Who takes antibiotics when they're ill? Antibiotic usage in Flusurvey

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Abstract

Background: Antibiotic resistance (ABR) is a growing public health problem caused by selection due to antibiotic use. Understanding who takes antibiotics, and why they do so, can help with the design and targeting of interventions for reducing prescription rates and hence unnecessary antibiotic use.

Methods: We used an internet-based open community cohort, Flusurvey, to assess levels of antibiotic use in the UK. Participants were asked whether they had taken antibiotics during each period in which they reported any symptoms (an "episode"). We conducted a multivariate regression analysis to determine the effect of covariates on antibiotic usage rate.

Results: We analysed, 31,784 episodes from 6,667 participants and found that participants reported consuming antibiotics in 4.5% episodes over the years 2012-2017. Of those episodes where an antibiotic was reported as being taken, 15% reported no visit to a medical service in this episode despite prescriptions being required for antibiotic use in the UK.

Multivariate regression showed that antibiotic usage was increased under the reported presence of both ILI and fever symptoms. Similarly, if you visited a medical centre the rates of antibiotic usage increased.

Conclusions: We found that antibiotics are used in 4.5% of illness episodes reported in a community cohort, and that a relatively high rate of antibiotic use was not associated with a visit to a medical centre (and hence potentially no prescription).

Introduction

Antibiotic resistance (ABR) is a growing public health problem (World Health Organisation 2018). ABR is selected by the use of antibiotics, and hence the informed reduction in antibiotic use is a public health priority. Understanding who uses antibiotics, and if there are any population covariates that make someone more likely to take antibiotics when unwell, can help to target interventions.

Over 75% of healthcare antibiotics are prescribed in primary care (Ashiru-Oredope et al. 2013). However, the composition of the population taking antibiotics is unclear. Previous work exploring variance in antibiotic prescribing has focused mainly on snapshots of the entire primary care community (Shallcross et al. 2017; Wang et al. 2009; Dolk et al. 2018). Here, we used an existing internet-based open community cohort, Flusurvey, to determine if any population covariates could be linked to the likelihood of taking antibiotics specifically when reporting cold or flu-like symptoms. This dataset, of episodes of reported illness, provides a unique opportunity to profile the UK population's antibiotic prescription patterns. Importantly, we were able to explore a snapshot of antibiotic usage in those reporting having influenza-like-illness (ILI) symptoms, to compare those taking antibiotics to those not. This is highly relevant as the majority of antibiotic prescriptions in English primary care were for infections of the respiratory tract (Dolk et al. 2018).

Importantly, antibiotics do not kill viruses such as influenza. This does not mean that antibiotic usage when infected with 'flu has no consequence. Instead, the impact of taking antibiotics when there is no bacterial infection is to potentially select for resistance in the host microbiome (bystander effect). This could result in a reservoir of resistant bacteria in a host which may cause infection at a later date.

The key drivers of antibiotic use in previous work have been age, with highest rates in the elderly (Dolk et al. 2018), and being female (Dolk et al. 2018; Shallcross et al. 2017). English guidelines recommend that antibiotic treatment should be avoided for self-limiting respiratory tract infections unless the patient is at high risk of serious complications because of a pre-existing comorbidity (NICE 2008). Hence, previous analysis of electronic health care records suggested that specific comorbidities could increase the rate of antibiotic prescribing by more than one-third (Shallcross et al. 2017) and that patient populations with higher reported limiting long-term illness rates have higher prescribing levels (Wang et al. 2009). Geographical setting has also been linked to differences: large differences in the level of antibiotic prescribing exist across Europe (Goossens et al. 2005) and across the UK (Public Health England 2017; Dolk et al. 2018). Previous analysis has shown that high antibiotic prescribing has been associated with practices in the north of England (Wang et al. 2009). Higher levels of education in parents have also been linked to lower levels of antibiotic prescribing in children in a single county Sweden (Mangrio et al. 2009). However, data from a larger area suggests that socioeconomic differences cannot explain differences in antibiotic prescribing rates (Hedin et al. 2006).

Information on many of these factors are included in the baseline questionnaire of Flusurvey and hence can be analysed here. This work could then inform new interventions designed specifically at certain sub-groups before, or when, they report being ill. For example, educational interventions or targetting of General Practitioners to understand which of their patient population are most likely to ask for antibiotics.

Our aim was to determine the characteristics that determine whether a person reporting symptoms of illness (from a runny nose to a fever), will take an antibiotic. We used a Bayesian approach.

Methods

Data

Included in this study were episodes of illness from any resident of the UK recruited into Flusurvey between 2012 and 2017. Flusurvey was approved by the London School of Hygiene and Tropical Medicine Ethics Committe (Application number 5530). Details of the survey structure and recruitment can be found in a previous publication (Adler et al. 2014).

