**Neuraminidase inhibitor use in adults presenting to hospital with suspected influenza: a questionnaire-based survey of practice among hospital physicians**

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# Abstract

## Background

UK Public Health England (PHE) guidelines recommend the liberal use of neuraminidase inhibitors (NAIs) in hospitalised adults with suspected influenza and are aligned with international guidelines. NAI use is recommended to start as early as possible and empirical use is recommended whilst awaiting laboratory results. Current UK hospital physician knowledge, attitudes, and practises regarding the use of NAIs, and levels of adherence to guideline recommendations are not known.

## Methods

This online, cross-sectional questionnaire-based survey of self-reported prescribing practice using clinical scenarios, was distributed to secondary care physicians involved in the assessment of adults presenting to hospital with suspected influenza. The primary outcome measure was adherence to PHE guidelines.

## Results

There were 237 respondents to the survey. 157 (67%) of 233 respondents reported awareness of PHE guidelines. Adherence to guidelines in the clinical scenarios ranged from 56% (95% CI 49-63%) to 72% (95% CI 66-79%) with considerable variability between specialities (p=0.0008). Not treating suspected cases was common as was withholding of NAIs whilst awaiting laboratory results, despite the acknowledgment of prolonged turnaround times. 73 of 220 (33%) respondents reported that concerns about NAI efficacy influenced their prescribing.

## Conclusions

Concordance with national guidelines for the treatment of influenza is sub-optimal. Lack of guideline awareness and concerns over the effectiveness of NAIs are contributing factors. This study highlights a disparity between public health policy and clinical practice and suggests that strategies that promote rapid diagnostic testing and adherence to treatment guidelines are required.

## Study registration

This study is registered with the ISRCTN:18249297

# Keywords

Influenza, neuraminidase inhibitor, oseltamivir, survey

# Introduction

The influenza virus causes seasonal epidemics leading to excess hospitalisations and deaths every year, principally in adults with co-morbidity and the elderly [1, 2]. Annual seasonal influenza vaccine is recommended for these groups [3] however protection is sub-optimal [4]. The rate of hospitalisation in adults with influenza has been estimated at 5 to 20 per 100,000 overall [5] but is much higher in the elderly [6]. In adults hospitalised with influenza 10-30% are admitted to critical care units and 3-15% will die in hospital [7, 8].

The effectiveness of neuraminidase inhibitors (NAIs) for the treatment of influenza has been the source of much debate [9]. The original placebo controlled trials of NAIs were performed mainly in otherwise healthy patients with uncomplicated influenza and showed a modest reduction in the duration of illness symptoms and viral shedding [10, 11]. Hospitalised adults with already complicated disease represent a priority for NAI treatment but no placebo controlled trials have been performed in this group. There is now a large body of data from observational studies which have consistently shown clinical benefits of NAIs in this group, including reduction in mortality [12-19]. Consistent with this evidence, Public Health England (PHE) guidelines recommend the use of NAIs for hospitalised adults and are strongly aligned with international guidelines [20-22] and supported by a recent UK Department of Health commissioned review [23]. As early NAI treatment is associated with better outcomes [19, 24, 25] and the turnaround time of laboratory testing is generally 1-2 days, empirical use is recommended at the point of presentation, whilst awaiting results.

Internationally there is great variation in the use of NAIs for influenza, including for hospitalised adults [26, 27]. Current knowledge, attitudes, and prescribing practises regarding the use of NAIs and adherence to PHE guidelines among front-line UK physicians are not known. We sought to address this evidence gap by performing a cross-sectional survey of practice among front-line UK physicians involved in the initial assessment of, and decisions to prescribe NAIs in, adults presenting to secondary care with suspected influenza.

# Methods

## Survey method

We performed an online, cross-sectional questionnaire-based survey of self-reported practice using the web-based survey tool SurveyMonkey. UK physicians involved in the initial assessment of adults presenting to hospital with suspected influenza, and the decision to use NAIs, were invited to complete the questionnaire. Entry into a prize draw was offered as an incentive to complete the questionnaire. Following conceptualisation and a scoping exercise the questionnaire was designed by a panel and piloted internally at University Hospital Southampton NHS Foundation Trust. The questionnaire format and questions were subsequently adapted to improve validity and reliability. It was then e-mailed to potential participants via the following specialist societies: the British Infection Association, the British Thoracic Society, the British Geriatrics Society and the Society of Acute Medicine. To increase the coverage and response rate the introductory letter and questionnaire were also emailed out to physicians via the R&D departments at NHS trusts (the full list of participating NHS trusts is detailed in the supplementary appendix, S1). The survey was sent out a further two times at monthly intervals to maximise response rate.

