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Equine influenza vaccination as reported by horse owners and factors influencing their decision to vaccinate or not

W. Bambra, J.M. Daly, N.R. Kendall, D.S. Gardner, M. Brennan and J.H. Kydd*

School of Veterinary Medicine and Science, University of Nottingham, Sutton Bonington, Loughborough, Leicestershire, LE12 5RD, United Kingdom

* Corresponding author Julia.kydd@nottingham.ac.uk Tel 44(0)115 9516448

Willbambra@outlook.com

Janet.daly@nottingham.ac.uk

Nigel.kendall@nottingham.ac.uk

David.gardner@nottingham.ac.uk

Marnie.brennan@nottingham.ac.uk

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Abstract

Background: Equine influenza virus is a highly contagious respiratory pathogen that causes pyrexia, anorexia, lethargy and coughing in immunologically naïve horses. Vaccines against equine influenza are available and vaccination is mandatory for horses that participate in affiliated competitions, but this group forms a small proportion of the total horse population. The aims of this study were to: i) identify the equine influenza vaccination rate as reported in 2016 by horse owners in the United Kingdom (UK); ii) examine the demographics of owners and horses which were associated with significantly lower influenza vaccination rates and iii) explore factors that influence horse owners' decisions around influenza vaccine uptake.

Results: Responses from 4,837 UK horse owners who were responsible for 10,501 horses were analysed. An overall equine influenza vaccination rate of 80% (8385/10501) was reported. Several owner demographic characteristics were associated with significantly lower ($p \leq 0.05$) reported equine influenza vaccination rates including: some geographical locations, increasing horse owner age, annual household income of less that £15,000 and owning more than one horse. Horse-related features which were associated with significantly lower reported equine influenza vaccination rates included age ranges of ≤4 years and ≥ 20 years, use as a companion or breeding animal or leaving their home premises either never or at most once a year. The most common reasons cited for failing to vaccinate horses was no competition activity, lack of exposure to influenza and expense of vaccines. In contrast, the most common underlying reasons given by horse owners who vaccinated their horse were protection of the individual horse against disease, veterinary advice and to protect the national herd. Owners of vaccinated horses had less previous experience of an influenza outbreak or adverse reaction to vaccination compared with owners of unvaccinated horses.

Conclusions: This study documented a high rate of equine influenza vaccination as reported by owners in a substantial number of horses in the UK, but this does not reflect the level of protection. Sub-populations of horses which were less likely to be vaccinated and the factors that influence each owner's decision around vaccination of their horses against equine influenza were identified, but may alter following the 2019 European influenza outbreak. This information may nevertheless help veterinary surgeons identify "at-risk" patients and communicate more personalised advice to their horse-owning clients. It may also influence educational campaigns about equine influenza directed to horse owners, which aim to improve uptake of vaccination against this pathogen.

Key words: equine influenza, vaccine, vaccination, prevalence, decisions, survey, horse owners

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1. Introduction

Equine influenza A virus causes a contagious respiratory tract infection (Paillot, 2014; Sack, 2019), with 100% morbidity in populations of naïve animals that are exposed. Clinical signs in naïve horses include pyrexia, lethargy and anorexia, a harsh dry cough and serous nasal discharge (Wood et al., 2006). In primed horses, clinical signs are more mild and of shorter duration. In the majority of horses, the mortality rate arising from equine influenza is low, but secondary bacterial infection, which presents as a mucopurulent nasal discharge and an extended fever, can increase mortality in a small number of cases (Wood et al., 2006). The majority of equine influenza virus transmission occurs through close contact between infectious and naïve individuals, but this virus is highly infectious and can also be spread by transport of infected animals, contaminated personnel and equipment or in a wind-borne aerosol over 1-2 km, as reported in South Africa and Australia (Guthrie et al., 1999; Davis et al., 2009).

In 2007, a notable outbreak of equine influenza occurred in unvaccinated horses in Australia, which was previously free of the disease (Callinan, 2008; Webster, 2011). The cost of controlling this equine influenza outbreak amongst the naïve Australian horse population and regaining the country’s disease-free status was estimated at approximately 270 million Australian dollars (Callinan, 2008), demonstrating the potentially large economic impact of such an outbreak. Other recent notable equine influenza outbreaks have occurred in unvaccinated horses and donkeys in India and Nigeria (Virmani et al., 2010; World Organisation for Animal Health (OIE), 2019a), vaccinated horses in Japan (Yamanaka et al., 2008) and both vaccinated and

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unvaccinated horses in the UK, Ireland and France in 2019 (Newton, 2019; Animal Health Trust, 2020).

Inactivated whole virus vaccines have been used against equine influenza since the 1960s. A range of vaccines, including subunit and recombinant virus products is currently available (Paillot, 2014; Daly and Murcia, 2018). For complete protection, these vaccines rely primarily on generating cell-mediated immunity (Hannant and Mumford, 1989; Paillot et al., 2006b; Paillot et al., 2007) and a strong, but often short-lived, antibody immune response to protect against exposure to homologous virus (Paillot et al., 2006a). Correlates of protection for cell mediated immunity remain to be identified. However a correlation between existing antibody levels, as measured by single radial haemolysis (SRH), and protection of horses against infection with a homologous strain of influenza virus has been established. Thus clinical (e.g. absence of fever, cough) or virological (significant reduction in nasopharyngeal virus shedding) protection against homologous strains requires $\geq$85mm^2 or $\geq$154mm^2 SRH antibody areas respectively (Mumford and Wood, 1992).

In April 2019, the recommendations of the World Organisation for Animal Health (OIE) expert advisory panel on equine influenza advised that vaccines should contain representative strains of both the H3N8 Florida sub-lineages, namely clade 1 (e.g. A/equine/South Africa/04/2003-like or A/equine/Ohio/2003-like) and clade 2 (e.g. A/equine/Richmond/1/2007-like) (World Organisation for Animal Health (OIE), 2019b). These recommendations, which are reviewed annually, have remained the same between 2010 and 2019. In the UK, the so-called H3N8 American strains, Florida clades 1 and 2 circulate currently (Animal Health Trust, 2020). Here, three vaccines are available against equine influenza, only one of which complies with the current OIE recommendations to include both H3N8 Florida clade 1 and clade 2 (ProteqFlu, Boehringer Ingelheim; A/equine/Ohio/2003 and A/equine/Richmond/2007;(Animal Health Trust, 2020)). The other two vaccines contain European and American (Kentucky) strains (Equip F, Zoetis; A/equine/Borlange/1991; A/equine/Kentucky/1998) or European and Florida clade 1 strains (Equilis Prequenza, MSD Animal Health; A/equine/Newmarket/2/1993; A/equine/South Africa/2003) respectively (Durham, 2019). However despite these apparent shortcomings, shortly after a third vaccination of yearling horses, all three vaccines stimulated single radial haemolysis antibody responses against Florida clade 2 strain (A/equine/Richmond/1/2007) which are associated with clinical and virological protective immunity (Dilai et al., 2018) and Equip F shows cross protection against virulent challenge for representative strains of Florida clades 1 and 2 (Paillot et al., 2008; Bryant et al., 2010; Paillot, 2015) . Nevertheless, if influenza infection occurs in vaccinated animals, clinical signs are more mild and of shorter duration. However, in addition to providing complete or partial protection of individuals against infection, the aim of vaccination is to reduce the amount of virus shed from the nasopharynx and thus limit the spread of infection to other equids. In the UK, influenza vaccination (at least annual) is compulsory for horses competing under the regulations of affiliated organisations such as the British Horseracing Authority (Thoroughbred horseracing), British Show Jumping, British Eventing and Federation Equestre Internationale, but there is no mandatory vaccination of non-competitive, leisure horses imposed by the UK government.

