

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

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## Abstract

**Background:** Antibiotic resistance 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 unnecessary antibiotic use and hence overall antibiotic exposure.

**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, 10% reported no visit to, or contact with, a medical service in this episode despite prescriptions being required for antibiotic use in the UK.

Multivariate regression showed that antibiotic usage was increased if a participant reported visiting or contacting a medical centre. The presence of influenza like illness (ILI)&fever symptoms or an underlying medical risk factor also substantially increased antibiotic usage. When taking into account other covariates, we found no correlation between gender and antibiotic usage.

**Conclusions:** We found that antibiotics are used in 4.5% of illness episodes reported in a community cohort, and that ILI&fever symptoms were highly correlated with antibiotic use suggesting a potential large burden of inappropriate use.

# 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 primary care community (Shallcross et al. 2017; Wang et al. 2009; Dolk et al. 2018) (CHECK-all UK?). 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 usage 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 co-morbidity (NICE 2008). Hence, previous analysis of electronic health care records suggested that specific co-morbidities 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 targeting 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 Committee (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 were included and where a substantial difference was seen.

## Analysis

We performed a Bayesian multivariate regression analysis. For each of the  $n$  episodes in the Flusurvey data, we had a set of observations  $((y_i, w_i), i = 1, \dots, n)$ , 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  $w_i = w_{i1}, \dots, w_{in}$  are the co-variate 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 co-variate coefficients ( $\beta_j$ ) parameters with mean 0 and variance 10.

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

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

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

We analysed the following logistic models for  $\theta$ , where  $i$  is episode number:

$$\begin{aligned}
M1 : \text{logit}(\theta) &= a + bw_{i,\text{gender}} + cw_{i,\text{age}} + dw_{i,\text{ili.fever}} + eaw_{i,\text{vaccine.this.year}} \\
&+ fw_{i,\text{freq.contact.children}} + gw_{i,\text{underlying.risk}} + hw_{i,\text{visit.or.contact.medical.service}} + iaw_{i,\text{freq.contact.elderly}}
\end{aligned}
\tag{4}$$

$$M2 : \text{logit}(\theta) = a[\text{visit.or.contact.medical.service}] + bw_{i,\text{gender}} + cw_{i,\text{age}} + dw_{i,\text{ili.fever}} + eaw_{i,\text{vaccine.this.year}}
\tag{6}$$

$$\begin{aligned}
&+ fw_{i,\text{freq.contact.children}} + gw_{i,\text{underlying.risk}} + iaw_{i,\text{freq.contact.elderly}} \\
a[\text{visit.medical.service}] &\sim \text{Normal}(0, \sigma_v)
\end{aligned}
\tag{7}$$

$$\sigma_v \sim \text{Cauchy}(0, 40)
\tag{9}$$

For all models:  $c(a, b, c, d, ea, f, g, h, ia) \sim \text{Normal}(0, 10)$ . We chose to use a “logit” link function for  $\theta$  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 or contact with a medical service) for antibiotic use, the second model’s intercept was segregated by the binary co-variate of whether a participant had made contact with or visited 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 co-variate 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 coefficients (i.e. those least influencing antibiotic prescribing) were removed systematically from M1 (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 refitted 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.  $N(1, 10)$ ).

# 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 16.1% of participants accounted for 100% of the episodes where antibiotics were reported as being taken. 77.6% of participants who reported taking an antibiotic only did so for one episode, whilst 7% took antibiotics in 3 or more episodes, accounting for 19.3% of all episodes with reported antibiotic use.

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

## Antibiotic usage rates

Mean antibiotic usage rates were relatively stable across the seasons at between 3.7 and 5.4% of episodes having reported antibiotic use (Figure 1). Exploring antibiotic usage rates by each co-variate 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, or contacted, in 12.4% of episodes. Of those episodes where a visit to or contact with a medical centre was reported, an antibiotic was reported as being taken in 32.9% (see Table 2 & Supplementary). Of those episodes where an antibiotic was reported as being taken, 89.9% also reported visiting or contacting a medical service, i.e. 10.1% 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 and Supplementary). All covariates were binary except for age which was regularized by subtracting the mean and dividing by the standard deviation.