The survey used a combination of closed question statements and open ended free-text comments. The first question confirmed the appropriateness of the respondent to complete the questionnaire. The questionnaire contained questions relating to demographic data, local testing methods for influenza and turnaround time for results, knowledge of national treatment guidelines, and factors affecting physician’s decisions to use NAIs. It was made clear that the clinical scenarios all took place during periods of peak influenza transmission. There were 4 separate clinical scenarios representing the 4 categories of patients considered for NAI treatment in national and international guidelines: (i) uncomplicated influenza with no risk factors for subsequent complicated disease, presenting within 48 hours of symptom onset; (ii) uncomplicated influenza with risk factors for subsequent complicated disease, presenting within 48 hours of symptom onset; (iii) already complicated disease presenting within 48 hours of symptom onset; (iv) complicated (life threatening) disease presenting after 48 hours of symptom duration. Respondents were asked to pick responses from a list of options with the choice to add free text comments to justify their answers or provide additional details. In addition there was provision for free text comments at the end of the survey for respondents to mention any other relevant factors or opinions. Responses were anonymised. The full survey is available in the supplementary appendix, S2.

## Statistical methods

Anonymised data was entered into a dedicated database and cleaned. Analysis was conducted using Prism version 6·0 (GraphPad Software Inc; La Jolla, California) and Stata version 13·1 (StataCorp, College Station, Texas). The primary outcome measure was concordance with PHE guidelines as measured by the proportion of respondents selecting the appropriate responses for each scenario. Baseline characteristics were summarised using appropriate descriptive statistics. The level of respondent concordance with PHE guidelines for each scenario was calculated as an overall proportion and then for individual specialities. Results for all 4 Scenarios were pooled to give a combined estimate of guideline concordance for all respondents and then calculated for the individual specialities and compared across them (Chi squared test). Where 95% confidence intervals are presented, the Copper-Pearson ‘Exact’ method is used. Sample size was calculated based on an estimate of the population of UK adult physicians (consultant and registrar level) involved in the initial assessment of patients presenting to hospital with suspected influenza, of approximately 8,000. Using a confidence level of 95% and a maximum acceptable margin of error of 7%, 192 respondents were needed to estimate adherence to PHE guidelines for the scenarios.

## Qualitative methods

Free-text comments from the scenarios and other sections were sought to yield detailed views on the use of NAIs and to explore potential reasons underlying the responses in the clinical scenarios. Free-text comments were repeatedly studied independently by two researchers who then inductively identified emerging themes and collated responses within them.

# Results

Between 20th July 2015 and 1st Feb 2017 237 respondents completed the survey. It was not possible to calculate the response rate as the speciality societies and R&D departments who distributed the survey were unable to give details on the numbers of eligible physicians.

226(95%) of 237 respondents reported being regularly involved in the assessment and management of patients with influenza. Details of the respondent’s grade and speciality, other baseline characteristics and awareness of guidelines are summarised in table 1. 180(77%) of 233 respondents provided estimates of the turnaround time for laboratory testing at their institution and most (96[53%] of 180) reported a turnaround time of 24-72 hours, figure 1.

Concordance with PHE guidelines in the 4 scenarios ranged from 56% (95%CI 49-63%) to 72% (95%CI 66-79%). For scenario 1 PHE guidelines do not recommend treatment with NAIs. 140(63%) of 222 respondents reported that they would not treat with NAIs, 75(34%) reported that they would treat with NAIs and 6(3%) reported ‘other’ practice. For scenario 2 PHE guidelines recommend treating with NAIs empirically whilst awaiting results. 123(56%) of 220 respondents reported that they would treat empirically with NAIs, 53(24%) of 220 reported that they would withhold NAIs whilst awaiting the results of PCR testing, 35(16%) of 220 reported that they would not treat with NAIs and 9 (4%) reported ‘other’ practice. For scenario 3 PHE guidelines recommend treating with NAIs empirically whilst awaiting results. 157(72%) of 216 respondents reported that they would treat empirically with NAIs, 33(15%) reported that they would withhold NAIs whilst awaiting the results of PCR testing, 20(9%) reported that they would not treat with NAIs and 10(4%) reported other practice. For scenario 4 PHE guidelines recommend treating with NAIs empirically whilst awaiting results. 140(66%) of 210 respondents reported that they would treat empirically with NAIs, 29(14%) reported that they would withhold NAIs whilst awaiting the results of PCR testing, 35(17%) reported that they would not treat with NAIs and 6(3%) reported other practice. Across all scenarios 7% to 35% reported that they would not test for influenza.