Despite the requirements for compulsory vaccination in some disciplines, there have been periodic epidemics of equine influenza, particularly in unvaccinated animals in the UK in 2003 (Newton et al., 2006) and more recently in 2019 (Newton, 2019; Animal Health Trust, 2020). In the latter, Thoroughbred horseracing was cancelled for six days, resulting in a substantial interruption to racehorse training and racing schedules and financial losses to the economy. Non-Thoroughbred horses and equestrian events were also affected, which required dissemination of consistent advice to veterinary surgeons and horse-owners, particularly in relation to booster vaccination (Newton, 2019) (https://www.aht.org.uk/disease-surveillance/equiflunet; https://www.britishhorseracing.com/regulation/equine-influenza-update/).

Mathematical models show a dramatic reduction of influenza outbreaks among groups of vaccinated horses (reviewed in Daly et al. (2013)). However, the efficacy of influenza vaccines depends on a close match between the virus strain(s) incorporated in the vaccine and the strain(s) circulating in the field. Where there is a mismatch between the vaccine strain and circulating virus, much higher levels of antibody are required to prevent an individual from becoming infected. From mathematical models, it is estimated that vaccine coverage of 40% of the population is sufficient to prevent outbreaks involving homologous strains, i.e. provide “herd immunity” (Park et al., 2009). However, as the virus evolves over time, the effectiveness of vaccines containing older strains is reduced, increasing the risk of outbreaks occurring (Park et al., 2004). Models have illustrated that, following an accumulation of 4 or 5 amino acid changes in key regions of the virus, at least 70% of horses must be vaccinated to provide herd immunity and with 6 changes, this figure increases to at least 95% (Park et al., 2009).

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A limited number of studies into the influenza vaccination status of leisure or pet horses in the UK have been conducted. These have described the influenza vaccination rate as reported by horse-owners ranging between 79% and 91% (Hotchkiss et al., 2007; Boden et al., 2013; Ireland et al., 2013). In contrast, based on sales of influenza virus vaccines in the UK, which can only be prescribed and administered by veterinary surgeons, the estimated annual vaccination rate is <50% (MSD, 2017). Recent data estimates that there are between 847,000 and 1,350,000 horses in the UK (Boden et al., 2012; British Equestrian Trade Association (BETA), 2019). A total of 4,098 horses (98.3%), asses (0.2%) and mules (1.5%) were imported (Food and Agricultural Organization of the United Nations (FAO), 2017), but it is likely that the majority of imported horses were high value bloodstock or racing Thoroughbreds or sports horses. In one national survey, 98% (3419/3482) of respondents reported that they rode (Boden et al., 2013), with 1.8 million riding at least once a month in the past 12 months (British Equestrian Trade Association (BETA), 2019). Another report stated that around 60% of riders compete in non-affiliated events (British Equestrian Trade Association (BETA), 2015). These data indicate the size and mobility of the leisure horse population within the UK, but their influenza vaccination status and factors which influence vaccine decisions by owners are unknown. The aims of this study were first to identify the equine influenza vaccination rate as reported in 2016 by horse owners in the United Kingdom (UK), second, to examine the demographics of owners and horses which were associated with significantly lower reported influenza vaccination rates and third, to explore factors that influence horse-owners' decisions around influenza vaccine uptake.

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2. Materials and Methods

2.1 Survey Design

This study was approved by the School of Veterinary Medicine and Science's Research and Ethics committee (University of Nottingham) and participants gave informed consent. A modified tailored design was used to create a mixed method directional survey in English via esurveycreator®, applying the authors' expertise in equine infectious respiratory viral disease (JMD and JHK). A pilot survey was completed by 15 individual volunteers who were horse owners, including veterinary students, riders and horse trainers and thus formed a convenience sample: two questions were removed and four shortened to produce the final survey (Supplementary Figure 1) in which each participant was asked a total of 29 questions, of which 26 were compulsory to progress. The directional nature allowed appropriate yet consistent phrasing and collection of relevant data, depending on whether participants vaccinated their horse or not. Only one completion was permitted per participant and the survey took approximately 10 minutes, although participants could exit the survey and resume later. To determine any variation in vaccination status of horses owned by the same person, the survey allowed collection of data for up to 5 horses per participant, all of which were anonymised. Closed questions were used to collect information on the geographical location, age, gender and income of participants, the age and reported vaccination status of their horses, as well as the purpose for which they were kept and frequency of leaving their home premises for any reason, including a hack. The assumption was made that horse(s) were located in the same geographical region as their owners. In some questions, participants were asked to indicate how much they agreed with several statements on an eight-option Likert scale ranging from strongly disagree (1) to strongly agree (7), with an eighth option for ‘does not apply’. To collect information on how influential different factors were on horse owners’ decisions to vaccinate against equine influenza, a separate set of statements was presented to participants who reported vaccinating either all, some or none of their horses. Owners used a visual analogue scale ranging from 0 (no influence) to 100 (significant influence) to assess nine pre-determined categories. These categories were horse welfare, competition requirements, financial situation, advice from their vet, scientific reports, national herd protection, online forums and social media, opinions of friends or pony club recommendations. There was one open question to record any additional factors that affected participants’ decisions around vaccination. The survey was released online on the 5th July 2016 and closed on the 19th October 2016.

2.2 Survey Distribution

The online survey titled “Calling all horse owners”, was distributed and publicised through a number of media outlets, including a University of Nottingham press release, regional TV news, a national equestrian magazine and equestrian associations *via* their members’ mailing lists. The survey was also heavily promoted at regular intervals on social media platforms. A poster with a QR code and web address for the survey was displayed on notice boards at local equine retail stores, selected competitions and livery stables (Supplementary Figure 2). Participants who completed the survey were entered into a prize draw to win £150 worth of vouchers.

2.3 Data and thematic analysis

Data were downloaded into Microsoft Excel 2010 (Microsoft®, Redmond, USA) and imported into the statistical analysis program GenStat (GenStat®, v19, VSNi

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International Ltd., Rothampsted, UK). Odds ratios (ORs) with 95% confidence intervals (CI) were generated from ordinal and multinomial logistic regression analysis to examine the strength of the relationship between categorical variables and reported vaccination status and represent the strength of any predictive factors. An OR not equal to 1, with confidence intervals which did not overlap the confidence intervals of the null value (OR=1) was considered significant ($p \leq 0.05$). OR reference categories were selected as the median by GenStat or based on the most logical selection. Owner ages were grouped in an attempt to reflect young adults, adults, middle aged adults and those of elderly status. Owner reference categories were selected as 18-25 years, because this age range is most likely to be competing and a salary range of £15,000-£34,999, because it included the national average income of £28,600 in 2016 (Office for National Statistics, 2017). Horse ages were grouped into six categories at 5 year intervals for convenience and to reflect the stage of their training / ridden career e.g. horses 0-4 years were likely to be un-ridden or in the early stages of ridden training, whereas horses >20 years tend to compete less. Thus horse related reference categories were selected as 5-9 years (the age when horses commonly start to compete). Other reference categories were chosen arbitrarily. Chi-squared tests with Yates' correction were used to assess the statistical independence between use of horse and reported vaccination status. The statistical significance of the variations between median values of those respondents who reported vaccinating their horses against equine influenza virus and those who did not were analysed using Mann-Whitney U tests. For all statistical tests, $p \leq 0.05$ was considered significant. All data presented relate to vaccination against equine influenza virus as reported by horse owners and for most analyses, each horse was treated as an individual, with no allowance made for horses owned by the same

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person. The exceptions were the analysis of the influence of previous experience of a horse owner in relation to an influenza outbreak, adverse reaction and reasons which influenced horse owners around influenza vaccination. In these instances, the vaccination status of all horses owned by the same person was identified as either all vaccinated or all non-vaccinated or a mix of vaccinated and non-vaccinated ("both").