Briefly, participants recruited into Flusurvey were asked a set of background questions at the start of the influenza season. There was then a weekly email asking participants to complete a symptoms survey. If participants reported any symptoms in their weekly symptoms survey, they were asked "Did you take medication for these symptoms (tick all that apply)?". One possible medication was "Antibiotics". This record, of taking antibiotics or not, by episode is analysed here.

An episode is defined as:... ?? how much detail?

Episodes were excluded if there was no information on whether they had visited a medical service in this episode ("GP", "hospital", "A&E", "Other" or "waiting for an appointment") which removed 571 episodes ($< 2\%$ of total possible episodes). Further episodes were removed as there was no information on their age (237), whether they had received an influenza vaccine this year (45), whether they had a fever (94) or if they reported health score greater than 100 (15).

Covariate identification

We considered all risk factors from Flusurvey that were potentially associated with differences in antibiotic usage rates. These were then plotted in a univariate analysis against antibiotic usage rates (see Supplementary). Only those where there were sufficient data on both the covariate and antibiotic usage rates were included and where a substantial difference was seen (e.g. region was excluded).

Analysis

We performed a Bayesian multivariate regression analysis. For each of the n episodes in the Flusurvey data, we had a set of observations $((y_i, w_i), i = 1, ..., n)$, where y_i was a binary response such that $y_i = 1$ if a participant in Flusurvey reported taking an antibiotic during this episode, and $y_i = 0$ if not. The $w_i = w_{i1}, ...w_{in}$ are the covariate values for each participant for this episode, mentioned above. Our logistic regression model then estimated the binomial probability of receiving an antibiotic or not (y_i).

We assumed Normal priors for all covariate coefficients (β_j) parameters with mean 0 and variance 10.

$$y_i \sim Binomial(1, \theta) \tag{1}$$

$$\theta = a + \sum_{0<j<n} \beta_j w_{ij} \tag{2}$$

$$\beta_j \sim Normal(0, 10) \tag{3}$$

We analysed the following logistic models for θ, where i is episode number:

$$M1 : logit(\theta) = a + bw_{i,gender} + cw_{i,age} + dw_{i,ili.fever} + eaw_{i,vaccine.this.year} \quad (4)$$
$$+ fw_{i,freq.contact.children} + gw_{i,underlying.risk} + hw_{i,visit.medical.service} + iaw_{i,freq.contact.elderly} \quad (5)$$
$$M2 : logit(\theta) = a[visit.medical.service] + bw_{i,gender} + cw_{i,age} + dw_{i,ili.fever} + eaw_{i,vaccine.this.year} \quad (6)$$
$$+ fw_{i,freq.contact.children} + gw_{i,underlying.risk} + hw_{i,visit.medical.service} + iaw_{i,freq.contact.elderly} \quad (7)$$
$$a[visit.medical.service] \sim Normal(0, \sigma_v) \quad (8)$$
$$\sigma_v \sim Cauchy(0, 40) \quad (9)$$

For all models: $c(a, b, c, d, ea, f, g, h, ia) \sim Normal(0, 10)$. We chose to use a "logit" link function for θ to constrain the output to lie between zero and one (as required for a probability). The "logit" link function is defined as the log-odds function.

M1 and M2 included all covariates with sufficient data (see Supplementary). To account for the need for a prescription (through a visit to a medical service) for antibiotic use, the seoncd model's intercept was segregated by the binary covariate of whether a participant had made a medical visit in this episode.

Parameter estimation

We implemented the models in R 3.3.3 (Team 2008) using the "rethinking" package (McElreath 2016) and Stan (Team 2018). The models were fit to the data using the "map2stan" function which uses Monte Carlo Markov Chain (MCMC) sampling to generate posterior distributions for all covariate coefficients. All models were linear. For all models, 4 Markov chains were run (in parallel) with 6,000 iterations, of which the first 1,000 were rejected as burn-in in order to ensure the convergence of the parameters. Convergence was assessed using the Brooks-Gelman-Rubin statistic (Rhat) and the effective sample size of the chains (n_eff). Specifically, we required the statistics Rhat<1.1 and n_eff >8,000 for each parameter in the model. We also monitored convergence by plotting trace and autocorrelation plots of the samples.

Model comparison

We compared the set of plausible models using the Watanabe-Akaike information criterion (WAIC) (Watanabe 2010). The WAIC is an estimate of out-of-sample deviance. Small values of WAIC indicate a good fit. We also calculated pWAIC: the estimated effective number of parameters to give an idea of how flexible each model is in fitting the sample, and the standard error of the WAIC estimate. To compare models, we calculate the Akaike weight, which is an estimate of the probability that the model will make the best predictions on new data, conditional on the set of models considered (Wagenmakers and Farrell 2004). The model with the greatest weight is likely to do the best at prediction.

Further model generation

After fitting these models to the data, the smallest coeffecients (i.e. those least influecing antibiotic prescribing) were removed systematically from M3 (the simpler of the above two models). This process of backward elimination gave a further three models: Model 3 is Model 1 with the smallest fitted coefficient set to zero, Model 4 is Model 1 with the smallest two coefficients set to zero etc. These Models were refit to the data and all models compared.