When combining the results from all 4 scenarios, concordance with PHE guidelines was 64%(95%CI 61-68%) overall and varied significantly by speciality (p=0.0008). Among individual specialities adherence was highest amongst infection specialists (Microbiologists 74%[95%CI 67 to 80%] and Infectious Diseases physicians 72%[95%CI 64-79%]) and lowest for Emergency physicians (56%[95%CI 46-67%]). Adherence to PHE guidelines for the 4 scenarios is shown in figure 2a-d and combined results for all scenarios are shown in figure 3.

220(93%) of 237 respondents reported factors that influenced their use of NAIs, table 2. 73 of 22(33%) respondents reported that concerns about NAI efficacy influenced their decisions on NAI prescribing. 41(19%) and 29(13%) of 220 reported that concerns over the side effects and concerns over NAI resistance respectively, influenced their prescribing decisions. 36(16%) of 220 reported that a history of influenza vaccination influenced their NAI prescribing decision.

Commonest themes emerging from free-text comments were: the lack of routine use of NAIs for suspected influenza in participant’s institutions and the perceived lack of effectiveness of NAIs. Additional themes included perceived discouragement of liberal influenza testing and empirical NAI use due to hospital infection control policies, and the perception that pneumonia was not caused by influenza viruses. Themes and examples of individual responses are given in table 3.

# Discussion

Our study demonstrates overall sub-optimal concordance to national guidelines for the treatment of influenza with NAIs and considerable variation between physician specialities. This includes not using NAIs in patients presenting to hospital with suspected influenza, not testing patients with suspected influenza and the practice of withholding NAI treatment whilst awaiting laboratory results. It suggests that a lack of knowledge of guidelines and ongoing concerns over the effectiveness of NAIs may be major contributing factors to this practice. Our study also reveals other potential contributing factors in the under-utilisation of influenza testing and NAIs use such as hospital infection control policies.

Our study is the first, to our knowledge, to examine in detail current UK physician NAI prescribing practices and to explore their underlying knowledge, beliefs and attitudes, and therefore fills an important knowledge gap. The ongoing concerns over the effectiveness of NAIs for influenza reported by respondents may originate from media attention surrounding the Cochrane review authors’ publicised concerns over the lack of data transparency from industry-sponsored studies [9]. These concerns related to the original placebo controlled studies of NAIs which were largely conducted in healthy people, and have now been addressed by subsequent independent meta-analyses [11]. These studies are of questionable relevance to the use of NAIs in hospitalised adults who represent the group at highest risk of poor outcomes and arguably have the most to benefit from an effective antiviral treatment. Although no placebo controlled trials have ever been performed in this group, the results of multiple separate observational studies have consistently suggested improved clinical outcomes with NAI treatment [12-18, 25]. A large, well-controlled meta-analysis using patient level data from nearly 30,000 hospitalised patients with pandemic H1N1 influenza A demonstrated a reduction in mortality in adults treated with NAIs, which extended beyond 48 hours of symptom duration in critically ill patients [19]. It is highly unlikely that placebo controlled trials will ever be performed in this patient group due to the obvious ethical constraints and so management recommendations for severe influenza will continue to derive from observational studies.

The practice of withholding of NAIs until laboratory results are available despite the reported acknowledgement of the prolonged turnaround time of laboratory testing is concerning. Multiple studies have shown that earlier treatment with NAIs is associated with superior clinical outcomes [19, 24, 25] and so treatment at the point of initial assessment is clearly desirable. This practice may derive from concerns over the side effects highlighted by the Cochrane review authors, however these are typically mild and are less pertinent in the hospitalised cohort, especially among the critically ill. The concerns reported by respondents over the generation of resistance are also largely unjustified since empirically treating patients who subsequently test negative for influenza cannot credibly generate resistance, and the development of resistance in those who do have influenza and are treated has been rare with current influenza strains. A history of influenza vaccination should not influence empirical NAI use as influenza vaccine effectiveness is only moderate in adults with comorbidity and is even lower in the elderly, and so many patients hospitalised with influenza will have a history of vaccination [4].