Thematic analysis was used to interpret the qualitative data arising from one open question, which aimed to capture other factors which influenced horse owners' decisions on equine influenza vaccination. The response(s) by each horse owner was assigned to one or more codes which were in turn amalgamated into themes. The topic of each theme was either one which arose from quantitative data analysis or novel, as appropriate.

3. Results

3.1 Survey inclusion criteria

The final survey was started by 6,547 participants. Participants who did not complete the survey (1,242), those who lived outside the UK (468) and those who owned only donkeys were excluded. Therefore final data for analysis comprised a maximum of 4,837 owners of a total of 10,501 horses. Throughout the results, the number of responses to individual questions are detailed. Full details of the numbers, percentages and statistical analysis including odds ratios with 95% confidence intervals, z statistics and *p* values are shown in Supplementary Tables 1 and 2.

3.2 Demographics of survey participants and regional distribution

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The majority of participants were female (98.5%, 4765/4837) and were aged between 41–60 years (43%, 2061/4837). The annual household income ‘£15,000 to £34,999’ was most common, with 30% (1469/4837) of participants in this category (Table 1). Most horse owners owned one horse (40%; 1955/4837). All UK regions were represented, ranging from 0.8% (41/4837) respondents in Greater London to 19% (926/ 4837) in the South East of England and 14% in both the South West (668/4837) and East of England (675/4837). Respondents from all other areas represented <10% of the total number of participants.

3.3 Equine influenza virus vaccination rate and regional distribution

The overall reported equine influenza virus vaccination rate was 80% (8385/10501). The highest reported influenza vaccination rate, 85% (1656/1954), was in horses owned by participants who lived in the South East (Figure 1a). Odds ratio analysis using East Midlands as a reference category (79%; 786/989), showed that horse owners in the South East of England were more likely to vaccinate (85%, 1656/1954; p=0.0003) whereas those in Wales (63%, 334/528; p<0.0001), the South West (73%,1056/1443;p=0.0004), West Midlands (73%, 624/849; p=0.0026) and Scotland (74%, 679/916; p=0.0057) were significantly less likely to vaccinate (Figure 1a; Supplementary Table 1, Section 1a).

3.4 Horse owner-related factors associated with reported influenza vaccination

3.4.1 Gender and age

There was no significant difference between the gender of an owner and the reported equine influenza vaccination status of their horse(s) (p=0.129; Supplementary Table 1, Section 1b). Compared with the reference category of 18-25

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years (83%, 1588/1911), owners in all age groups $\geq$26 years were significantly less likely to report vaccinating their horse(s) against equine influenza virus (26-40 years, 79%; 2534/3207, p=0.002; 41-60 years, 78%, 3716/4793, p<0.001; >60 years, 70%, 415/590, p<0.001; Figure 1b; Supplementary Table 1, Section 1c).

3.4.2 Income

The reference category of '£15,000-£34,999' was chosen as representative of the average UK salary of £28,600 in 2016 (Office for National Statistics, 2017). Compared with the reference category (78%, 2402/3063), horses owned by participants with an annual household income of 'Less than £15,000' had the lowest reported equine influenza vaccination rates (69%, 806/1162, p<0.0001). Participants earning '£55,000-£74,999' and '£95,000 or more' had significantly higher reported equine influenza vaccination rates (83%, 901/1086; p=0.0014; 86%, 526/621, p=0.0004 respectively; Figure 1c; Supplementary Table 1, Section 1d) compared with the reference category.

3.4.3 Number of horses owned

Reported equine influenza vaccination rates were highest when only one horse was owned (88%, 1721/1957; Figure 1d; Supplementary Table 1, Section 1e). Odds ratio analysis using one horse as the reference category showed that reported vaccination rates were significantly lower if more than one horse was owned (2 horses, 81%, 2241/2765, p<0.0001; 3 horses 79%, 1651/2090, p<0.0001; 4 horses, 76%, 1028/1344, p<0.001; 5 horses 73%, 648/890, p<0.001; > 5 horses, 66%, 964/1455, p<0.001).

3.5 Horse-related factors associated with reported influenza vaccination

3.5.1 Age

Horses in the age category of 10-14 years had the highest reported equine influenza vaccination rates (84%, 2062/2456) while the reported lowest vaccination rates were seen in horse age category 25->36 years (55%, 316/579; Figure 2a; Supplementary Table 1, Section 2a). The median age of horses reportedly vaccinated was 11 years, whereas the median age of reported non-vaccinated horses was 15 years ($p<0.001$). The reference category of 5-9 year old horses had a reported vaccination of 83% (2728/3275). Using this reference value, horses in each of the age categories 0-4, 20-24 and 25->36 years were significantly less likely to be reported as vaccinated (72%, 809/1120, $p<0.0001$; 69%, 813/1172, $p<0.0001$; 55%, 316/579, $p<0.0001$ respectively).

3.5.2 Use

The highest reported equine influenza vaccination rates were recorded in horses used for competitions, whether affiliated and unaffiliated (88%, 918/1047; 86%, 2047/2389 respectively; Figure 2b; Supplementary Table 1, Section 2b). The lowest reported equine influenza vaccination rates were noted in horses used solely for breeding or companionship (64%, 141/220 and 67%, 1552/2293, respectively). The reference category of hacking had 79% (2603/3289) reported vaccinated. Odds ratio analysis showed the reported influenza vaccination rates were significantly higher for horses in affiliated and unaffiliated competitions but lower in horses used solely for breeding or as companions (affiliated competitions $p<0.0001$; non-affiliated competitions $p<0.0001$; breeding $p<0.0001$; companion, $p<0.0001$). Vaccination of horses used for leisure riding approached significance (leisure riding p=0.052; Figure 2b).

3.5.3 Frequency of leaving yard

Horses that left the premises at which they were stabled on a daily basis had the highest reported equine influenza vaccination rates (83%, 127/153). The reference category of leaving once a month had 75% (298/396) reported vaccination rates; in comparison with this, horses that left their home premises less than once a year (54%, 63/116, p<0.0001), once a year (60%, 37/62, p=0.011) or never (30%, 96/324, p<0.0001) had significantly lower reported vaccination rates (Figure 2c; Supplementary Table 1, Section 2c). Horses which left daily (83%, 127/153, p=0.05) or 2-6 times a week (80%, 1158/1444, p=0.032) or 2-3 times a month (82%, 719/879, p=0.007) were significantly more likely to be reported as vaccinated against equine influenza compared with the reference category.

3.6 Owner-related factors associated with reported equine influenza vaccination

3.6.1 Underlying reasons

Owners were asked to indicate on a visual analogue Likert scale how influential various factors were on their decision to vaccinate their horse(s) against equine influenza. The eight options ranged from "*Strongly disagree*" (1) to "*Strongly agree*" (8) with "*neutral*" (4) and *"does not apply"* (0) available. The majority of horse owners who reported vaccinating their horse against equine influenza agreed slightly, moderately or strongly with the statement "I vaccinate to protect my horse from equine influenza" (86%, 2846/3624), followed by national herd protection (43%, 1547/3624) or vet's advice (43%, 1523/3624; Figure 3a; Supplementary Table 1,

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Section 3a). In contrast, of horse owners who reported not vaccinating their horse against equine influenza, the majority selected "My horse does not compete in affiliated competitions" (65%, 793/1215), followed by horse not exposed (42%, 512/1215) and expense (36%, 435/1215; Figure 3b; Supplementary Table 1, Section 3b). Responses relating to the most popular reason for reported vaccination or non-vaccination in each category were polarised towards "strongly agree".