Informed priors

Using prior information, we also tested whether the model fit was improved by setting the priors for gender, age, frequent contact with children, having a risk factor and visiting a medical service to have a mean greater than 0 (i.e. $N(1, 10)$).

Table 1: Antibiotic prescription usage by participants

Number of episodes where antibiotic consumption was reported	Number of participants	Total number of episodes with antibiotic consumption
0	5594	0
1	833	833
2	165	330
3	43	129
4	22	88
5	6	30
6	1	6
7	1	7
9	2	18

Results

Data Description

A total of 31,784 episodes were analysed from 6,667 participants. Antibiotics were taken in 1,441 (4.5%) of episodes (see Supplementary). The maximum number of episodes per participant was 34, whilst the mean and standard deviation were 4 and 5 respectively.

1,073 participants reported taking an antibiotic during any of their episodes (Table 1). Thus 16% of participants accounted for 100% of the episodes where antibiotics were reported as being taken. 78% of partipants who reported taking an antibiotic only did so for one episode, whilst 7% took antibiotics in 3 or more episodes, accounting for 19% of all episodes with reported antibiotic use.

Antibiotic usage rates

Mean antibiotic usage rates were relatively stable across the seasons at between 3.74 and 5.4% of episodes having reported antibiotic use (Figure 1). Exploring antibiotic usage rates by each covariate revealed substantial differences (see Table 2 & Supplementary).

Children (<18yo) and the elderly (>65) had higher rates of antibiotic usage than others (Figure 1) at mean levels of 5.3% and 7.2% of episodes, across all included Flusurvey seasons.

In the UK, a prescription is required for almost all antibiotics. In this analysis, a medical service was visited in 9% of episodes. Of those episodes where a visit to a medical centre was reported, an antibiotic was reported as being taken in 42% (see Table 2 & Supplementary). Of those episodes where an antibiotic was reported as being taken, 85% also reported visiting a medical service, i.e. 15% of episodes where an antibiotic was taken may not have had a prescription for this antibiotic usage.

Multivariate analysis

The final covariates included in the multivariate analysis were: age, influenza like illness (ILI) with fever, influenza vaccine received this year, whether a participant visited a medical service during this episode, gender, frequent contact with children or elderly, and underlying health issue (e.g. diabetes) (see Table 2). All covariates were binary except for age which was regularized by subtracting the mean and dividing by the standard deviation.