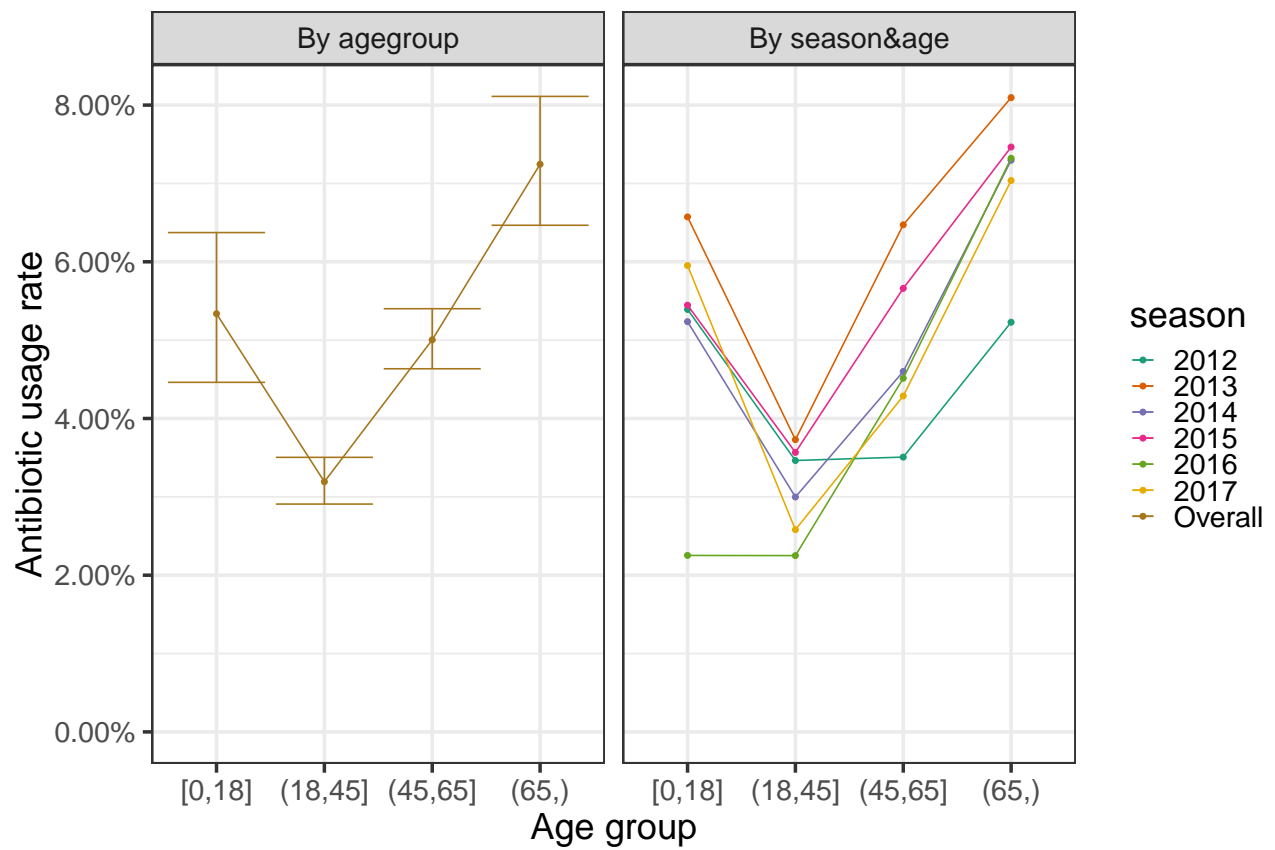


Figure 1: Antibiotic usage rate by age and season. Note that here antibiotic usage rate is per episode of illness.



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
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
Main activity		1312	64	4.9
	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
	true	2284	132	5.8

## Model analysis

### Models compared: M1 & M2

The first two models compared were M1 & M2:

$$M1 : \theta = a + bw_{i,gender} + cw_{i,age} + dw_{i,ili.fever} + eaw_{i,vaccine.this.year} \quad (10)$$

$$+ fw_{i,freq.contact.children} + gw_{i,underlying.risk} + hw_{i,visit.or.contact.medical.service} + iaw_{i,freq.contact.elderly} \quad (11)$$

$$M2 : \theta = a[visit.or.contact.medical.service] + bw_{i,gender} + cw_{i,age} + dw_{i,ili.fever} + eaw_{i,vaccine.this.year} \quad (12)$$

$$+ fw_{i,freq.contact.children} + gw_{i,underlying.risk} + hw_{i,visit.or.contact.medical.service} + iaw_{i,freq.contact.elderly} \quad (13)$$

$$a[visit.medical.service] \sim Normal(0, \sigma_v) \quad (14)$$

$$\sigma_v \sim Cauchy(0, 40) \quad (15)$$

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).

Table 3: Model comparison output.