3.6.2 Impact of previous experience of equine influenza outbreak or adverse vaccine reaction

For this analysis, participants were split into three groups based on whether they reported vaccinating: (i) all of their horses (*'vaccinate'* = 75%, 3623/4837); (ii) some but not all of their horses (*'both'* = 13%, 629/4837); (iii) none of their horses (*'non-vaccinate'* = 13%, 585/4837). A small number of participants had experienced an equine influenza outbreak as diagnosed by a vet (5%, 242/4837; Supplementary Table 1, Section 3c) or had observed a self-assessed "adverse reaction" to equine influenza vaccination (19%, 933/4837; Supplementary Table 1, Section 3d). Compared with the 'non-vaccinated' reference group, owners in the 'vaccinate' group were significantly less likely to have had any experience of an equine influenza outbreak (4%, 152/3623; $p<0.0001$; Figure 4a) or to have observed a self-assessed "adverse reaction" to equine influenza vaccination (16%, 598/3623; $p<0.001$; Figure 4b).

3.6.3 Importance of underlying reasons

The influence of nine pre-determined factors on horse owners' decisions to vaccinate against equine influenza was assessed using a visual analogue scale ranging from 0

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(no influence) to 100 (significant influence). These categories were horse welfare, competition requirements, financial situation, advice from their vet, scientific reports, national herd protection, online forums and social media, opinions of friends or pony club recommendations. Data were analysed according to the number of horses up to a maximum of five owned by one individual which were reported as '*vaccinated'* by their owners, ranging from all vaccinated (5/5) to none vaccinated (0/5). In all groups, horse welfare was the most influential factor (median scores of 96, 80-95 and 76 out of 100 for the *'vaccinate'* n=3623, '*both'* n=629 and *'non-vaccinate'* n=585' groups respectively; Supplementary Table 1, Section 3e). For horse owners who reported vaccinating all five or at least two of their five animals, competition requirements, advice from their vet and scientific reports were most influential and had median scores that were significantly different from horse owners in the "*non-vaccinate*" group ($p<0.001$). Protection of the national herd gained influence with increasing numbers of horses reported vaccinated. In contrast, horse owners who reported vaccinating 1-3 of their five reported horses indicated that their financial position was more influential (range of median scores 50-58) than owners who vaccinated all five horses (median score 10) or none (median score 27). See Supplementary Table 1, Section 3e for interquartile ranges.

3.7 Thematic analysis

A total of 508 horse owners answered the open question "Please state any other factors that affect your decision on equine influenza vaccination" and analysis revealed 15 over-arching themes (Supplementary Table 2). Responses were also categorised as positive, mixed or negative attitudes towards influenza vaccination and representative quotes are shown in Supplementary Figure 3. The most common

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responses which were associated with a negative attitude towards vaccination included adverse vaccine reactions and minimal exposure to new horses. Factors cited by horse owners that had a positive attitude to influenza vaccination included insurance requirements and a sense of responsibility, although numbers of responses were small. Mixed attitudes to vaccination arose following advice from their vet or a local influenza outbreak.

4. Discussion

In this study, an overall reported equine influenza vaccination rate of 80% among 10,501 horses was obtained from an online survey of horse owners in the United Kingdom during 2016, but this does not reflect the level of protection. This rate is comparable to the 79% (n=873) and 82% (n=797) rates previously found in mainland Britain (Hotchkiss et al., 2007; Ireland et al., 2013), but lower than others (91%, n=4601; (Boden et al., 2013). These consistently high overall equine influenza vaccination rates reported by respondents are at odds with the estimated number of 530,000 vaccine doses sold by pharmaceutical companies in 2013, which equates to an estimated 53% vaccination rate (MSD, 2017). This suggests that a significant number of horses are not vaccinated annually which, until the 2019 influenza outbreak in the UK was the minimum interval recommended by vaccine manufacturers and various equine authorities. Several potential explanations for this discrepancy may be proposed. First, the high reported vaccination rate may be self-selection bias whereby more horse-owners who vaccinated their horses participated. This is a recognised failing of an electronic survey approach (Sax et al., 2003; Bethlehem, 2010), but this method permits access by large numbers of people easily; the number of individual UK households with internet access has increased dramatically in recent years to 89% in 2016 (Office for National Statistics, 2016). Second, the survey's publicity title, "Calling all horse owners" attempted to minimise sampling bias by avoiding the use of the word "vaccination". Nevertheless it is possible that horse-owners who are actively engaged with their horses' health were more likely to complete the survey. One qualitative study on attitudes to vaccination revealed that veterinary surgeons divided farmers into three groups, namely proactive, receptive to advice or disengaged (Richens et al., 2016); similar groups are likely to exist amongst horse owners. Third, the survey relied on recall by owners, who were not questioned specifically about the product administered or the frequency and time since last vaccination as this was deemed too unreliable; the question simply asked whether their horse had been vaccinated against equine influenza at some point in their memory. Ireland et al. (2013) reported that 4% of horses vaccinated against equine influenza received their last vaccination more than one year previously, thereby failing to meet manufacturer's recommendations of at least annual vaccination in most horses or even bi-annual vaccination in high-risk populations. Others reported that 6% of the horses received vaccinations once every 2 years (Mellor et al., 2001). Accessing veterinary records would have improved the quality of the data, but was too difficult logistically with the numbers of respondents and horses.

The study had several strengths, for example, horse owners could record the vaccination status of up to five horses, which captured differences in reported vaccination status within horses owned by the same person. The directional nature also allowed collection of relevant data, depending on whether participants reported

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vaccinating their horse or not. In addition, completion of the questions relating to vaccination was compulsory, largely because Boden et al. (2013) found that 20% of participants skipped the vaccination question in their survey, leading to the possibility that non-response bias led to an under-representation of non-vaccinated horses. A total of 81% of participants completed the current survey, likely encouraged by the use of a prize draw, regular publicity on social media and the ability to resume at a later date (Edwards et al., 2002; Boden et al., 2013). The completion rate decreased as the survey progressed, indicating that length may have discouraged some participants to complete and emphasising the need to avoid over-long surveys. The assumption that horse(s) are located in the same region as their owners was based on the finding by Boden (Boden et al., 2013) who reported that just over 90% of respondents to their survey kept their horses within 10 miles of their own home. In the current survey, Greater London was the least represented region by respondents, corresponding with the low density of horses reported in this area, whereas the high number of participants in areas such as the South East and the South West corresponded with the high density of horses in these regions (Boden et al., 2012).

After completion of this survey, there was a widespread outbreak of equine influenza (American lineage, Florida clade 1 sub-lineage) amongst vaccinated and non-vaccinated horses throughout the United Kingdom, Ireland and France in 2019, which led to the suspension of Thoroughbred horse racing in the UK for 6 days (https://www.aht.org.uk/disease-surveillance/equiflunet). Prior to this outbreak and after the previous widespread outbreak in 2003, one mathematical model predicted that with annual booster vaccination, more frequent outbreaks of equine influenza

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involving a smaller number of horses would be the trend (reviewed in (Daly et al., 2013)). Up until 2013, the pattern of influenza outbreaks supported the model, but despite the high rate of equine influenza vaccination reported by horse-owners in the current and other studies, this was insufficient to prevent the substantial 2019 incursion. The size of the 2019 outbreak suggests that vaccination levels were insufficient to afford protection of the national herd. One potential explanation is that the true annual vaccination rate is lower than reported by horse owners and closer to that reported by pharmaceutical companies. In addition, a mismatch between the 2019 influenza virus strain and the strains included in current vaccines may mean that a higher rate of vaccination is required to achieve herd immunity. The substantial size and well-publicised impacts of the 2019 influenza outbreak may assist in improving the actual uptake of vaccines against this virus by horse owners.