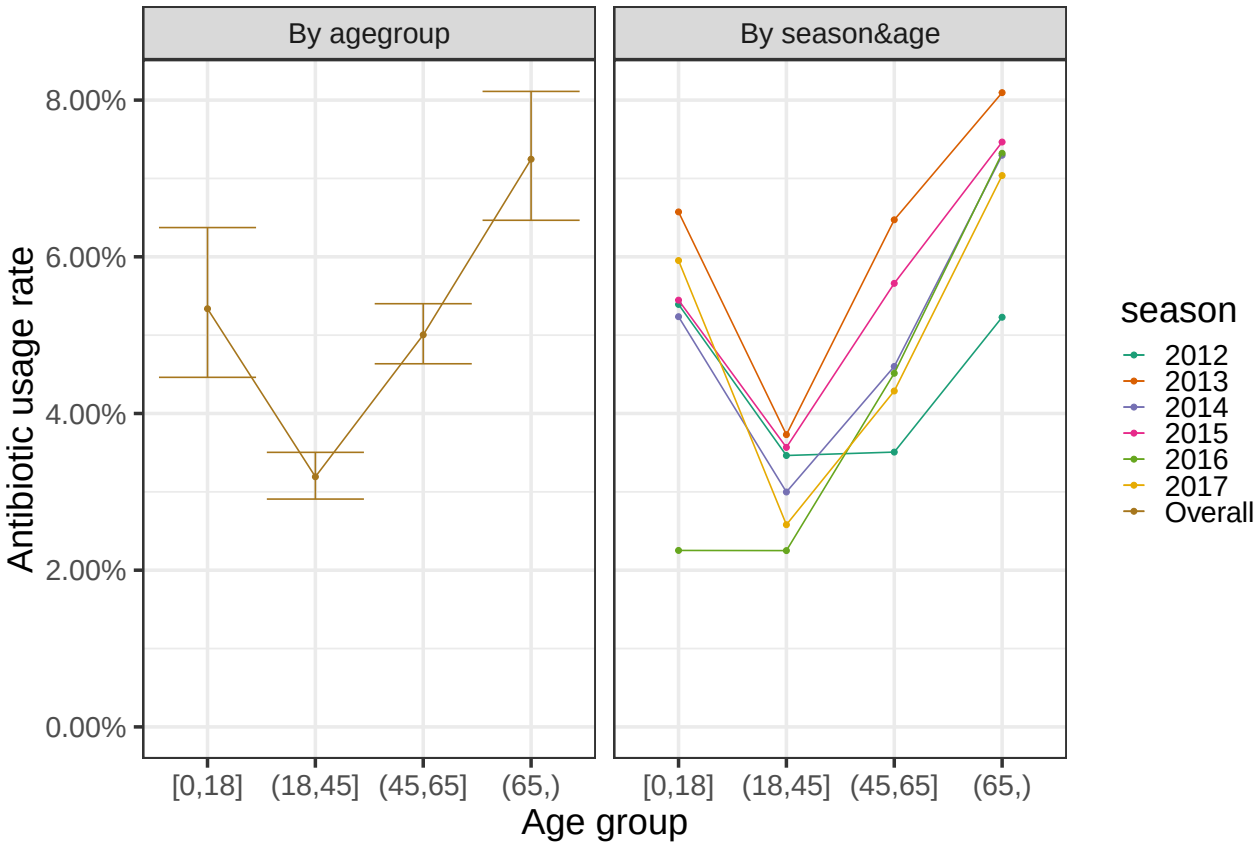


Figure 1: Antibiotic usage rate by age and season. Note that here antibiotic usage rate is per episode of illness.

Table 2: Characteristics of the participants. Blanks in the category column indicate no data provided for the episode.

Type	Category	Number of episodes	Antibiotic usage reported	Mean antibiotic usage rate (%)
Age group	[0,18]	2136	114	5.3
	(18,45]	13375	427	3.2
	(45,65]	12450	623	5.0
	(65,)	3823	277	7.2
Region	channel islands	24	1	4.2
	east midlands	1756	91	5.2
	east of england	3466	157	4.5
	london	7350	292	4.0
	north east england	827	37	4.5
	north west england	2372	129	5.4
	northern ireland	315	16	5.1
	scotland	1974	88	4.5
	south east england	5413	267	4.9
	south west england	2462	114	4.6
	wales	1108	49	4.4
	west midlands	2021	100	4.9
	yorkshire and the humber	2357	80	3.4
	isle of man	11	2	18.2
Vaccine this year?	yes	12366	733	5.9
	no	19418	708	3.6
	All	3395	416	12.3
	All	17131	396	2.3
	All	1057	10	0.9
	All	963	15	1.6
	All	4381	423	9.7
	All	4444	129	2.9
	All	291	46	15.8
	All	122	6	4.9
Education status	no.education	701	55	7.8
	education.gcse	2095	151	7.2
	education.alevels	3783	229	6.1
	education.bsc	7928	340	4.3
	education.msc	14144	523	3.7
	education.stillin	1821	79	4.3
		1312	64	4.9
Main activity	paid employment full time	14516	514	3.5
	paid employment part time	3956	185	4.7
	self employed	2051	101	4.9
	school	3224	133	4.1
	home maker	1147	58	5.1
	unemployed	344	13	3.8
	long term leave	435	40	9.2
	retired	5509	368	6.7
	other	602	29	4.8
No visit to medical service	false	2917	1227	42.1
	true	28867	214	0.7
ILI symptoms	false	23422	662	2.8
	true	7573	731	9.7
		789	48	6.1
ILI plus fever symptoms	false	29247	1055	3.6
	true	2537	386	15.2
Freq. contact with children	false	26237	1151	4.4
	true	5547	290	5.2
Freq. contact with elderly	false	29500	1309	4.4

Model analysis

Models compared: M1 & M2

The first two models compared were M1 & M2:

$$M1 : \theta = a + bw_{i,gender} + cw_{i,age} + dw_{i,ili.fever} + eaw_{i,vaccine.this.year} \quad (10)$$
$$+ fw_{i,freq.contact.children} + gw_{i,underlying.risk} + hw_{i,visit.medical.service} + iaw_{i,freq.contact.elderly} \quad (11)$$
$$M2 : \theta = a[visit.medical.service] + bw_{i,gender} + cw_{i,age} + dw_{i,ili.fever} + eaw_{i,vaccine.this.year} \quad (12)$$
$$+ fw_{i,freq.contact.children} + gw_{i,underlying.risk} + hw_{i,visit.medical.service} + iaw_{i,freq.contact.elderly} \quad (13)$$
$$a[visit.medical.service] \sim Normal(0, \sigma_v) \quad (14)$$
$$\sigma_v \sim Cauchy(0, 40) \quad (15)$$

For all models: $c(a, b, c, d, ea, f, g, h, ia) \sim Normal(0, 10)$

Model fit

When comparing the goodness of fit of the first two models, we find that Model 1&2 had very similar WAIC values (Table 3). Despite Model 2 having more parameters, the estimated effective number of parameters was the same for Models 1&2 (pWAIC value) as some parameters posteriors were close to zero (e.g. the coefficient of gender). The Akaike Weight values suggest that Models 1&2 may be equally as good at prediction as each other.