	WAIC	pWAIC	Difference in WAIC	Akaike weight	SE of WAIC estimate	Difference in SE
Model1_priors	6603	9	0	0.26	148.50	
Model2_priors	6603	9	0	0.25	148.49	0.067
Model2	6603	9	0	0.25	148.46	0.062
Model1	6603	9	0	0.24	148.50	0.070

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).

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.

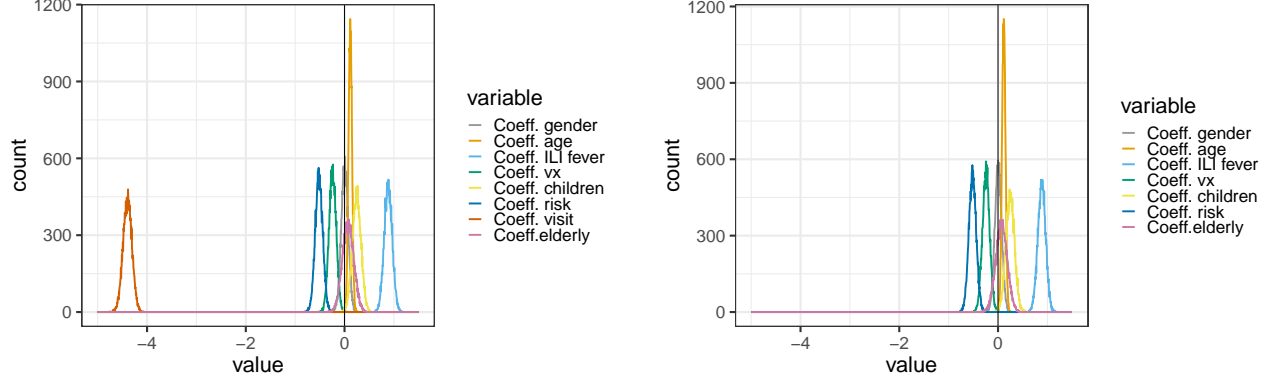


Figure 2: Posterior samples for each model (not including the intercept parameters, see Supplementary)

## 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 of gender (*b*), frequent contact with the elderly (*ia*) and then age (*c*) were removed.

$$M3 : \text{logit}(\theta) = a + cw_{i,age} + dw_{i,ili.fever} + eaw_{i,vaccine.this.year} \quad (16)$$

$$+ fw_{i,freq.contact.children} + gw_{i,underlying.risk} + hw_{i,visit.or.contact.medical.service} \quad (17)$$

$$+ iaw_{i,freq.contact.elderly} \quad (18)$$

$$M4 : \text{logit}(\theta) = a + cw_{i,age} + dw_{i,ili.fever} + eaw_{i,vaccine.this.year} \quad (19)$$

$$+ fw_{i,freq.contact.children} + gw_{i,underlying.risk} + hw_{i,visit.or.contact.medical.service} \quad (20)$$

$$M5 : \text{logit}(\theta) = a + dw_{i,ili.fever} + eaw_{i,vaccine.this.year} \quad (21)$$

$$+ fw_{i,freq.contact.children} + gw_{i,underlying.risk} + hw_{i,visit.or.contact.medical.service} \quad (22)$$

$$(23)$$

Comparing all fitted models (Table 4) suggests that the Models were highly similar in terms of model fit (WAIC values), but that Model 4 is overwhelmingly the best at model prediction (with an Akaike weight of 57%) followed by Model 3 (25%). The original Model 1 and 2 have 9% of the weight, whilst Model 5 can be ignored. This suggests that antibiotic prescribing is most associated with those parameters remaining in Model 4: age, ILI plus fever, 'flu vaccine status, frequent contact with children, underlying risk factors and whether there has been a visit to or contact with a medical service.

Table 4: Model comparison output.

	WAIC	pWAIC	Difference in WAIC	Akaike weight	SE of WAIC estimate	Difference in SE
Model4	6599	7	0	0.57	148.37	
Model3	6601	8	2	0.25	148.42	1.209
Model2	6603	9	4	0.09	148.46	1.214
Model1	6603	9	4	0.09	148.50	1.222
Model5	6609	6	10	0.00	148.40	6.992