Another potential reason for physicians failing to perform influenza testing and treating empirically with NAIs revealed by this survey was the issue of hospital infection control policies mandating isolation in patients tested for influenza or prescribed NAIs, whilst awaiting definitive results. Single-occupancy rooms are a limited resource in most UK hospitals and so isolating large numbers of patients with suspected influenza can lead to impairment of patient flow through acute areas. Physicians may therefore feel discouraged from testing patients with suspected influenza and treating empirically with NAIs. The consequences of failing to diagnose hospitalised patients with influenza are serious for both patients and hospitals and nosocomial outbreaks of influenza lead to multiple ward closures and avoidable patient deaths every year.

One potential solution to these problems may be the introduction of molecular point-of-care testing (POCT) for influenza. We published a randomised controlled trial evaluating routine molecular POCT in hospitalised adults demonstrated improved adherence to guidelines for the treatment of influenza and more rapid administration of NAIs compared to standard clinical care [28]. A subsequent randomised controlled trial of molecular POCT for influenza in hospitalised adults as part of a ‘test and treat’ strategy with NAIs, showed dramatic improvements in the detection of influenza and the appropriate use of antivirals, including faster administration, compared with standard clinical care. Additionally, this was the first randomised controlled trial to show that molecular POCT is associated with improvements in influenza patients’ clinical outcomes, which is likely to be attributable to the rapid and near universal administration of NAIs in patients with influenza [29]. A host-response finger prick point-of-care test for respiratory viruses that gives results in 10 minutes may also have the potential to facilitate rapid antiviral use in hospitalised patients with influenza [30, 31].

The strengths of this survey include the sampling of a broad range of physician specialists involved in the initials assessment of patient presenting with suspected influenza from across the entire UK. Although we were unable to calculate the response rate for our study, it is likely to be low, and therefore we cannot exclude the possibility of non-response bias. The number of respondents does however represent an adequate sample size for the estimated population of UK physicians involved in the initial assessment of patient presenting to hospital with suspected influenza, and so our overall conclusions are likely to be valid and reproducible. Survey responses obviously represent self-reported practice which may not accurately represent actual practice and so the findings of the study should ideally be corroborated by examining laboratory and pharmacy data. Of note the use of NAI in hospitalised adults with confirmed influenza was 65% and 62% in the control groups of the aforementioned randomised controlled trials of routine molecular POCT for respiratory viruses, which is consistent with the results in this survey [28, 29].

## Conclusions

This study demonstrates sub-optimal concordance with current PHE guidelines for the treatment of suspected influenza among UK physicians, with considerable variability across specialities. Lack of confidence in the effectiveness of NAIs seems to be a contributing factor in this. Acknowledging and highlighting this discrepancy between public health policy and clinical practice is an important first step in improving the care of patient with influenza. As there are unlikely to ever be definitive trials evaluating the efficacy of NAIs in hospitalised adults, and a wealth of observational studies now supports their use in this patient group, efforts should now focus on improving physician knowledge and adherence to current management guidelines.

# Acknowledgments

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# Conflict of interest statement

Conflict of interest disclosure: TWC reports grants from NIHR and DRIVE EU, personal fees from Biomerieux and BioFire diagnostics, Roche, Cidara Therapeutics, Synairgen, and Randox Laboratories, non-financial support from Biomerieux and BioFire diagnostics. The other authors declare no competing interests.

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# Ethics approval and consent to participate

As this was a web-based questionnaire-based survey of practise among physicians, specific written informed consent from participants was not deemed necessary - consent being implied by the decision to take part in the survey (a process made clear on the Surveymonkey webpage). Ethical approval was granted by University of Southampton Faculty of Medicine Ethics Committee on the 25th of September 2015: ID: 17321.

# Availability of data and materials

The datasets used and/or analysed during the current study are available from the senior author on reasonable request.

# Authors’ Contributions

TWC, PJL and NJB contributed to the conception and design of the study. TWC, NJB and AKM participated in the acquisition and analysis of the data. TWC developed the first draft of the manuscript. All authors participated in the review and revision of the manuscript and the approval of the final version.