In order to ensure a population is protected against an equine influenza outbreak with a homologous strain, at least 70% of horses must be vaccinated annually (Baker, 1986) and this rises to 95% if at least 6 amino acid HA substitutions arise (Park et al., 2009). Notably vaccination rates among some groups of horses reported here were significantly lower. This is concerning because in a population which is partially immune to influenza, the index case that triggers an outbreak is usually a seronegative horse (ie non-vaccinated or vaccinated >6 months previously) (Wood, 1991). Several factors appeared to influence the reported equine influenza vaccination rate, including owner's age ≥26 years old. It may be that older participants are less likely to compete in affiliated competition, removing any compulsory requirement for influenza vaccination of their horses. In contrast, a survey of dog, cat and rabbit owners reported that participants over the age of 55 years were more likely to say their pets had received booster vaccinations (PDSA, 2019). There was a significant association between annual household income and equine influenza vaccination rates, with participants on annual household incomes lower than the national average salary less likely to vaccinate their horse(s) against equine influenza. Vaccine cost was also important in Australian horse-owners who failed to vaccinate their horses against Hendra virus (Goyen et al., 2017). Owners located in the municipality of Wales reported the lowest rate of influenza vaccination but it is likely that confounding factors, in particular the use of horse, contribute to the regional trends observed. For example, Wales has very few affiliated eventing competitions for which vaccination is compulsory. Nevertheless a lower booster vaccination of pets (dogs, cats and rabbits) has been reported in Wales elsewhere (PDSA, 2019) so animals in this municipality may be more vulnerable to infectious disease.

The reported equine influenza vaccination rate was inversely proportional to the number of horses owned. Thus 88% of owners reported that 'horse 1' was vaccinated, but this fell to 69% for 'horse 5', a pattern also observed by Koskinen (2014a) in Finland. This suggests that survey participants are more likely to record vaccinated horses first and before unvaccinated horses, which may have influenced data in previous studies that only analysed the first horse per participant (Hotchkiss et al., 2007; Boden et al., 2013; Koskinen, 2014a). In addition, Boden et al. (2013) assumed that all horses owned by a participant had the same equine influenza vaccination status. However, the current survey revealed that 13% of participants vaccinated some, but not all the horse(s) they owned. If all horses owned by one participant were assumed to have the same vaccination status, a vaccination rate of

88% would have been found instead of 80%, illustrating the effect such an approach can have. It may also be speculated that as the number of horses owned and age of owners increase, their use may become more diverse (e.g. athletes, companionship, retired or bloodstock), for which equine influenza vaccination may be perceived as unnecessary.

Significant differences were detected between age groups of horses and their reported equine influenza vaccination status. The highest reported vaccination rates were seen in horse age categories spanning 5 to 14 years. The eldest horses (category $\geq$ 20 years), and the youngest horses (category $\leq$4 years) were less likely to be vaccinated against equine influenza, with an even lower figure (63%) of horses <1 year old reportedly vaccinated, although this is likely to include foals which were too young to be vaccinated. Koskinen (2014a) similarly found that participants gave ‘too old’ and ‘too young’ as reasons for non-vaccination. The use or activity level of a horse is likely to be a confounding factor, with both the youngest and eldest horses unlikely to be competing or ridden regularly.

The use of horses influenced reported influenza vaccination rates, with the highest rates found in horses used in affiliated competitions. However, some horses competing in affiliated competitions were reported as not vaccinated against equine influenza, despite the mandatory vaccination specifications. This sub-optimal equine influenza vaccination rate may illustrate the necessity for stricter enforcement of regulations at affiliated competitions; stricter monitoring has been introduced by many regulatory authorities and shows since the 2019 influenza outbreak (Horse of the Year Show, 2019). In the UK, equine influenza vaccination is recorded on each horse’s paper passport, which legally, must accompany the horse at all times. There is no legal requirement for leisure horse owners in the UK to vaccinate their horses, unless competing in affiliated events. No central equine influenza vaccination electronic database exists, unlike selected equine sports in some countries (e.g. Finnish Trotting and Breeding Association; (Koskinen, 2014b; Koskinen, 2014a)). Instead officials at events involving athletic horses are responsible for checking vaccination status on the horse’s arrival at the event. At each Thoroughbred race course or international competition, official Veterinary Officers employed by the British Horseracing Authority or FEI inspect passports prior to each horse entering the stables. Inspection by officials at affiliated national competitions (e.g. British Show Jumping, British Dressage etc) has been formalised since the 2019 influenza outbreak but is often reliant on amateur volunteers, with a veterinary surgeon on-call for advice. However, this study aimed to target the large numbers of leisure horse owners, who have freedom of choice around influenza vaccination, who do not compete and are therefore not required to vaccinate their horses. Although the reported vaccination rate was high (~80%), there were clearly sub-groups of horses owned by some groups of horse owners where the rate of vaccination was substantially lower. Therefore further education of horse owners about the benefits of influenza vaccination in the prevention of infection and thus improving the welfare of their horse, which was noted as an important influential factor in decision making, may be useful in altering behaviour.

Only 30% of horses that never left their home premises were reported as vaccinated against equine influenza. The frequency with which horses leave their home premises is likely to be linked to the purpose for which they are kept. Horses used for breeding or companionship rather than competing in affiliated competition were reported as less likely to be vaccinated against equine influenza. Koskinen (2014a) and McGowan et al. (2010) also found breeding, retired and companion horses were less likely to be vaccinated against equine influenza. Lack of exposure to new horses has previously been documented as a common reason for non-vaccination (Ireland et al., 2013; Koskinen, 2014a). In the current study, “minimal exposure to new horses” was stated frequently in the free text as a reason for not vaccinating against equine influenza. Participants who did not vaccinate strongly agreed with the statement regarding non-vaccination because of lack of affiliated competition requirements. Therefore further education of horse owners about the highly contagious nature of equine influenza and the 1-2km distance over which virus can be transmitted as a wind-borne aerosol (Guthrie et al., 1999; Davis et al., 2009; Cullinane et al., 2010) may be required.

When horse owners were asked about factors that influenced their decision to vaccinate against equine influenza, the welfare of their horses was the most important. The main reason behind owners not vaccinating their horse against equine influenza was their non-participation in affiliated competitions and ownership of a horse that suffered an adverse reaction, which may be related to owners’ increased age and life experience. Adverse events have been identified as a barrier to vaccination in dogs and cats (Belshaw et al., 2018). In the UK, adverse reactions should be reported to the Veterinary Medicines Directorate who collate and disseminate information to vaccine manufacturers. Here, an adverse event was not defined but includes a failure to protect against challenge infection (more accurately described as vaccine breakdown) and reactions involving clinical signs or illness,

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including very rarely, anaphylaxis. The latter is more likely to concern individual horse owners. If adverse events are a barrier to the uptake of influenza vaccination by a sub-group of horse owners, more publicly available data is required to describe, for example, their form, frequency, any association with the inoculation site or administration method or predisposition by horse breed or age. Minor reactions (clinical signs) involving mild and transient heat and pain (tenderness) at the injection site are likely to be detected by horse owners and perhaps classified as “adverse”, without realising that such inflammation is a necessary pre-requisite for the stimulation of an effective adaptive immune response. A marked adverse reaction involving more severe inflammation may result in horses developing a very stiff neck, with severely restricted movement, which requires adaptions to enable them to eat and drink normally. In these instances, it may be that repeated administration of vaccines which contain non-viral components such as tissue culture derived proteins e.g. egg proteins and stabilizers e.g. bovine serum albumin can lead to the development of IgE mediated, hypersensitivity Type I reactions in animals with a genetic predisposition for this response (Gershwin et al., 2012). Thus although difficult, further research and then education of horse owners about the range of adverse influenza vaccine reactions may provide data to re-assure and encourage vaccine uptake.

