.37; p=0.134)
Any referrals	12/1302 (0.92%)	11/1375 (0.80%)	0.86 (0.38, 1.94; p=0.721)	1.08 (0.42, 2.79; p=0.870)

*Multivariate model controls for gender, age, highest educational qualification, smoking status, whether there are children aged under 16 years living in the household, any comorbid condition, index of multiple deprivation score and the number of times the patient reported consulting a doctor about an respiratory tract infection in the 12 months prior to the study.

†Reported as the mean (SD). The median is 0 and the IQR is (0, 0). The range is 0–8.

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BMJ Open 2017;7:009769corr1. doi:10.1136/bmjopen-2015-009769corr1



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