# References

1. Thompson WW, Shay DK, Weintraub E, et al. Influenza-associated hospitalizations in the United States. *JAMA* 2004;292(11):1333-40.

2. Thompson WW, Shay DK, Weintraub E, et al. Mortality associated with influenza and respiratory syncytial virus in the United States. *JAMA* 2003;289(2):179-86.

3. World Health Organization (WHO), Regional Office for Europe: WHO/Europe recommendations on influenza vaccination during the 2016/2017 Winter Season. September 2016. <http://www.euro.who.int/data/assets/pdffile/0003/321843/recommendations-influenza-vaccination-2016-2017-winter-season-en.pdf>. Accessed July 2017.

4. Tanner AR, Dorey RB, Brendish NJ, Clark TW. Influenza vaccination: protecting the most vulnerable. *Eur Respir Rev* 2021; 30: 200258

5. Dao CN, Kamimoto L, Nowell M, et al. Emerging Infections Program Network: adult hospitalizations for laboratory-positive influenza during the 2005-2006 through 2007-2008 seasons in the United States. *J Infect Dis* 2010;202(6):881-8.

6. Widmer K, Zhu Y, Williams JV, et al. Rates of hospitalizations for respiratory syncytial virus, human metapneumovirus, and influenza virus in older adults. *J Infect Dis* 2012;206(1):56-62.

7. Mauskopf J, Klesse M, Lee S, et al. The burden of influenza complications in different high-risk groups: a targeted literature review. *J Med Econ* 2013;16(2):264-77.

8. Li G, Yilmaz M, Kojicic M, et al. Outcome of critically ill patients with influenza virus infection. *J Clin Virol* 2009;46(3):275-8.

9. Jefferson T, Doshi P. Multisystem failure: the story of anti-influenza drugs. *BMJ* 2014;348:g2263.

10. Jefferson T, Jones MA, Doshi P, et al. Neuraminidase inhibitors for preventing and treating influenza in healthy adults and children (Review). *Cochrane Database Syst Rev* 2014;(4):CD008965.

11. Dobson J, Whitley RJ, Pocock S, et al. Oseltamivir treatment for influenza in adults: a meta-analysis of randomised controlled trials. *Lancet* 2015;385(9979):1729-37.

12. McGeer A, Green KA, Plevneshi A, et al. Antiviral therapy and outcomes of influenza requiring hospitalization in Ontario, Canada. *Clin Infect Dis* 2007;45(12):1568-75.

13. Hanshaoworakul W, Simmerman JM, Narueponjirakul U, et al. Severe human influenza infections in Thailand: Oseltamivir treatment and risk factors for fatal outcome. *PLoS One* 2009;4(6):e6051.

14. Lee N, Choi KW, Chan PK, et al. Outcomes of adults hospitalised with severe influenza. *Thorax* 2010;65(6):510-5.

15. Yu H, Feng Z, Uyeki TM, et al. Risk factors for severe illness with 2009 pandemic influenza A (H1N1) virus infection in China. *Clin Infect Dis* 2011;52(4):457-65.

16. Louie JK, Yang S, Acosta M, et al. Treatment with neuraminidase inhibitors for critically ill patients with influenza A (H1N1)pdm09. *Clin Infect Dis* 2012;55(9):1198-204.

17. Lee N, Leo YS, Cao B, et al. Neuraminidase inhibitors, superinfection and corticosteroids affect survival of influenza patients. *Eur Respir J* 2015;45(6):1642-52.

18. Hsu J, Santesso N, Mustafa R, Brozek J, Chen YL, Hopkins JP, et al. Antivirals for treatment of influenza: a systematic review and meta-analysis of observational studies. *Ann Intern Med* 2012;156(7):512-24.

19. Muthuri SG, Venkatesan S, Myles PR, Leonardi-Bee J, Al Khuwaitir TS, Al Mamun A, et al. Effectiveness of neuraminidase inhibitors in reducing mortality in patients admitted to hospital with influenza A H1N1pdm09 virus infection: a meta-analysis of individual participant data. *Lancet Respir Med* 2014;2(5):395-404.

20. PHE guidance on use of antiviral agents for the treatment and prophylaxis of seasonal influenza. Public Health England (2016-17). Version 7.0. October 2016. https://www.gov.uk/government/uploads/system/uploads/attachment\_data/file/580509/PHE\_guidance\_antivirals\_influenza\_2016\_2017.pdf. Accessed July 2017.