Additional potential future research around the motivation, barriers and decision-making processes undertaken by horse owners with regard to uptake of vaccination may provide further insight into this complex process. In parents, vaccine hesitancy of their children is well recognised and has been defined by the World Health Organisation as “a behaviour, influenced by a number of factors including issues of confidence (do not trust a vaccine or a provider), complacency (do not perceive a need for a vaccine or do not value the vaccine) and convenience (access)" (Edwards and Hackell, 2016), Multiple factors influence parents when making decisions about vaccination of their children (Rhodes, 2017; Smith et al., 2017), with concern about cost, adverse effects, attitudes to vaccination, trust and information availability featuring consistently. In pet owners (dogs, cats and rabbits), there has been a sustained reduction since 2016 in the proportion who report a primary vaccination of young animals or booster vaccination of adults, with the most common reasons for not vaccinating cited as "too expensive", "lack of contact with other animals" and "unnecessary" (PDSA, 2019). The owner's age, education level and gross household income were all influential factors. In dog-owners, vaccination of their pets against rabies virus in Texas, USA increased following a change from annual to triennial vaccination (Rogers, 2011), indicating the influence of vaccine intervals in owner compliance. However, reducing the frequency of equine influenza vaccinations is unlikely because protective immunity is relatively short-lived (~ 6 months) and the concurrent circulation of multiple influenza strains of different sub-lineages means that cross-protective immunity induced by an annual vaccination interval is insufficient to prevent clinical signs of disease. During the widespread 2019 influenza outbreak in western Europe, vaccine breakdown was detected in 31-34% of horses which had been vaccinated annually but succumbed to infection, (Gildea et al., 2018; Fougerolle et al., 2019) implying that the level and / or duration of protective immunity stimulated by the current vaccination protocols was insufficient to provide clinical protection against infection with heterologous strains. The reasons and risk factors underlying vaccine breakdown therefore requires additional research and in particular the immunity gap during a primary vaccination course (Daly and Murcia,

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2018) and sexual dimorphism in susceptibility to infection (Barquero et al., 2007; Ryan et al., 2015). Furthermore an estimated 10% of the equine population respond poorly to influenza vaccination, by consistently generating antibody levels below the thresholds required for clinical and virological protection (Daly et al., 2004; Baguelin et al., 2010; Gildea et al., 2011; Gildea et al., 2013); the underlying causes may include genetic background, poor administration interval compliance or vaccine degradation. Regardless of the underlying reasons, these animals are likely to act as index cases during an outbreak. In Australia, vaccination uptake against Hendra virus, which can be fatal for horses and people was 11-17%. Reasons cited for the poor initial uptake included vaccine safety, cost and effectiveness (Manyweathers et al., 2017b). Improved vaccination uptake was triggered by a nearby infection outbreak (Manyweathers et al., 2017a) and vets played an important advisory role, which concurs with data from owners involving dog and cat vaccination (Belshaw et al., 2018). Increased odds ratios for non-vaccination against Hendra virus included non-vaccination against strangles, handling more than 3 horses each week, concerns over the motivation of veterinary surgeons to make money, the side effects and lack of efficacy of vaccines and non-vaccination of other pets (Goyen et al., 2017); these insights may inform future research on risk factors associated with poor compliance around influenza vaccination. Thus many studies show that the factors which influence vaccination uptake in animals and people are complex and may be inter-related. Hence future studies to identify motivation and barriers to influenza vaccination of horses may prove beneficial in altering behaviour and improving vaccine uptake by horse-owners and thus limit or prevent disease caused by harmful, infectious pathogens.

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5. Conclusions

In conclusion, this study documented a high rate of equine influenza vaccination as reported by owners in a substantial number of horses in the UK. However time since last vaccination or product administered and therefore the potential level of protection against influenza infection was unknown. Nevertheless, it identified sub-populations of horses which were less likely to be vaccinated and provided novel insights into the factors that influence owners' decisions around vaccination of their horses against equine influenza. Although these factors may alter subtly in response to the 2019 influenza outbreak in Europe, this information may nonetheless help veterinary surgeons identify "at-risk" patients and thus communicate more personalised advice to their horse-owning clients. It may also influence educational campaigns about equine influenza (e.g. the distance influenza can travel) directed to horse owners, which aim to improve uptake of vaccination against this highly infectious pathogen.

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Authors' contributions: JHK was responsible for the initial concept, questionnaire design, project supervision, manuscript preparation and had oversight of the whole project. WB designed and analysed the survey and prepared figures. JMD contributed to survey design and writing of the manuscript. NRK, MB and DSG advised on study design and DSG and WB undertook statistical analysis.

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Figure legends

Figure 1. Impact of horse-owner related factors on horse-owners' decision whether to vaccinate their horse against equine influenza virus. a) geographical region; b) owner's age; c) owner's salary; d) number of horses owned. No. of horses owned; n = 10,501. OR Odds Ratio with lower and upper 95% Confidence Intervals. Reference category is indicated by an OR of 1. Black dots: categories which are significantly different ($p \leq 0.05$) from the reference category. Grey dots: categories are not significantly different. Percent of horses reported by horse owners as vaccinated: a) East Midlands 85%, South East 85%, Wales 63%, South West 73%, West Midlands 73%, Scotland 74%; b) 18-25 years 83%, 26-40 years 79%, 41-60 years 78%, >60 years 70%; c) £15,000-£34,999 78%, >£95,000 86%, £55,000-£74,999 83%, <£15,000 69%; d) 1 horse 88%, 2 horses 81%, 3 horses 79%, 4 horses 76%, 5 horses 73%, >5 horses 66%.

Figure 2. Impact of horse-related factors on horse-owners' decision whether to vaccinate their horse against equine influenza virus. a) Horses' age (years), n = 10,483, b) Horses' use, n=12,473; c) Frequency of horse leaving yard, n = 4,836. OR Odds Ratio with lower and upper 95% Confidence Intervals. Reference value is indicated by an OR of one. Black dots: categories which are significantly different ($p \leq 0.05$) from the reference category. Grey dots: categories are not significantly different. Percent of horses reported by horse owners as vaccinated with age: a) 5-9 years 83%, 25->36 years 55%, 20-24 years 69%, 0-4 years 72%; b) hacking 79%, affiliated competitions 88%, unaffiliated competitions 86%, breeding 64%, companion 68%; c) once a month 75%, never 30%, once a year 60%, less than once

a year 54%, 2-3 times a month 82%, daily 83%, 2-6 times a week 80%, once a week 79%.

Figure 3. Reasons underlying horse owners’ decisions: a) to vaccinate n=3624. b) not to vaccinate against equine influenza virus. n=1215. x axis legend shows topic of each question; see Supplementary material for full text of questions.