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

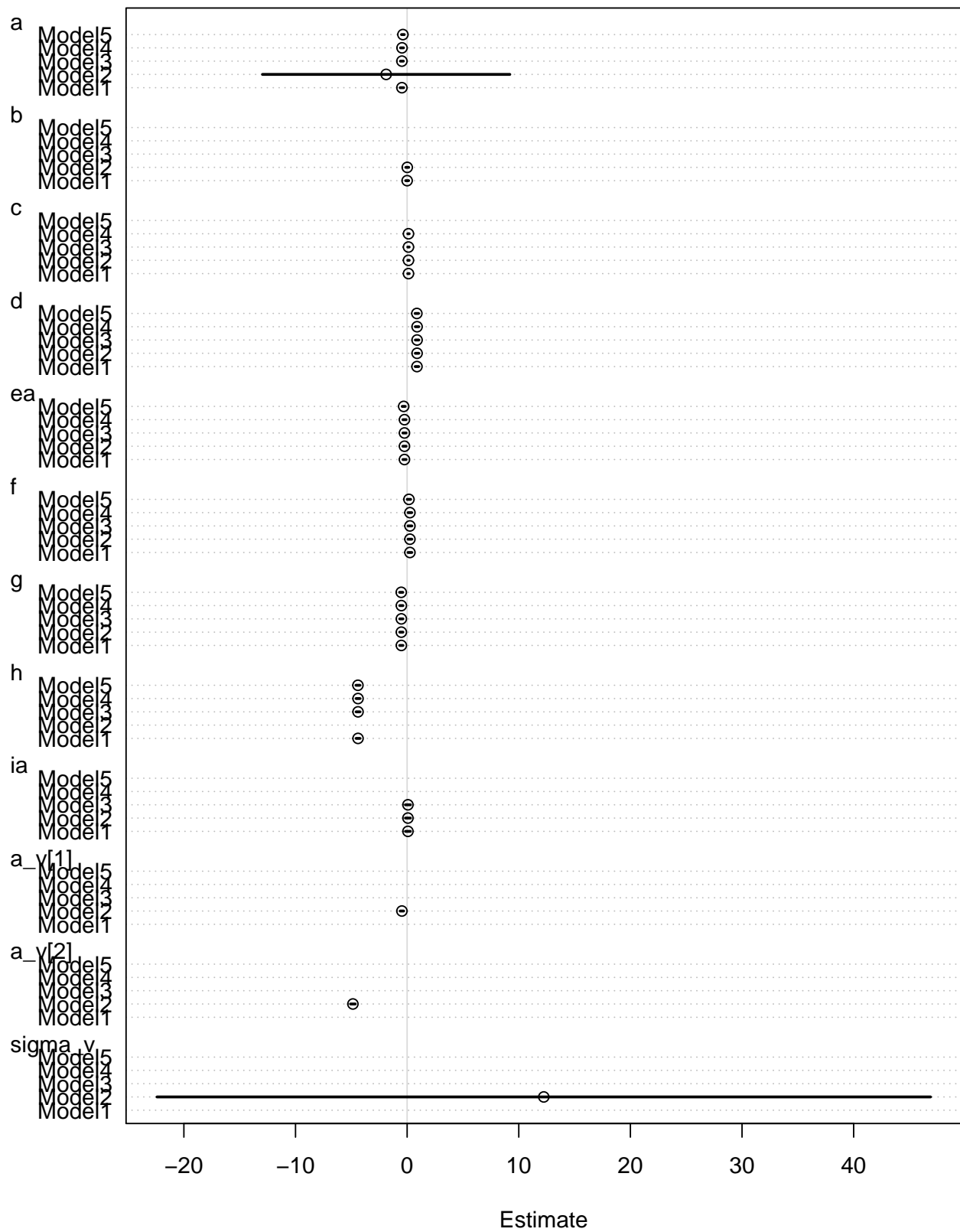


Figure 3: Posterior densities. Points are maximum a posteriori (MAP) estimates (the mode of the posterior distribution) and each black line segment is an 89 percent interval.

## Change in Odds

We can calculate the proportional change in odds (adjusted odds ratio) and relative effect of each coefficient from the optimal Model 4 (Table 5). Adjusting for the effects of other covariates, we found strong evidence for an impact on the odds of reporting taking an antibiotic whether an individual has visited, or had contact with, a medical centre (aOR with 89% credible interval (CI) of 0.01 [0.01, 0.01]). The odds were increased by more than 40% if an individual had ILI&fever symptoms (aOR with 89% CI 2.42 [2.2, 2.67]) or reduced by 40% if an individual had no additional risk factors (aOR with 89% CI 0.6 [0.54, 0.65]). All coefficients in Model 4 had aOR with 89% credible intervals that fell completely above or below 1.