When including slightly more informative priors (mean greater than 0) we found the model fit highly comparable: Model1_priors and Model2_priors had the very similar Akaike Weight values to Models1&2 suggesting that these priors have little impact (Table 3).

```
## Warning in compare(Model1, Model2, Model1_priors, Model2_priors): Different numbers of observations f
## Information criteria only valid for comparing models fit to exactly same observations.
## Number of observations for each model:
## Model1 31784
## Model2 31784
## Model1_priors 36654
## Model2_priors 36654
```

```
## Warning in waic_ptw1 - waic_ptw2: longer object length is not a multiple of
## shorter object length

## Warning in waic_ptw1 - waic_ptw2: longer object length is not a multiple of
## shorter object length

## Warning in waic_ptw1 - waic_ptw2: longer object length is not a multiple of
## shorter object length

## Warning in waic_ptw1 - waic_ptw2: longer object length is not a multiple of
## shorter object length
```

The posterior distributions for the parameter estimates for the coefficients are shown in Figures 2&3. Most are highly similar between the two models except for the intercept (which varies in model formulation, see Supplementary for plot).

```
## Using  as id variables
## Using  as id variables
```

Table 3: Model comparison output.

	WAIC	pWAIC	Difference in WAIC	Akaike weight	SE of WAIC estimate	Difference in SE
Model2	6603	9	0	0.51	148.46	
Model1	6603	9	0	0.49	148.50	0.065
Model2_priors	10650	9	4047	0.00	207.05	244.372
Model1_priors	10650	9	4047	0.00	207.02	244.350

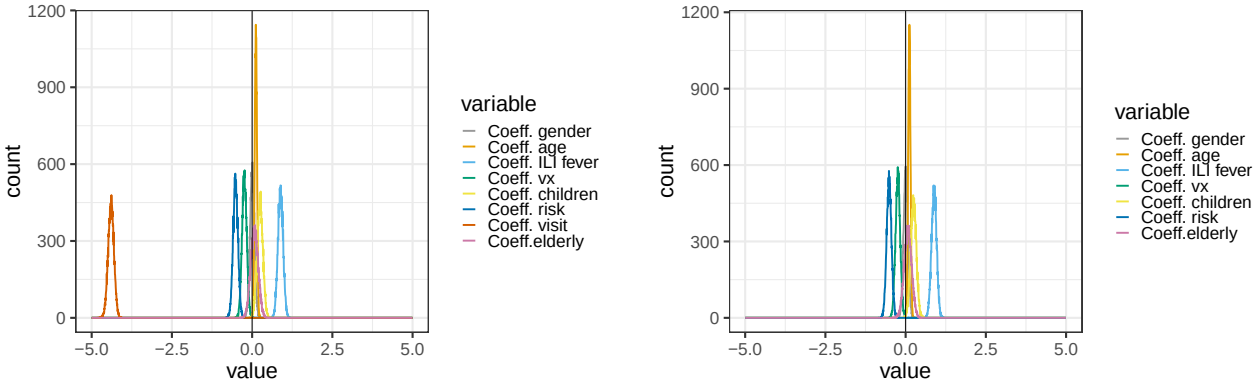


Figure 2: Posterior samples for each model (not including the intercept parameters, see Supplementary)

```
## Using  as id variables
## Using  as id variables
```

```
## Warning: Removed 24 rows containing missing values (geom_path).
```

```
## Warning: Removed 21 rows containing missing values (geom_path).
```

The biggest parameter coefficient is for ILI with fever (ignoring visit to medical service as this varies in formulation between the two models) - suggesting that those with the most serious illness are the most likely to take an antibiotic. The next highest coefficients are those associated with an underlying risk factor and whether the participant had the influenza vaccine.

Testing for associations

Using the above coefficient values we removed those least associated with antibiotic usage rates one by one. This gave three new models where, respectively, the coefficients c, ia and then b were removed.

$$M3 : \theta = a + bw_{i,gender} + dw_{i,ili.fever} + eaw_{i,vaccine.this.year} \tag{16}$$
$$+ fw_{i,freq.contact.children} + gw_{i,underlying.risk} + hw_{i,visit.medical.service} + iaw_{i,freq.contact.elderly} \tag{17}$$
$$M4 : \theta = a + bw_{i,gender} + dw_{i,ili.fever} + eaw_{i,vaccine.this.year} \tag{18}$$
$$+ fw_{i,freq.contact.children} + gw_{i,underlying.risk} + hw_{i,visit.medical.service} \tag{19}$$
$$M5 : \theta = a + dw_{i,ili.fever} + eaw_{i,vaccine.this.year} \tag{20}$$
$$+ fw_{i,freq.contact.children} + gw_{i,underlying.risk} + hw_{i,visit.medical.service} \tag{21}$$
$$\tag{22}$$

Comparing their model fit (Table 4) to the original Model 1 suggests that Model 1 is overwhelmingly still the best at model prediction, with all of the Akaike weight.