Figure 4. Previous experiences of horse-owners which influenced their decisions around equine influenza vaccination. a) influenza outbreak; b) adverse reaction following influenza vaccination. n = 4,837. Odds ratio (OR) with lower and upper 95% Confidence Intervals. Reference value is indicated by an OR of 1. Black dots: categories which are significantly different ($p \leq 0.05$) from the reference category. Grey dots: categories are not significantly different. Percent of owners with previous experience of: a) an outbreak with, non-vaccinated horses 8%, vaccinated horses 4%; b) an adverse reaction with, non-vaccinated horses 28%, vaccinated horses 16%.

Table 1. Demographics of horse owners who participated in the survey. Total number of respondents =4837. United Kingdom regional abbreviations: East Midlands, East of England, Greater London, North East, North West, Northern Ireland, Scotland, South East, South West, Wales, West Midlands, Yorkshire and the Humber.

Demographic	**Category Percent (number)**											
Gender	**Female**	**Male**										
Percent	98.5	1.5										
(No.)	(4765)	(72)										
Age (years)	**18-25**	**26-40**	**41-60**	**>60**								
Percent	21.0	31.2	42.6	5.2								
(No.)	(1017)	(1509)	(2061)	(250)								
Annual income (£1000s)	**<15**	**15-34.9**	**35-54.9**	**55-74.9**	**75-94.9**	**>95**	**I'd rather not say**					
Percent	12.2	30.4	21.1	10.5	5.3	5.1	15.4					
(No.)	(590)	(1469)	(1021)	(508)	(256)	(249)	(744)					
No. of horses owned	**1**	**2**	**3**	**4**	**5**	**>5**						
Percent	40.4	28.6	14.4	6.9	3.7	6.0						
(No.)	(1955)	(1381)	(696)	(336)	(178)	(291)						
Region	**E Mid**	**E Eng**	**G Lond**	**NE**	**NW**	**N Ireland**	**Scotland**	**SE**	**SW**	**Wales**	**W Mid**	**Y & H**
Percent	9.9	14.0	0.8	3.9	6.8	2.3	8.3	19.1	13.8	4.3	7.7	9.1
(No.)	(477)	(675)	(41)	(189)	(327)	(111)	(403)	(926)	(668)	(208)	(371)	(441)

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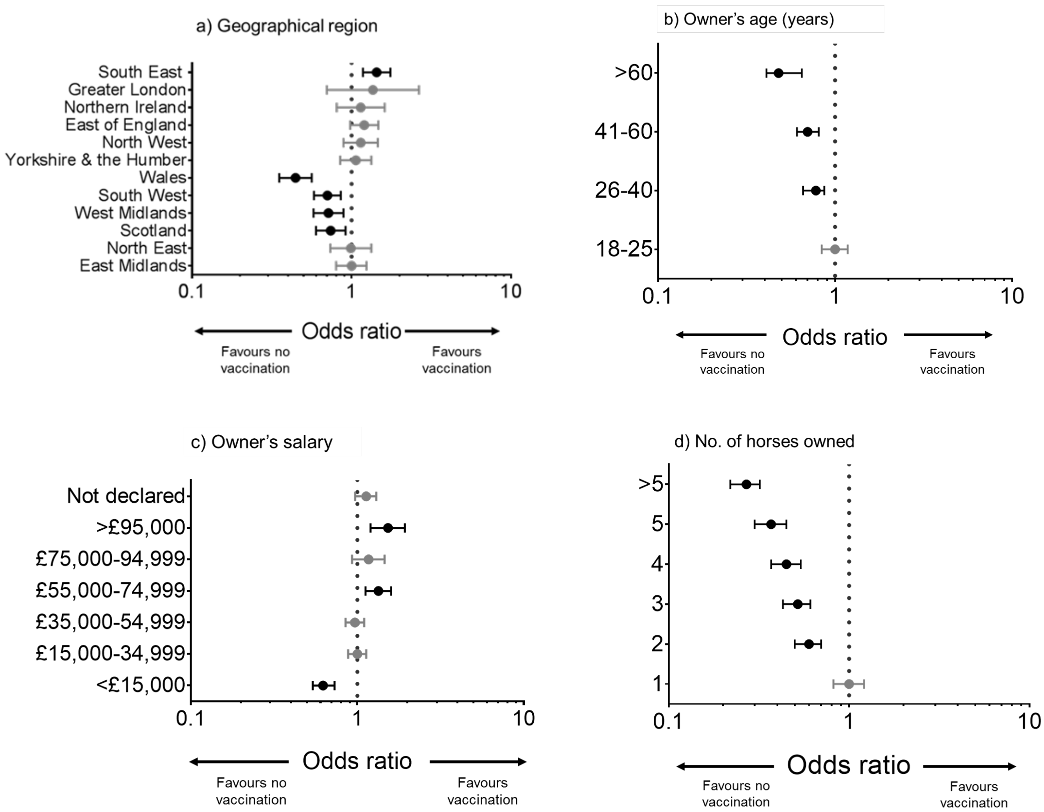
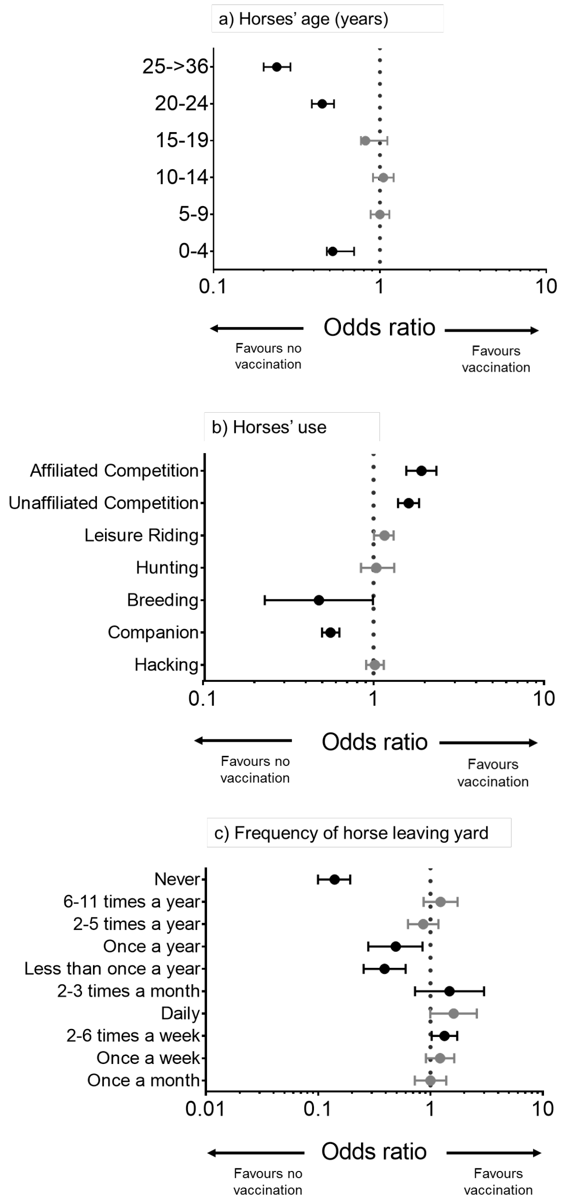
Figure 1



a) Geographical region
South East
Greater London
Northern Ireland
East of England
North West
Yorkshire & the Humber
Wales
South West
West Midlands
Scotland
North East
East Midlands
0.1
1
10
Odds ratio
Favours no vaccination
Favours vaccination
b) Owner's age (years)
>60
41-60
26-40
18-25
0.1
1
10
Odds ratio
Favours no vaccination
Favours vaccination
c) Owner's salary
Not declared
>£95,000
£75,000-94,999
£55,000-74,999
£35,000-54,999
£15,000-34,999
<£15,000
0.1
1
10
Odds ratio
Favours no vaccination
Favours vaccination
d) No. of horses owned
>5
5
4
3
2
1
0.1
1
10
Odds ratio
Favours no vaccination
Favours vaccination

Figure 2.



a) Horses' age (years)
25->36
20-24
15-19
10-14
5-9
0-4
0.1
1
10
Odds ratio
Favours no vaccination
Favours vaccination
b) Horses' use
Affiliated Competition
Unaffiliated Competition
Leisure Riding
Hunting
Breeding
Companion
Hacking
0.1
1
10
Odds ratio
Favours no vaccination
Favours vaccination
c) Frequency of horse leaving yard
Never
6-11 times a year
2-5 times a year
Once a year
Less than once a year
2-3 times a month
Daily
2-6 times a week
Once a week
Once a month
0.01
0.1
1
10
Odds ratio
Favours no vaccination
Favours vaccination

Figure 3.