21. United States Centers for Disease Control and Prevention. Influenza Antiviral Medications: Summary for Clinicians. Centers for Disease Control and Prevention; 2014. <https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm>. Accessed July 2017.

22. World Health Organisation. Clinical management of human infection with pandemic (H1N1) 2009: revised guidance. <http://www.who.int/csr/resources/publications/swineflu/clinical_management_h1n1.pdf>. Accessed July 2017.

23. The Academy of Medical Sciences and the Wellcome Trust. Use of neuraminidase inhibitors in influenza. October 2015. <https://acmedsci.ac.uk/file-download/38069-561595082cd83.pdf>. Accessed July 2017.

24. Kumar A. Early versus late oseltamivir treatment in severely ill patients with 2009 pandemic influenza A (H1N1): speed is life. *J Antimicrob Chemother* 2011;66(5):959-63.

25. Katzen J, Kohn R, Houk JL, Ison MG. Early Oseltamivir After Hospital Admission Is Associated With Shortened Hospitalization: A 5-Year Analysis of Oseltamivir Timing and Clinical Outcomes. *Clin Infect Dis.* 2019;69(1):52-58.

26. Appiah GD, Chaves SS, Kirley PD, et al. Increased Antiviral Treatment Among Hospitalized Children and Adults With Laboratory-Confirmed Influenza, 2010-2015. *Clin Infect Dis* 2017;64(3):364-367.

27. Sugaya N. Widespread use of neuraminidase inhibitors in Japan. *J Infect Chemother* 2011;17(5):595-601.

28. Brendish NJ, Malachira AK, Armstrong L, et al. Routine molecular point-of-care testing for respiratory viruses in adults presenting to hospital with acute respiratory illness (ResPOC): a pragmatic, open-label, randomised controlled trial. *Lancet Respir Med* 2017;5(5):401-411.

29. Clark TW, Beard KR, Brendish NJ, et al. Clinical impact of a routine, molecular, point-of-care, test-and-treat strategy for influenza in adults admitted to hospital (FluPOC): a multicentre, open-label, randomised controlled trial. *Lancet Respir Med*. 2020. S2213-2600(20)30469-0.

30. Beard K, Chan C, Mills S, Poole S, Brendish NJ, Clark TW. Evaluation of the Febridx Host Response Point-of-Care Test to Differentiate Viral From Bacterial Etiology in Adults Hospitalized with Acute Respiratory Illness During Influenza Season. *Open Forum Infect Dis* 2019; 6: S300–1.

31. Clark TW, Brendish NJ, Poole S, et al. Diagnostic accuracy of the FebriDx host response point-of-care test in patients hospitalised with suspected COVID-19. *J Infect* 2020. 81(4):607-613.

**Table 1**. Baseline characteristics of respondents, n=237.

|  |  |  |
| --- | --- | --- |
| **Variable** | **n** | **%** |
| **Primary place of work** |  |  |
| Tertiary referral centre | 101 | 42.6% |
| District general | 125 | 52.7% |
| Other | 11 | 4.6% |
| **Speciality** |  |  |
| Acute Medicine | 23 | 9.7% |
| Emergency Medicine | 28 | 11.8% |
| Geriatric Medicine | 28 | 11.8% |
| Infectious Diseases | 40 | 16.9% |
| Microbiology | 50 | 21.1% |
| Respiratory Medicine | 53 | 22.4% |
| Other\*\* | 15 | 6.3% |
| **Grade** |  |  |
| Consultant | 163 | 68.8% |
| Associate Specialist | 2 | 0.8% |
| Specialist Registrar | 60 | 25.3% |
| Trust grade | 10 | 4.2% |
| Other | 2 | 0.8% |
| **Duration Qualified** |  |  |
| ≤10 years | 57 | 24.1% |
| 11 to 20 years | 97 | 40.9% |
| 21 to 30 years | 60 | 25.3% |
| 31 to 40 years | 21 | 8.9% |
| >40 years | 2 | 0.8% |
| **Document awareness\*** |  |  |
| PHE Influenza treatment guidelines | 157 | 67.4% |
| Cochrane Review (2014) | 109 | 46.8% |

PHE, Public Health England. \*Assessed in 233 respondents

\*\*Responses included: virology, public health, general medicine,

diabetes, rheumatology, stroke medicine and respiratory high

dependency.