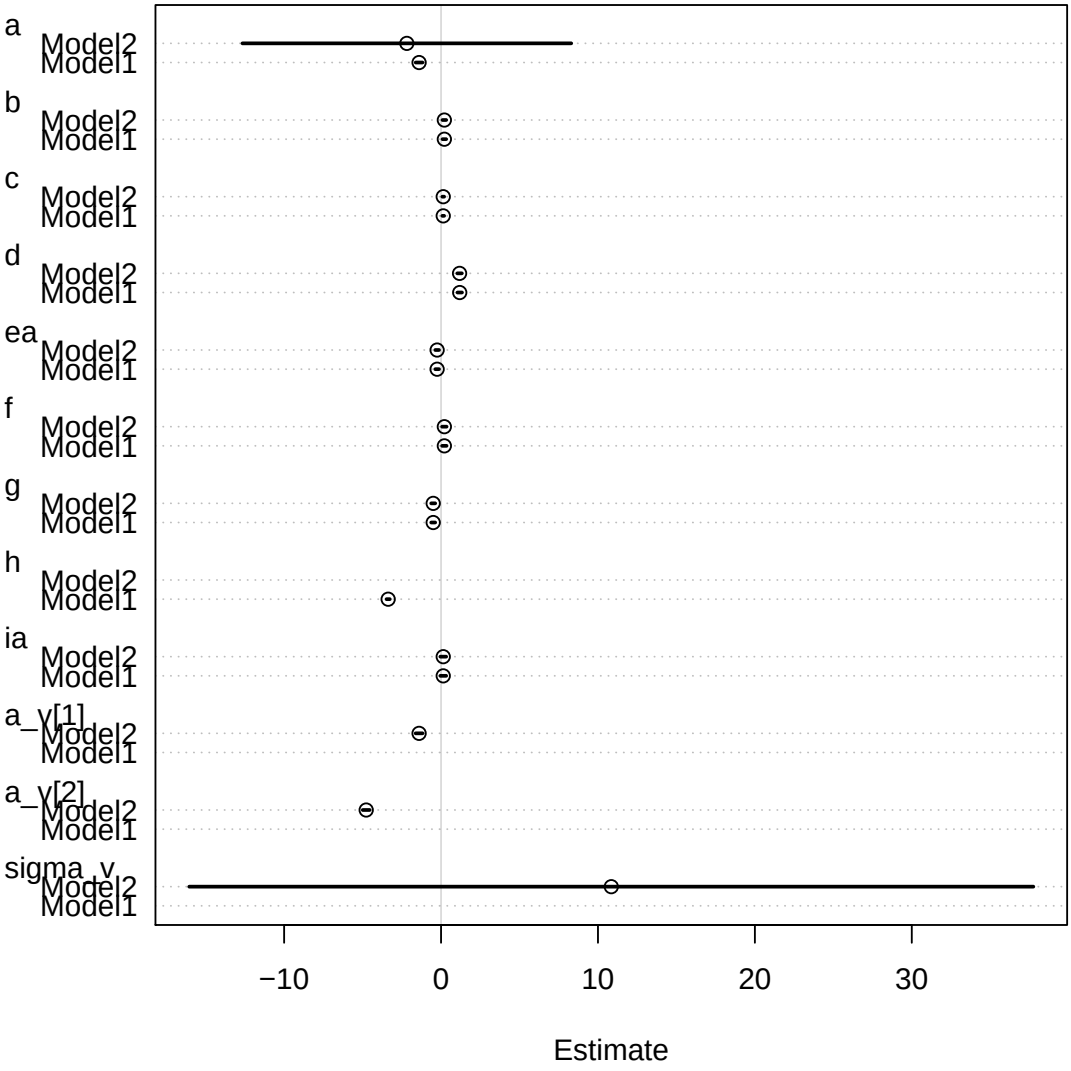


Figure 3: Posterior densities. Points are maximum a posteriori (MAP) estimates (the mode of the posterior distribution) and each black line segment is an 89% interval.

```
## Warning in compare(Model1, Model3, Model4, Model5): Different numbers of observations found for at le
## Information criteria only valid for comparing models fit to exactly same observations.
## Number of observations for each model:
## Model1 31784
## Model3 36654
## Model4 36654
## Model5 36654
```

```
## Warning in waic_ptw1 - waic_ptw2: longer object length is not a multiple of
## shorter object length
```

```
## Warning in waic_ptw1 - waic_ptw2: longer object length is not a multiple of
## shorter object length
```