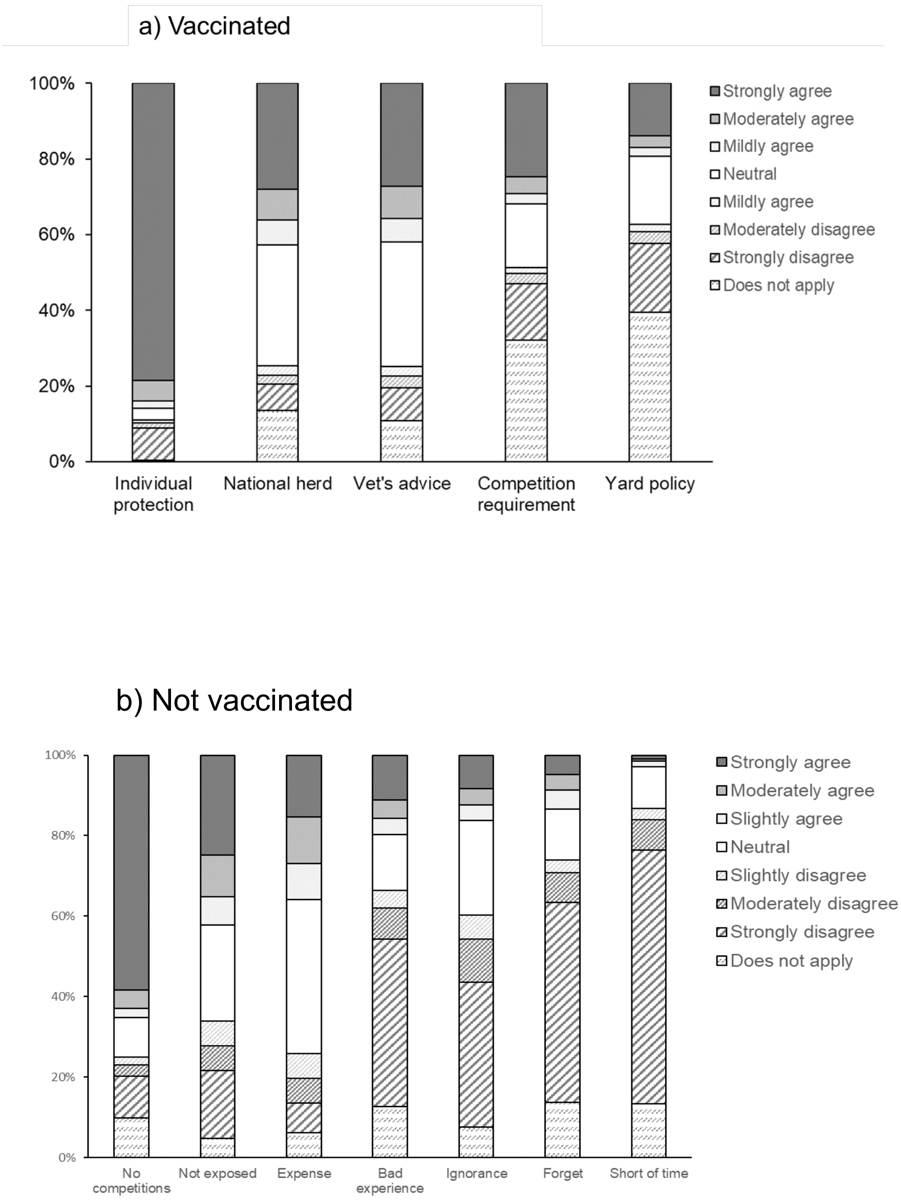
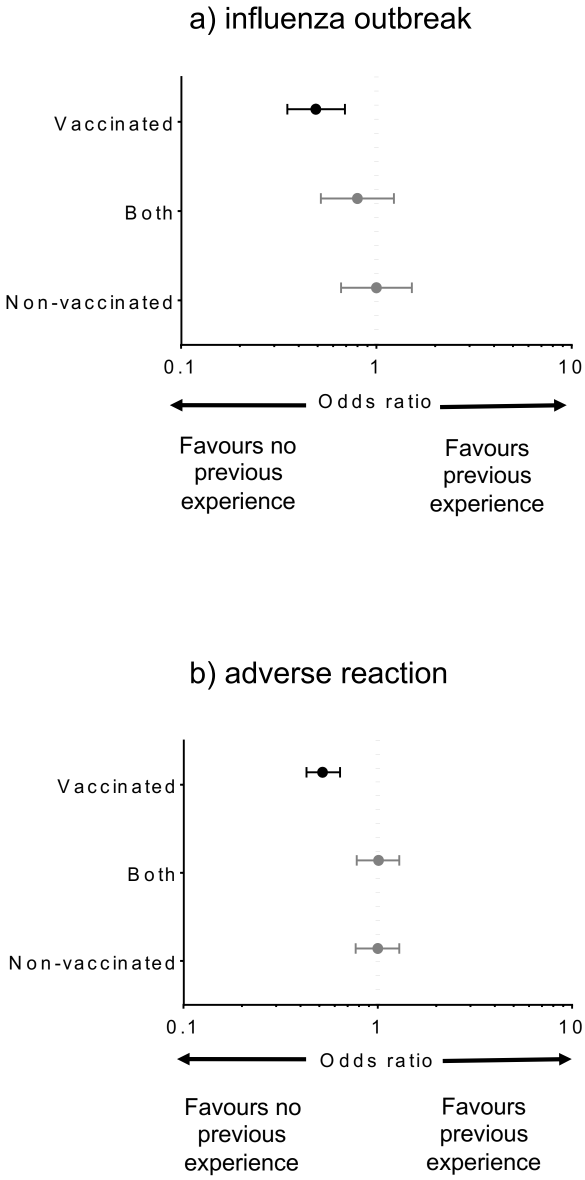

a) Vaccinated
100%
80%
60%
40%
20%
0%
Individual protection
National herd
Vet's advice
Competition requirement
Yard policy
Strongly agree
Moderately agree
Mildly agree
Neutral
Mildly agree
Moderately disagree
Strongly disagree
Does not apply
b) Not vaccinated
100%
80%
60%
40%
20%
0%
No competitions
Not exposed
Expense
Bad experience
Ignorance
Forget
Short of time
Strongly agree
Moderately agree
Slightly agree
Neutral
Slightly disagree
Moderately disagree
Strongly disagree
Does not apply

Figure 4


a) influenza outbreak
Vaccinated
Both
Non-vaccinated
0.1
1
10
Odds ratio
Favours no previous experience
Favours previous experience
b) adverse reaction
Vaccinated
Both
Non-vaccinated
0.1
1
10
Odds ratio
Favours no previous experience
Favours previous experience