Table 5: Coefficient effect for Model 4. The estimate of the coefficient is taken from a 20,000 posterior sample. The adjusted Odds Ratio (aOR) is calculated by taking the exponential of the coefficient. 'Absolute' is the mean absolute effect of the coefficient taking into account the mean intercept estimate. The ranges are all 89 percent credible intervals.

Variable	Estimate	Estimate range	aOR	Absolute
Intercept	-0.46	[-0.55,-0.37]	0.63 [0.58,0.69]	0.39
Coeff. age	0.12	[0.08,0.16]	1.13 [1.08,1.17]	0.42
Coeff. ILI fever	0.89	[0.79,0.98]	2.42 [2.2,2.67]	0.60
Coeff. vx	-0.24	[-0.33,-0.16]	0.78 [0.72,0.86]	0.33
Coeff. children	0.25	[0.15,0.36]	1.29 [1.16,1.43]	0.45
Coeff. risk	-0.52	[-0.61,-0.43]	0.6 [0.54,0.65]	0.27
Coeff. visit	-4.40	[-4.51,-4.28]	0.01 [0.01,0.01]	0.01

The same calculation for Model 1, highlights very similar changes in odds linked to the above coefficients but shows that the additional terms in Model 1 do not have aOR with 89% credible intervals that remain on one side of 1 (Supplementary).

The absolute values in Table 5 give the probability of reporting taking an antibiotic per episode taking into account the intercept. i.e. the absolute value of 0.4 for the intercept is the estimated mean probability of taking an antibiotic ignoring all other covariates. It can be seen that if an individual also has ILI&fever symptoms, then this probability increases to 0.6. Hence, this model suggests that, as shown with the aOR analysis, there is strong evidence for an impact of ILI&fever, having additional risk factors (co-morbidities) and visiting (or contacting) a medical centre but weaker evidence for a link to other covariates.

## 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 were presence of both ILI&fever symptoms, having additional risk factors and visiting, or contacting, a medical centre during an episode.

Hence, 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. The former suggests that, independently of whether it is a bacterial infection, worse symptoms are linked with more prescribing. Antibiotics are an inappropriate treatment for influenza-associated illness. Hence it is likely that much of the ILI with fever prescribing is inappropriate. The impact of this on resistance rates, with bystander selection if the infection is not bacterial, could be substantial.

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 co-morbidity (NICE 2008). Previous analysis of electronic health care records suggested that specific co-morbidities 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). Here we found that, of those episodes where antibiotics were prescribed 66% were from participants who had an underlying health issue. Although care must be taken to prevent unintended consequences (such as escalation of infection if not treated), this suggests that those with underlying health issues could be a focus for potential reductions in antibiotic use.

In the UK, a prescription is required for almost all antibiotics - potentially explaining the high correlation between medical centre visit (or contact) and antibiotic usage. 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 illness 12.4% visited a medical service. Of those episodes where an antibiotic was reported as being taken, 90% also reported visiting a medical service, i.e. 10% of episodes where an antibiotic was taken may not have had a prescription for this antibiotic usage.

This could be due to a lack of reporting professional medical contact in the survey, but still suggests a substantial proportion of antibiotic usage is occurring without prescription. The high correlation could also be partially explained by those that are more ill being more likely to seek professional care. We found some hint of this in the analysis of reported health score values (supplementary).

In contrast with previous studies (Shallcross et al. 2017; Brauer et al. 2016; Mor et al. 2015; Dolk et al. 2018), we did not find higher levels of antibiotic use in women once other covariates had been taken into account. Previous work has suggested that higher rates 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.

16% of participants accounted for 100% of the episodes where antibiotics were reported as being taken. This bias towards “heavy users” has been seen in previous studies (Malo et al. 2014; Shallcross et al. 2017). 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 re-attendance (Little et al. 1997; Williamson et al. 2006). This re-attendance link could also contribute to those reporting having received the influenza vaccine reporting higher levels of antibiotic use.

We did not see substantial trends in levels of prescribing across these 2012-2017 seasons which is reassuring but does not reflect the UK wide trends where decreases are being seen - CHECK if just hospital prescribing. We had no data on the specific antibiotics taken.

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, and age, were somewhat 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.

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 accurately record medical care visits nor whether an antibiotic was actually consumed (there may be confusion about what constitutes an antibiotic). It is also unclear how to exclude from the survey antibiotics that are being taken for treatment of non-ILI symptoms. We also 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 targeting these, whilst bearing in mind the complications - some sub-populations such as those with underlying health risks are likely to require more antibiotics.

Worryingly, the biggest driver of antibiotic prescribing in this analysis was having ILI&fever despite antibiotics being inappropriate for treating influenza. 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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