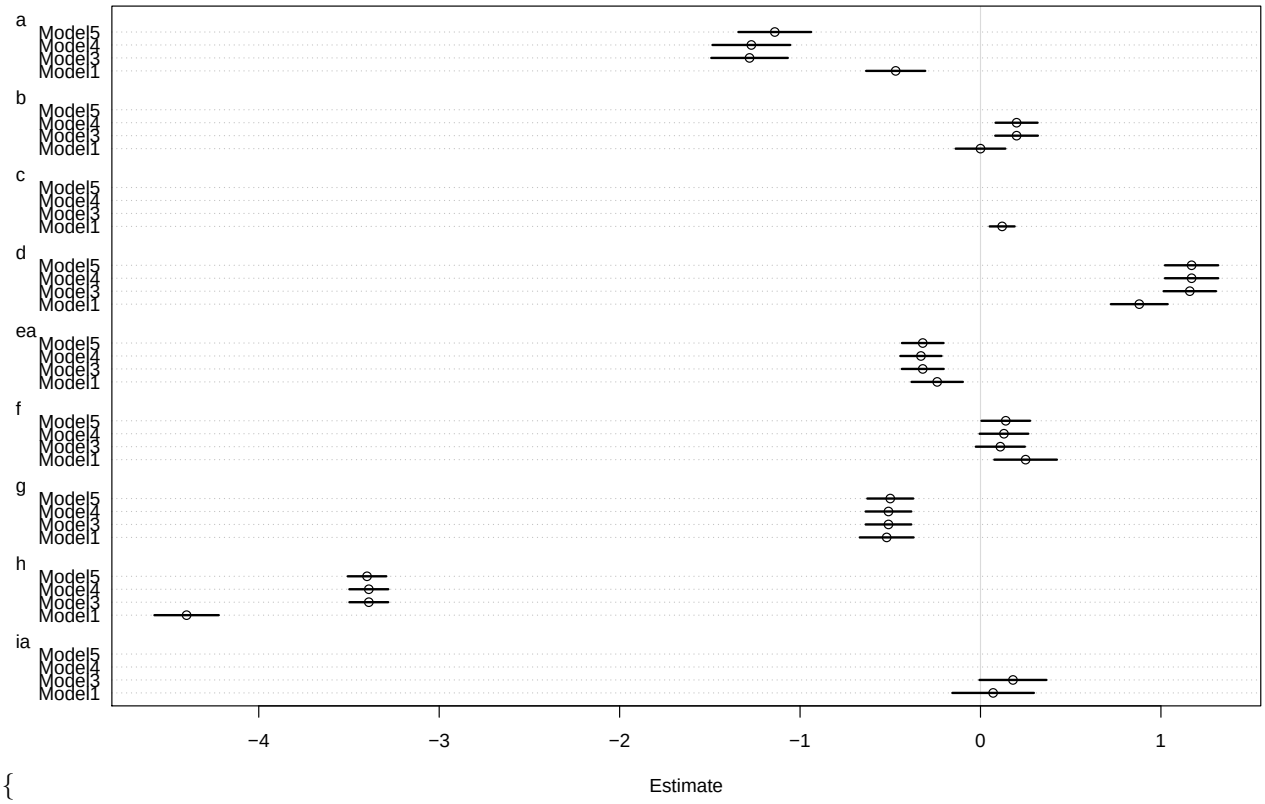
```
## Warning in waic_ptw1 - waic_ptw2: longer object length is not a multiple of
## shorter object length
```

Table 4: Model comparison output.

	WAIC	pWAIC	Difference in WAIC	Akaike weight	SE of WAIC estimate	Difference in SE
Model1	6603	9	0	1.00	148.50	
Model3	10671	8	4068	0.00	207.62	244.860
Model4	10672	7	4069	0.00	207.59	244.845
Model5	10682	6	4079	0.00	207.60	244.819

Looking at the coefficient estimates (Figure) shows the impact of removing the terms in Models 3-5.

\begin{figure}



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\caption{Posterior densitites. Points are maximum a posteriori (MAP) estimates (the mode of the posterior disstribution) and each black line segment is an 89% interval.} \end{figure}

Change in Odds

We can calculate the proportional change in odds (adjusted odds ratio) and relative effect of each coefficient from these model fits.

Table 5: Coefficient effect. The estimate is from the posterior sample. aOR stands for adjusted Odds Ratio. 'Absolute' is the mean absolute effect of the coefficient taking into account the mean intercept estimate.

Variable	Estimate	aOR	Absolute
Intercept	-0.47 [-0.57,-0.37]	0.63 [0.57,0.69]	0.39
Coeff. gender	0 [-0.08,0.09]	1 [0.92,1.1]	0.63
Coeff. age	0.12 [0.07,0.16]	1.12 [1.07,1.17]	0.70
Coeff. ILI fever	0.88 [0.79,0.98]	2.42 [2.2,2.67]	1.51
Coeff. vx	-0.24 [-0.33,-0.15]	0.79 [0.72,0.86]	0.49
Coeff. children	0.25 [0.14,0.35]	1.28 [1.15,1.42]	0.80
Coeff. risk	-0.52 [-0.61,-0.42]	0.6 [0.54,0.65]	0.37
Coeff. visit	-4.4 [-4.51,-4.29]	0.01 [0.01,0.01]	0.01
Coeff.elderly	0.07 [-0.07,0.21]	1.07 [0.93,1.24]	0.67

Discussion

This analysis aimed to explore what participant characteristics of the internet-based open community cohort, Flusurvey, could be linked to antibiotic prescribing. Within each reported illness episode, we found that approximately 5% of participants reported taking an antibiotic.