**Table 2**. Reported factors influencing respondent’s decisions to prescribe neuraminidase inhibitors to patient with suspected influenza (respondents could select multiple factors from the list), n=220.

|  |  |  |
| --- | --- | --- |
| **Factor** | **n** | **%** |
| Duration of illness | 120 | 54.5% |
| Presence of risk factors for complicated disease\* | 195 | 88.6% |
| Presence of already complicated or severe diseases (e.g. pneumonia or exacerbation of airways disease) | 176 | 80.0% |
| Concerns over the efficacy of oseltamivir | 73 | 33.2% |
| Concerns over the side effects of oseltamivir | 41 | 18.6% |
| Concerns over generating resistance to oseltamivir | 29 | 13.2% |
| A history of influenza vaccination for the current season | 36 | 16.4% |

\*Age >65, chronic cardiovascular, respiratory, renal, liver or neurological diseases, diabetes mellitus or immune suppression.

**Table 3**. Themes and individual responses from free-text comments

|  |  |
| --- | --- |
| Themes | Example comments |
| 1. Culture of non-routine use of NAIs in | ‘We don't currently use NAIs’ |
| institution | ‘I have never prescribed NAIs’ |
|  | ‘I do not prescribe NAIs for suspected influenza’ |
|  | ‘We hardly ever use NAIs here’ |
|  |  |
| 2. Perceived lack of effectiveness of NAIs | ‘I am unconvinced of any real benefit with oseltamivir’ |
|  | ‘This guy is ill so he'd get Tamiflu even though it'll do nothing’ |
|  | ‘I still think oseltamivir is rubbish despite the meta-analysis paper last year’ |
|  | ‘I don't think oseltamivir makes enough difference to dish it out prior to the results, which I will have within 24 hrs’ |
|  | ‘NAIs are widely perceived to be ineffective’ |
|  | ‘I'm not sure flu drugs make any difference, I'd like lots more good evidence that they actually work’  ‘I don't trust the drug companies to be honest about Tamiflu’ |
|  | ‘There is substantial doubt in my mind that oseltamivir is definitely beneficial in most patients with influenza and I rarely use it on those grounds’’ |
|  |  |
| 3. Perception that pneumonia is not caused by influenza viruses | ‘I would probably assume this is just community acquired pneumonia and not use NAIs ‘  ‘Sounds like community acquired pneumonia and I would treat as such, Tamiflu adds nothing’ |
|  |  |
| 4. Concerns over infection controls policies | ‘In the Medical Admissions Unit we have problems explaining to infection control staff and bed managers that patients on Tamiflu do not have confirmed influenza and so do not need isolation’ |
|  | ‘The panic that ensues when we test and need to isolate causes far more harm than not giving the Tamiflu ‘placebo’ to patients’ |

**Figure legends**

**Figure 1**. Reported turnaround time (hours) for laboratory influenza PCR testing at the respondents institution, n=180.

**Figure 2a-d**. Concordance with PHE guidelines for the 4 clinical scenarios, overall and by speciality. Scenario 1 (n=222); uncomplicated influenza in an adult without risk factors for developing complications, presenting within 48 hours of symptom onset. Scenario 2 (n=220); uncomplicated influenza in an adult with risk factors for developing complications, presenting within 48 hours of symptom onset. Scenario 3 (n=216); already complicated influenza in an adult, presenting within 48 hours of symptom onset. Scenario 4 (n=210); critical illness due to influenza, in an adult presenting after 48 hours of symptom onset.

**Figure 3**. Combined concordance with PHE guidelines for all scenarios, overall and by speciality.

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# Supplementary Appendix: S1

**List of participating NHS Trusts**

1. West Suffolk NHS Foundation Trust

2. The Shrewsbury and Telford Hospital NHS Trust

3. Salford Royal NHS Foundation Trust

4. Colchester Hospital University NHS Foundation Trust

5. Dorset County Hospital NHS Foundation Trust

6. Hull and East Yorkshire Hospitals NHS Trust

7. Torbay and South Devon NHS Foundation Trust

8. North Bristol NHS Trust

9. North Tees and Hartlepool Hospitals NHS Foundation Trust

10. University Hospitals Bristol NHS Foundation Trust

11. Medway NHS Foundation Trust

12. East Lancashire Hospitals NHS Trust

13. University Hospital Southampton NHS Foundation Trust

# Supplementary Appendix S2