The variables found to significantly increase antibiotic usage are presence of both ILI and fever symptoms, being female and having an underlying health issue. Similarly, if you had the influenza vaccine this year or visited a medical centre the rates of antibiotic usage increased.

In common with previous studies, we found higher levels of antibiotic use in women (Shallcross et al. 2017; Brauer et al. 2016; Mor et al. 2015; Dolk et al. 2018). This could be due to the either higher rates of urinary tract infection in this group or higher levels of consultation with their general practitioner (Hippisley-Cox J 2009). Unlike other studies, although we saw a trend for increasing use by age, this was not significant once adjusted for other covariates. This is likely to be linked to the fact that there is little data on children due to the survey design: adult participants are required to enter data on any children in their household.

Higher severity of illness (i.e. ILI with fever) as well as higher chance of complications (underlying health issue) were both associated with higher rates of prescribing. English guidelines recommend that antibiotic treatment should be avoided for self-limiting respiratory tract infections unless the patient is at high risk of serious complications because of a pre-existing comorbidity (NICE 2008). Previous analysis of electronic health care records suggested that specific comorbidities could increase the rate of antibiotic prescribing by more than one-third (Shallcross et al. 2017) and that patient populations with higher reported limiting long-term illness rates have higher prescribing levels (Wang et al. 2009).

Higher levels of prescribing in subsets of the population may be explained by the previously observed effect that prescribing for sore throat and acute otitis media increase reattendance (Little et al. 1997; Williamson et al. 2006). This reattendance link could also contribute to those reporting having received the influenza vaccine reporting higher levels of antibiotic use.

In the UK, a prescription is required for almost all antibiotics. A survey of the British population in 2003 suggested that less than 6% of the population have ever used, or given, an antibiotic without a prescription or advice from a health care professional (McNulty et al. 2007). In this analysis, for those reporting a bout of illnes 9% visited a medical service. Of those episodes where an antibiotic was reported as being taken, 85% also reported visiting a medical service, i.e. 15% of episodes where an antibiotic was taken may not have had a prescription for this antibiotic usage.

We did not see substantial differences by region although large differences in the level of antibiotic prescribing exist across Europe (Goossens et al. 2005) and across the UK (Public Health England 2017,Dolk2018). Previous analysis has shown that high antibiotic prescribing has been associated with practices in the north of England (Wang et al. 2009). It is likely that we did not have large enough sample sizes to detect the difference.

The strengths of this work relate to the data and the analysis. Flusurvey provides a unique snapshot into the behaviour of individuals when they are ill: i.e. this is representative of all individuals in a community and not just those that report to a medical service. Hence they would not be captured by standard surveys of primary care antibiotic use.

That frequent contact with children or the elderly, and age, were correlated with antibiotic prescribing suggests that transmission between age groups is an important dynamic for prescribing. It could also be a signal of the increased mixing within, rather than between, age groups. Those with more frequent contact with elderly are those who are elderly themselves.

As this relies on individuals reporting their symptoms and behaviours, one of the limitations of this analysis is that the data may not be completely accurate and that gaps in the reporting may exist. This self-reporting means that participants may not accruately record medical care visits nor whether an antibiotic was actually consumed. It is also unclear how to exclude from the survey antibiotics that are being

taken for treatment of non-ILI symptoms. Within this data limitation, we only consider Flusurvey "seasons" which are likely to be the peak antibiotic prescribing time [ref].

Future work could adapt the questions asked in the baseline survey of Flusurvey to explore race (Wang et al. 2009; Mangrio et al. 2009), level of deprivation (Unsworth and Walley 2001) and income (Kozyrskyj et al. 2004) - all previously shown to affect antibiotic prescribing rates. This analysis suggests that certain characteristics and contact populations of members of the community, who do not necessarily attend a medical centre, are linked to antibiotic prescribing. Future interventions to reduce antibiotic usage could consider targetting these, whilst bearing in mind the complications - some sub-populations such as those with underlying health risks are likely to require more antibiotics.

Antibiotics are an inappropriate treatment for influenza-associated illness. Hence it is likely that much of the ILI with fever prescribing is inappropriate. As it is the biggest driver of antibiotic prescribing in this analysis, future interventions could increase awareness and new rapid diagnostics to distinguish viral vs. bacterial infections at point of contact with medical care (e.g. GP surgeries) may have the biggest impact on prescribing, and potentially hence, resistance. (REF supplement PHE people)

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